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Drugs for preventing postoperative nausea and vomiting in adults after general anaesthesia: a network meta-analysis (Review)

Weibel S, Rücker G, Eberhart LHJ, Pace NL, Hartl HM, Jordan OL, Mayer D, Riemer M, Schaefer MS, Raj D, Backhaus I, Helf A, Schlesinger T, Kienbaum P, Kranke P

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[Intervention Review]

Drugs for preventing postoperative nausea and vomiting in adults after general anaesthesia: a network meta-analysis

Stephanie Weibel[1], Gerta Rücker[2], Leopold HJ Eberhart[3], Nathan L Pace[4], Hannah M Hartl[1], Olivia L Jordan[1], Debora Mayer[1], Manuel Riemer[1], Maximilian S Schaefer[5,6], Diana Raj[7], Insa Backhaus[8], Antonia Helf[1], Tobias Schlesinger[1], Peter Kienbaum[5], Peter Kranke[1]

[1]Department of Anesthesiology and Critical Care, University Hospital Wuerzburg, Wuerzburg, Germany. [2]Institute of Medical Biometry and Statistics, Faculty of Medicine and Medical Center – University of Freiburg, Freiburg, Germany. [3]Department of Anaesthesiology & Intensive Care Medicine, Philipps-University Marburg, Marburg, Germany. [4]Department of Anesthesiology, University of Utah, Salt Lake City, UT, USA. [5]Department of Anaesthesiology, University Hospital Düsseldorf, Düsseldorf, Germany. [6]Department of Anesthesia, Critical Care & Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA. [7]Department of Anaesthesia, Intensive Care Medicine and Pain Medicine, Queen Elizabeth University Hospital, Glasgow, UK. [8]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Contact address: Peter Kranke, kranke_p@ukw.de.

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ABSTRACT

Background

Postoperative nausea and vomiting (PONV) is a common adverse effect of anaesthesia and surgery. Up to 80% of patients may be affected. These outcomes are a major cause of patient dissatisfaction and may lead to prolonged hospital stay and higher costs of care along with more severe complications. Many antiemetic drugs are available for prophylaxis. They have various mechanisms of action and side effects, but there is still uncertainty about which drugs are most effective with the fewest side effects.

Objectives

• To compare the efficacy and safety of different prophylactic pharmacologic interventions (antiemetic drugs) against no treatment, against placebo, or against each other (as monotherapy or combination prophylaxis) for prevention of postoperative nausea and vomiting in adults undergoing any type of surgery under general anaesthesia

• To generate a clinically useful ranking of antiemetic drugs (monotherapy and combination prophylaxis) based on efficacy and safety

• To identify the best dose or dose range of antiemetic drugs in terms of efficacy and safety

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP), ClinicalTrials.gov, and reference lists of relevant systematic reviews. The first search was performed in November 2017 and was updated in April 2020. In the update of the search, 39 eligible studies were found that were not included in the analysis (listed as awaiting classification).

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Selection criteria

Randomized controlled trials (RCTs) comparing effectiveness or side effects of single antiemetic drugs in any dose or combination against each other or against an inactive control in adults undergoing any type of surgery under general anaesthesia. All antiemetic drugs belonged to one of the following substance classes: 5-HT_3 receptor antagonists, D_2 receptor antagonists, NK_1 receptor antagonists, corticosteroids, antihistamines, and anticholinergics. No language restrictions were applied. Abstract publications were excluded.

Data collection and analysis

A review team of 11 authors independently assessed trials for inclusion and risk of bias and subsequently extracted data. We performed pair-wise meta-analyses for drugs of direct interest (amisulpride, aprepitant, casopitant, dexamethasone, dimenhydrinate, dolasetron, droperidol, fosaprepitant, granisetron, haloperidol, meclizine, methylprednisolone, metoclopramide, ondansetron, palonosetron, perphenazine, promethazine, ramosetron, rolapitant, scopolamine, and tropisetron) compared to placebo (inactive control). We performed network meta-analyses (NMAs) to estimate the relative effects and ranking (with placebo as reference) of all available single drugs and combinations. Primary outcomes were vomiting within 24 hours postoperatively, serious adverse events (SAEs), and any adverse event (AE). Secondary outcomes were drug class-specific side effects (e.g. headache), mortality, early and late vomiting, nausea, and complete response. We performed subgroup network meta-analysis with dose of drugs as a moderator variable using dose ranges based on previous consensus recommendations. We assessed certainty of evidence of NMA treatment effects for all primary outcomes and drug class-specific side effects according to GRADE (CINeMA, Confidence in Network Meta-Analysis). We restricted GRADE assessment to single drugs of direct interest compared to placebo.

Main results

We included 585 studies (97,516 randomized participants). Most of these studies were small (median sample size of 100); they were published between 1965 and 2017 and were primarily conducted in Asia (51%), Europe (25%), and North America (16%). Mean age of the overall population was 42 years. Most participants were women (83%), had American Society of Anesthesiologists (ASA) physical status I and II (70%), received perioperative opioids (88%), and underwent gynaecologic (32%) or gastrointestinal surgery (19%) under general anaesthesia using volatile anaesthetics (88%).

In this review, 44 single drugs and 51 drug combinations were compared. Most studies investigated only single drugs (72%) and included an inactive control arm (66%). The three most investigated single drugs in this review were ondansetron (246 studies), dexamethasone (120 studies), and droperidol (97 studies).

Almost all studies (89%) reported at least one efficacy outcome relevant for this review. However, only 56% reported at least one relevant safety outcome.

Altogether, 157 studies (27%) were assessed as having overall low risk of bias, 101 studies (17%) overall high risk of bias, and 327 studies (56%) overall unclear risk of bias.

Vomiting within 24 hours postoperatively

Relative effects from NMA for vomiting within 24 hours (282 RCTs, 50,812 participants, 28 single drugs, and 36 drug combinations) suggest that 29 out of 36 drug combinations and 10 out of 28 single drugs showed a clinically important benefit (defined as the upper end of the 95% confidence interval (CI) below a risk ratio (RR) of 0.8) compared to placebo. Combinations of drugs were generally more effective than single drugs in preventing vomiting. However, single NK_1 receptor antagonists showed treatment effects similar to most of the drug combinations. High-certainty evidence suggests that the following single drugs reduce vomiting (ordered by decreasing efficacy): aprepitant (RR 0.26, 95% CI 0.18 to 0.38, high certainty, rank 3/28 of single drugs); ramosetron (RR 0.44, 95% CI 0.32 to 0.59, high certainty, rank 5/28); granisetron (RR 0.45, 95% CI 0.38 to 0.54, high certainty, rank 6/28); dexamethasone (RR 0.51, 95% CI 0.44 to 0.57, high certainty, rank 8/28); and ondansetron (RR 0.55, 95% CI 0.51 to 0.60, high certainty, rank 13/28). Moderate-certainty evidence suggests that the following single drugs probably reduce vomiting: fosaprepitant (RR 0.06, 95% CI 0.02 to 0.21, moderate certainty, rank 1/28) and droperidol (RR 0.61, 95% CI 0.54 to 0.69, moderate certainty, rank 20/28).

Recommended and high doses of granisetron, dexamethasone, ondansetron, and droperidol showed clinically important benefit, but low doses showed no clinically important benefit. Aprepitant was used mainly at high doses, ramosetron at recommended doses, and fosaprepitant at doses of 150 mg (with no dose recommendation available).

Frequency of SAEs

Twenty-eight RCTs were included in the NMA for SAEs (10,766 participants, 13 single drugs, and eight drug combinations). The certainty of evidence for SAEs when using one of the best and most reliable anti-vomiting drugs (aprepitant, ramosetron, granisetron, dexamethasone, ondansetron, and droperidol compared to placebo) ranged from very low to low. Droperidol (RR 0.88, 95% CI 0.08 to 9.71, low certainty, rank 6/13) may reduce SAEs. We are uncertain about the effects of aprepitant (RR 1.39, 95% CI 0.26 to 7.36, very low certainty, rank 11/13), ramosetron (RR 0.89, 95% CI 0.05 to 15.74, very low certainty, rank 7/13), granisetron (RR 1.21, 95% CI 0.11 to 13.15, very low certainty, rank 10/13), dexamethasone (RR 1.16, 95% CI 0.28 to 4.85, very low certainty, rank 9/13), and ondansetron (RR 1.62, 95% CI 0.32 to 8.10, very low certainty, rank 12/13). No studies reporting SAEs were available for fosaprepitant.

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Frequency of any AE

Sixty-one RCTs were included in the NMA for any AE (19,423 participants, 15 single drugs, and 11 drug combinations). The certainty of evidence for any AE when using one of the best and most reliable anti-vomiting drugs (aprepitant, ramosetron, granisetron, dexamethasone, ondansetron, and droperidol compared to placebo) ranged from very low to moderate. Granisetron (RR 0.92, 95% CI 0.80 to 1.05, moderate certainty, rank 7/15) probably has no or little effect on any AE. Dexamethasone (RR 0.77, 95% CI 0.55 to 1.08, low certainty, rank 2/15) and droperidol (RR 0.89, 95% CI 0.81 to 0.98, low certainty, rank 6/15) may reduce any AE. Ondansetron (RR 0.95, 95% CI 0.88 to 1.01, low certainty, rank 9/15) may have little or no effect on any AE. We are uncertain about the effects of aprepitant (RR 0.87, 95% CI 0.78 to 0.97, very low certainty, rank 3/15) and ramosetron (RR 1.00, 95% CI 0.65 to 1.54, very low certainty, rank 11/15) on any AE. No studies reporting any AE were available for fosaprepitant.

Class-specific side effects

For class-specific side effects (headache, constipation, wound infection, extrapyramidal symptoms, sedation, arrhythmia, and QT prolongation) of relevant substances, the certainty of evidence for the best and most reliable anti-vomiting drugs mostly ranged from very low to low. Exceptions were that ondansetron probably increases headache (RR 1.16, 95% CI 1.06 to 1.28, moderate certainty, rank 18/23) and probably reduces sedation (RR 0.87, 95% CI 0.79 to 0.96, moderate certainty, rank 5/24) compared to placebo. The latter effect is limited to recommended and high doses of ondansetron. Droperidol probably reduces headache (RR 0.76, 95% CI 0.67 to 0.86, moderate certainty, rank 5/23) compared to placebo. We have high-certainty evidence that dexamethasone (RR 1.00, 95% CI 0.91 to 1.09, high certainty, rank 16/24) has no effect on sedation compared to placebo. No studies assessed substance class-specific side effects for fosaprepitant.

Direction and magnitude of network effect estimates together with level of evidence certainty are graphically summarized for all pre-defined GRADE-relevant outcomes and all drugs of direct interest compared to placebo in http://doi.org/10.5281/zenodo.4066353.

Authors' conclusions

We found high-certainty evidence that five single drugs (aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron) reduce vomiting, and moderate-certainty evidence that two other single drugs (fosaprepitant and droperidol) probably reduce vomiting, compared to placebo. Four of the six substance classes (5-HT_3 receptor antagonists, D_2 receptor antagonists, NK_1 receptor antagonists, and corticosteroids) were thus represented by at least one drug with important benefit for prevention of vomiting. Combinations of drugs were generally more effective than the corresponding single drugs in preventing vomiting. NK_1 receptor antagonists were the most effective drug class and had comparable efficacy to most of the drug combinations. 5-HT_3 receptor antagonists were the best studied substance class. For most of the single drugs of direct interest, we found only very low to low certainty evidence for safety outcomes such as occurrence of SAEs, any AE, and substance class-specific side effects.

Recommended and high doses of granisetron, dexamethasone, ondansetron, and droperidol were more effective than low doses for prevention of vomiting. Dose dependency of side effects was rarely found due to the limited number of studies, except for the less sedating effect of recommended and high doses of ondansetron.

The results of the review are transferable mainly to patients at higher risk of nausea and vomiting (i.e. healthy women undergoing inhalational anaesthesia and receiving perioperative opioids). Overall study quality was limited, but certainty assessments of effect estimates consider this limitation. No further efficacy studies are needed as there is evidence of moderate to high certainty for seven single drugs with relevant benefit for prevention of vomiting. However, additional studies are needed to investigate potential side effects of these drugs and to examine higher-risk patient populations (e.g. individuals with diabetes and heart disease).

PLAIN LANGUAGE SUMMARY

Which medicines work best to prevent people from being sick (vomiting) after an operation?

Why are people sick after an operation?

Feeling sick (nausea) or being sick (vomiting) is a common unwanted effect of general anaesthesia—medicine that makes people unconscious and unresponsive so they don't move or feel pain during an operation.

Most unwanted effects of general anaesthesia, including feeling or being sick, happen immediately and stop after a few hours, although some people may continue to feel sick for up to a day. If people carry on feeling or being sick, they might have to stay in hospital longer than expected and may experience other unwanted effects or complications.

Women are more likely to be sick after an operation, as are people taking opioid painkillers, those who have had motion sickness, and those who have been sick after previous operations.

Medicines to prevent people from being sick

Medicines called antiemetics are given to prevent people from feeling or being sick. These medicines may be given before or during anaesthesia.

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Antiemetic medicines are grouped into six main classes based on how they act. Combining medicines from different classes sometimes makes them work better.

Why we did this Cochrane Review

We wanted to find out which medicines work best to prevent people from being sick after an operation and cause the fewest unwanted effects. Some unwanted effects of antiemetic medicines include headache, constipation, movement disorders such as tremors, sleepiness, irregular heartbeat, and wound infection.

What did we do?

We searched for studies that looked at the use of antiemetic medicines in adults having general anaesthesia to prevent people from being sick afterwards.

We looked for randomized controlled studies, in which the treatments people received were decided at random. This type of study usually gives the most reliable evidence about the effects of a treatment.

Search date

We included evidence published up to November 2017; in April 2020, we found another 39 studies, which are not yet included in the analysis.

What we found

We found 585 studies in 97,516 people who were given antiemetic medicines before or during general anaesthesia. People included in the studies were more likely to be sick after anaesthesia, as 83% were women and 88% were taking opioid painkillers. Most studies were conducted in Asia, Europe, or North America.

These studies either measured how many people were sick in the first 24 hours after their operation or how many unwanted effects were reported, or both of these outcomes. Most studies compared medicines (given alone or in combination) with a dummy (placebo) treatment.

We compared all antiemetic medicines with each other using a mathematical method called network meta-analysis.

What were our main results and how reliable are these results?

Compared with placebo treatment, 10 out of 28 single medicines and 29 out of 36 combinations of medicines prevented people from being sick in the first 24 hours after their operation (282 studies). Combinations of antiemetic medicines generally worked better than single medicines given alone. However, aprepitant, casopitant, and fosaprepitant worked as well alone as most combinations of antiemetics. The single medicine that worked best in the ranking of all medicines was fosaprepitant, followed by casopitant, aprepitant, ramosetron, granisetron, dexamethasone, tropisetron, ondansetron, dolasetron, and droperidol.

We are confident that aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron prevent people from being sick. We are moderately confident about how well fosaprepitant and droperidol work, but this finding may change when further evidence becomes available. We are uncertain about how well casopitant, tropisetron, and dolasetron work.

Not all studies looked at serious, life-threatening unwanted effects. We are uncertain how many of these effects were reported when taking an antiemetic medicine and whether serious, life-threatening unwanted effects occur at a similar rate or are reduced compared to placebo (28 studies).

Of the best medicines with most reliable evidence for preventing being sick, granisetron and ondansetron probably made little to no difference in the occurrence of unwanted effects compared to placebo, whereas dexamethasone and droperidol may cause fewer unwanted effects than placebo. We are uncertain about unwanted effects with aprepitant and ramosetron (61 studies). We found no studies looking at unwanted effects for fosaprepitant.

We are less confident about unwanted effects of other antiemetic medicines because we found little reliable evidence about this. Our results for unwanted effects are likely to change when further evidence is available.

Conclusions

For people at higher risk, we found that some antiemetic medicines work well to prevent them from being sick after general anaesthesia. The best antiemetic medicines with reliable evidence were aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron, followed by fosaprepitant and droperidol.

However, we did not find enough reliable evidence about potential unwanted effects to rank these medicines reliably according to how well they are tolerated.

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SUMMARY OF FINDINGS

Summary of findings 1. Primary summary of findings

Primary summary of findings'

Estimates of effects and certainty of the evidence of antiemetic drugs for prevention of postoperative nausea and vomiting in adults after general anaesthesia

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (single drugs and drug combinations)*

Comparator (reference): placebo (or no treatment)

Outcomes: all primary outcomes and drug class-specific adverse effects**

Setting: inpatient and outpatient

Outcomes	Effects and confidence in the estimate of effects (network meta-analysis)													
	Aprepitant*		**Ramosetron***		**Granisetron***		**Dexamethasone***		**Ondansetron***		**Fosaprepitant***		**Droperidol***	
Vomiting (or dry retching) within 24 hours postoperatively														
Total studies: 282; total participants: 50,812; number of treatments: 65 (36 drug combinations, 28 single drugs, placebo)														
Placebo (comparator) 300 per 1000[a] (30%)	**RR 0.26** (0.18 to 0.38) Network estimate	222 fewer per 1000 (246 fewer to 186 fewer)	**RR 0.44** (0.32 to 0.59) Network estimate	168 fewer per 1000 (204 fewer to 123 fewer)	**RR 0.45** (0.38 to 0.54) Network estimate	165 fewer per 1000 (186 fewer to 138 fewer)	**RR 0.51** (0.44 to 0.57) Network estimate	147 fewer per 1000 (168 fewer to 471 fewer)	**RR 0.55** (0.51 to 0.60) Network estimate	135 fewer per 1000 (147 fewer to 120 fewer)	**RR 0.06** (0.02 to 0.21) Network estimate	282 fewer per 1000 (294 fewer to 237 fewer)	**RR 0.61** (0.54 to 0.69) Network estimate	117 fewer per 1000 (138 fewer to 93 fewer)
	⊕⊕⊕⊕ **High** Confidence in network estimate		⊕⊕⊕⊕ **High** Confidence in network estimate		⊕⊕⊕⊕ **High** Confidence in network estimate[1]		⊕⊕⊕⊕ **High** Confidence in network estimate[1]		⊕⊕⊕⊕ **High** Confidence in network estimate[1]		⊕⊕⊕⊖ **Moderate** Confidence in network estimate due to incoherence		⊕⊕⊕⊖ **Moderate** Confidence in network estimate due to publication bias and heterogeneity[1,2]	

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Rank 65 (0.0607)	**Rank 20** (0.6760) rank 3 of 28 single drugs		**Rank 36** (0.4361) rank 5 of 28 single drugs		**Rank 38** (0.4234) rank 6 of 28 single drugs		**Rank 41** (0.3588) rank 8 of 28 single drugs		**Rank 48** (0.2974) rank 13 of 28 single drugs		**Rank 4** (0.9189) rank 1 of 28 single drugs	**Rank 55** (0.2320) rank 20 of 28 single drugs	
	Based on 94 participants (1 RCT) and indirect evidence (84%)		Based on 618 participants (6 RCTs) and indirect evidence (32%)		Based on 2270 participants (16 RCTs) and indirect evidence (18%)		Based on 4804 participants (43 RCTs) and indirect evidence (27%)		Based on 14,435 participants (77 RCTs) and indirect evidence (21%)		Based on indirect evidence only	Based on 6156 participants (41 RCTs) and indirect evidence (22%)	
Serious adverse events (SAEs) within 7 days postoperatively													
Total studies: 28; total participants: 10,766; number of treatments: 22 (8 drug combinations, 13 single drugs, placebo)													
Placebo (comparator) 14 per 1000[b] (1.43%)	**RR 1.39** (0.26 to 7.36) Network estimate	5 more per 1000 (10 fewer to 89 more)	**RR 0.89** (0.05 to 15.74) Network estimate	2 fewer per 1000 (13 fewer to 206 more)	**RR 1.21** (0.11 to 13.15) Network estimate	3 more per 1000 (12 fewer to 170 more)	**RR 1.16** (0.28 to 4.85) Network estimate	2 more per 1000 (10 fewer to 54 more)	**RR 1.62** (0.32 to 8.10) Network estimate	9 more per 1000 (10 fewer to 99 more)	**No studies were found that looked at SAEs**	**RR 0.88** (0.08 to 9.71) Network estimate	2 fewer per 1000 (13 fewer to 122 more)
	⊖⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations, imprecision, incoherence[3]		⊕⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations and imprecision[4]		⊕⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations and imprecision[5]			⊕⊕⊖⊖ **Low** Confidence in network estimate due to imprecision[6]	
Rank 14 (0.5020)	**Rank 17** (0.4421) rank 11 of 13 single drugs		**Rank 8** (0.5366) rank 7 of 13 single drugs		**Rank 16** (0.4612) rank 10 of 13 single drugs		**Rank 15** (0.4632) rank 9 of 13 single drugs		**Rank 20** (0.3708) rank 12 of 13 single drugs			**Rank 7** (0.5430) rank 6 of 13 single drugs	
	Based on indirect evidence only		Based on 236 participants (1 RCT) and indirect evidence (46%)		Based on 401 participants (2 RCTs) and indirect evidence (7%)		Based on 376 participants (3 RCTs) and indirect evidence (4%)		Based on 833 participants (3 RCTs) and indirect evidence (34%)			Based on 304 participants (2 RCTs) and indirect evidence (24%)	

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Any adverse events (any AEs) within 7 days postoperatively													
Total studies: 61; total participants: 19,423; number of treatments: 27 (11 drug combinations, 15 single drugs, placebo)													
Placebo (comparator) 377 per 1000[b] (37.68%)	**RR 0.87** (0.78 to 0.97) Network estimate	49 fewer per 1000 (83 fewer to 11 fewer)	**RR 1.00** (0.65 to 1.54) Network estimate	0 fewer/more per 1000 (132 fewer to 204 more)	**RR 0.92** (0.80 to 1.05) Network estimate	30 fewer per 1000 (75 fewer to 19 more)	**RR 0.77** (0.55 to 1.08) Network estimate	87 fewer per 1000 (170 fewer to 30 more)	**RR 0.95** (0.88 to 1.01) Network estimate	19 fewer per 1000 (45 fewer to 4 more)	**No studies were found that looked at any AE**	**RR 0.89** (0.81 to 0.98) Network estimate	41 fewer per 1000 (72 fewer to 8 fewer)
	⊕⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations, imprecision, incoherence		⊕⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊕⊕⊖ **Moderate** Confidence in network estimate due to imprecision		⊕⊕⊖⊖ **Low** Confidence in network estimate due to study limitations and imprecision		⊕⊕⊖⊖ **Low** Confidence in network estimate due to study limitations and imprecision			⊕⊕⊖⊖ **Low** Confidence in network estimate due to study limitations and imprecision	
Rank 23 (0.3129)	**Rank 6** (0.6589) rank 3 of 15 single drugs		**Rank 18** (0.4159) rank 11 of 15 single drugs		**Rank 11** (0.5436) rank 7 of 15 single drugs		**Rank 4** (0.7526) rank 2 of 15 single drugs		**Rank 16** (0.4655) rank 9 of 15 single drugs			**Rank 10** (0.6164) rank 6 of 15 single drugs	
	Based on indirect evidence only		Based on 173 participants (2 RCTs) and indirect evidence (43%)		Based on 699 participants (6 RCTs) and indirect evidence (3%)		Based on 1152 participants (6 RCTs) and indirect evidence (82%)		Based on 4892 participants (12 RCTs) and indirect evidence (4%)			Based on 1622 participants (2 RCTs) and indirect evidence (21%)	
Headache within 7 days postoperatively													
Total studies: 208; total participants: 42,445; number of treatments: 53 (29 drug combinations, 23 single drugs, placebo)													
Placebo (comparator)	**RR 0.86** (0.35 to 2.11) Network estimate	13 fewer per 1000 (62 fewer	**RR 1.13** (0.93 to 1.37) Network estimate	12 more per 1000 (7 fewer to 36 more)	**RR 1.20** (1.01 to 1.42) Network estimate	19 more per 1000 (1 more to 40 more)	**RR 0.85** (0.63 to 1.13) Network estimate	14 fewer per 1000 (36 fewer to 12 more)	**RR 1.16** (1.06 to 1.28) Network estimate	15 more per 1000 (6 more to 27 more)	**No studies were found that looked at headache**	**RR 0.76** (0.67 to 0.86)	23 fewer per 1000 (32 fewer

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96 per 1000[b] (9.56%)	Network estimate	to 107 more)											Network estimate	to 13 fewer)
	⊕⊕⊝⊝ **Low** Confidence in network estimate due to imprecision[6]		⊕⊕⊝⊝ **Low** Confidence in network estimate due to study limitations and imprecision		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations, imprecision, incoherence		⊕⊕⊝⊝ **Low** Confidence in network estimate due to imprecision[6]		⊕⊕⊕⊝ **Moderate** Confidence in network estimate due to imprecision				⊕⊕⊕⊝ **Moderate** Confidence in network estimate due to study limitations	
Rank 31 (0.4543	**Rank 24** (0.5349) rank 10 of 23 single drugs		**Rank 40** (0.3416) rank 16 of 23 single drugs		**Rank 45** (0.2914) rank 19 of 23 single drugs		**Rank 19** (0.5806) rank 8 of 23 single drugs		**Rank 44** (0.3082) rank 18 of 23 single drugs				**Rank 13** (0.6563) rank 5 of 23 single drugs	
	Based on 120 participants (1 RCT) and indirect evidence (73%)		Based on 1529 participants (14 RCTs) and indirect evidence (38%)		Based on 1639 participants (15 RCTs) and indirect evidence (43%)		Based on 1678 participants (13 RCTs) and indirect evidence (52%)		Based on 12,260 participants (57 RCTs) and indirect evidence (22%)				Based on 3679 participants (22 RCT) and indirect evidence (26%)	
Constipation within 7 days postoperatively														
Total studies: 43; total participants: 11,481; number of treatments: 23 (10 drug combinations, 12 single drugs, placebo)														
Placebo (comparator) 74 per 1000[b] (7.39%)	**RR 1.03** (0.59 to 1.80) Network estimate	2 more per 1000 (30 fewer to 129 more)	**RR 0.74** (0.39 to 1.40) Network estimate	19 fewer per 1000 (45 fewer to 30 more)	**RR 0.59** (0.21 to 1.63) Network estimate	30 fewer per 1000 (58 fewer to 47 more)	**RR 0.83** (0.21 to 3.25) Network estimate	13 fewer per 1000 (58 fewer to 167 more)	**RR 1.02** (0.71 to 1.46) Network estimate	1 more per 1000 (21 fewer to 34 more)	**No studies were found that looked at constipation**		**No studies were found that looked at constipation**	
	⊝⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations, impre-		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊕⊝⊝ **Low** Confidence in network estimate due to imprecision[6]		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]					

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	cision, incoherence[3]								
Rank 12 (0.4889)	**Rank 14** (0.4638) rank 7 of 12 single drugs	**Rank 5** (0.6692) rank 3 of 12 single drugs	**Rank 2** (0.7350) rank 1 of 12 single drugs	**Rank 7** (0.5802) rank 5 of 12 single drugs		**Rank 13** (0.4677) rank 6 of 12 single drugs			
	Based on indirect evidence only	Based on 280 participants (2 RCTs) and indirect evidence (84%)	Based on 230 participants (3 RCTs) and indirect evidence (13%)	Based on 327 participants (3 RCTs) and indirect evidence (19%)		Based on 1475 participants (8 RCTs) and indirect evidence (12%)			
Wound infection within 7 days postoperatively									
Total studies: 32; total participants: 4369; number of treatments: 10 (3 drug combinations, 6 single drugs, placebo)									
Placebo (comparator) 4 per 1000[b] (0.44%)	**No studies were found that looked at wound infection**	**No studies were found that looked at wound infection**	**No studies were found that looked at wound infection**	**RR 0.91** (0.45 to 1.87) Network estimate	0 fewer/more per 1000 (2 fewer to 3 more)	**RR 1.28** (0.01 to 115.24) Network estimate	1 more per 1000 (4 fewer to 457 more)	**No studies were found that looked at wound infection**	**No studies were found that looked at wound infection**
				⊕⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊖⊖⊖ **Very low** Confidence in network estimate due to imprecision and incoherence[7]			
Rank 10 (0.3885)				**Rank 8** (0.4272) Rank 5 of 6 single drugs		**Rank 9** (0.3974) rank 6 of 6 single drugs			
				Based on 3199 participants (24 RCTs) and indirect evidence (1%)		Based on indirect evidence only			
Extrapyramidal symptoms within 7 days postoperatively									
Total studies: 64; total participants: 10,724; number of treatments: 30 (13 drug combinations, 16 single drugs, placebo)									

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Placebo (comparator) 8 per 1000[b] (0.79%)	**No studies were found that looked at extrapyramidal symptoms**		**RR 0.73** (0.01 to 37.44) Network estimate	2 fewer per 1000 (8 fewer to 292 more)	**RR 0.90** (0.23 to 3.57) Network estimate	1 fewer per 1000 (6 fewer to 21 more)	**RR 0.70** (0.17 to 2.80) Network estimate	2 fewer per 1000 (7 fewer to 14 more)	**RR 0.73** (0.39 to 1.38) Network estimate	2 fewer per 1000 (5 fewer to 3 more)	**No studies were found that looked at extrapyramidal symptoms**	**RR 1.36** (0.89 to 2.08) Network estimate	3 more per 1000 (1 fewer to 9 more)
			⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations, imprecision, incoherence[3]		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊕⊝⊝ **Low** Confidence in network estimate due to imprecision[6]		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]			⊕⊕⊝⊝ **Low** Confidence in network estimate due to imprecision[6]	
Rank 22 (0.4778)			**Rank 8** (0.5409) Rank 5 of 16 single drugs		**Rank 12** (0.5109) Rank 6 of 16 single drugs		**Rank 4** (0.5865) Rank 2 of 16 single drugs		**Rank 3** (0.6026) Rank 1 of 16 single drugs			**Rank 29** (0.3456) Rank 15 of 16 single drugs	
			Based on indirect evidence only		Based on 330 participants (5 RCTs) and indirect evidence (37%)		Based on 1031 participants (4 RCTs) and indirect evidence (49%)		Based on 751 participants (7 RCTs) and indirect evidence (53%)			Based on 3270 participants (22 RCTs) and indirect evidence (11%)	
Sedation within 7 days postoperatively													
Total studies: 117; total participants: 21,440; number of treatments: 44 (19 drug combinations, 24 single drugs, placebo)													
Placebo (comparator) 130 per 1000[b] (13%)	**RR 0.43** (0.01 to 21.65) Network estimate	74 fewer per 1000 (129 fewer to 870 more)	**RR 0.89** (0.72 to 1.10) Network estimate	14 fewer per 1000 (36 fewer to 13 more)	**RR 1.00** (0.86 to 1.17) Network estimate	0 fewer/more per 1000 (18 fewer to 22 more)	**RR 1.00** (0.91 to 1.09) Network estimate	0 fewer/more per 1000 (12 fewer to 12 more)	**RR 0.87** (0.79 to 0.96) Network estimate	17 fewer per 1000 (41 fewer to 5 fewer)	**No studies were found that looked at sedation**	**RR 0.99** (0.96 to 1.01) Network estimate	1 fewer per 1000 (5 fewer to 1 more)

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	⊕⊝⊝⊝ **Very low** Confidence in network estimate due to imprecision and incoherence[7]	⊕⊕⊝⊝ **Low** Confidence in network estimate due to study limitations and imprecision		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊕⊕⊕ **High** Confidence in network estimate		⊕⊕⊕⊝ **Moderate** Confidence in network estimate due to imprecision[1]			⊕⊕⊝⊝ **Low** Confidence in network estimate due study limitations[8]	
Rank 26 (0.4880)	**Rank 10** (0.6518) Rank 6 of 24 single drugs	**Rank 13** (0.6263) Rank 8 of 24 single drugs		**Rank 24** (0.4996) Rank 15 of 24 single drugs		**Rank 25** (0.4982) Rank 16 of 24 single drugs		**Rank 9** (0.6623) Rank 5 of 24 single drugs			**Rank 18** (0.5152) Rank 11 of 24 single drugs	
	Based on indirect evidence only	Based on 581 participants (5 RCTs) and indirect evidence (85%)		Based on 850 participants (9 RCTs) and indirect evidence (33%)		Based on 1290 participants (9 RCTs) and indirect evidence (2%)		Based on 6092 participants (36 RCTs) and indirect evidence (39%)			Based on 3739 participants (21 RCTs) and indirect evidence (1%)	
Arrhythmia within 7 days postoperatively												
Total studies: 25; total participants: 5067; number of treatments: 18 (5 drug combinations, 12 single drugs, placebo)												
Placebo (comparator) 43 per 1000[b] (4.25%)	**No studies were found that looked at arrhythmia**	**RR 1.30** (0.80 to 2.10) Network estimate	13 more per 1000 (9 fewer to 47 more)	**RR 0.95** (0.04 to 21.59) Network estimate	2 fewer per 1000 (41 fewer to 885 more)	**RR 0.81** (0.44 to 1.51) Network estimate	8 fewer per 1000 (24 fewer to 22 more)	**RR 1.27** (0.47 to 3.43) Network estimate	12 more per 1000 (23 fewer to 104 more)	**No studies were found that looked at arrhythmia**	**RR 0.88** (0.31 to 2.48) Network estimate	4 fewer per 1000 (20 fewer to 64 more)
		⊕⊕⊝⊝ **Low** Confidence in network estimate due to imprecision[6,9]		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊕⊝⊝ **Low** Confidence in network estimate due to imprecision[6]		⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]			⊕⊝⊝⊝ **Very low** Confidence in network estimate due to study limitations and imprecision[5]	
Rank 13		**Rank 18** (0.3138)		**Rank 8** (0.4688)		**Rank 6** (0.5380)		**Rank 17** (0.3492)			**Rank 7** (0.4981)	

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(0.4400)			Rank 12 of 12 single drugs		Rank 5 of 12 single drugs	Rank 3 of 12 single drugs		Rank 11 of 12 single drugs			Rank 4 of 12 single drugs	
			Based on 140 participants (1 RCT), no indirect evidence available		Based on 50 participants (1 RCT) and indirect evidence (35%)	Based on 189 participants (3 RCTs) and indirect evidence (2%)		Based on 1643 participants (4 RCTs) and indirect evidence (16%)			Based on 659 participants (7 RCTs) and indirect evidence (22%)	
QT prolongation within 7 days postoperatively												
Total studies: 18; total participants: 4440; number of treatments: 13 (4 drug combinations, 8 single drugs, placebo)												
Placebo (comparator) 21 per 1000[b] (2.12%)	**RR 0.96** (0.19 to 4.92) Network estimate	1 fewer per 1000 (17 fewer to 82 more)	**RR 0.62** (0.08 to 4.76) Network estimate	8 fewer per 1000 (19 fewer to 79 more)	**No studies were found that looked at QT prolongation**	**RR 0.75** (0.05 to 12.06) Network estimate	5 fewer per 1000 (20 fewer to 232 more)	**RR 0.93** (0.18 to 4.76) Network estimate	1 fewer per 1000 (17 fewer to 79 more)	**No studies were found that looked at QT prolongation**	**RR 1.29** (0.71 to 2.34) Network estimate	6 more per 1000 (6 fewer to 28 more)
	⊕⊖⊖⊖ **Very low** Confidence in network estimate due to imprecision and incoherence[7]		⊖⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations, imprecision, incoherence[3]			⊕⊖⊖⊖ **Very low** Confidence in network estimate due to study limitations and imprecision[5]		⊕⊕⊖⊖ **Low** Confidence in network estimate due imprecision[6]			⊕⊕⊖⊖ **Low** Confidence in network estimate due imprecision[6]	
Rank 6 (0.4552)	**Rank 9** (0.4264) Rank 6 of 8 single drugs		**Rank 3** (0.6133) Rank 2 of 8 single drugs			**Rank 4** (0.5370) Rank 3 of 8 single drugs		**Rank 5** (0.4773) Rank 4 of 8 single drugs			**Rank 11** (0.3348) Rank 8 of 8 single drugs	
	Based on indirect evidence only		Based on indirect evidence only			Based on 149 participants (1 RCT) and indirect evidence (49%)		Based on 60 participants (1 RCT) and indirect evidence (82%)			Based on 303 participants (3 RCTs) and indirect evidence (1%)	

NMA-SoF table definitions:

- Network estimates are reported as risk ratio (RR) with confidence interval.
- Anticipated absolute effects compare two risks by calculating the difference between risks of the intervention group and the control group.

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- Certainty of evidence (confidence) is reported for network estimates only.
- Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments. Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.
- Information is given on the numbers of participants and studies included in the direct comparison and the contribution of indirect evidence (indirect evidence proportion).

* Selection criteria for presentation of interventions in this primary 'Summary of findings table': single antiemetic drugs of direct interest with important beneficial effect and with high or moderate certainty of evidence for the primary outcome (vomiting) were selected for presentation. These were aprepitant, ramosetron, granisetron, dexamethasone, ondansetron, fosaprepitant, and droperidol.

** Relevant adverse effects were selected according to the substance class: NK1 receptor antagonists (aprepitant, fosaprepitant): headache; 5-HT3 receptor antagonists (ramosetron, granisetron, ondansetron): headache, constipation; corticosteroids (dexamethasone): wound infection; D2 receptor antagonists (droperidol): extrapyramidal symptoms, sedation, arrhythmia, QT prolongation

GRADE Working Group grades of evidence (certainty of evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes to baseline risks (assumed control risks):

[a] Baseline risk (assumed control risk) for vomiting within 24 hours was obtained from the consensus guideline on postoperative nausea and vomiting (Gan-2014). The general incidence of vomiting after surgery is about 30%.

[b] The baseline risk is based on the total events of all placebo groups included in the relevant outcome of the current network meta-analysis (mean control group risk across studies).

Explanatory footnotes to the ratings of the confidence in the network estimates:

[1] Evidence only for recommended and high doses because low doses showed no clinically important effect.

[2] Serious concerns for publication bias and heterogeneity. Publication bias and heterogeneity are overlapping domains for which we downgraded only once.

[3] Serious concerns for study limitations and incoherence, and very serious concerns for imprecision.

[4] Very serious concerns for study limitations and imprecision.

[5] Serious concerns for study limitations and very serious concerns for imprecision.

[6] Very serious concerns for imprecision.

[7] Very serious concerns for imprecision and serious concerns for incoherence.

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[8] Very serious concerns for study limitations.

[9] Poorly connected to the network. Only direct evidence is available.

Summary of findings 2. Summary of findings (vomiting within 24 hours postoperatively)

BENEFIT

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: vomiting (or dry retching) within 24 hours postoperatively

Setting: inpatient and outpatient

Total studies: 282 RCTs **Total participants:** 50,812 **Number of treatments:** 65 **Geometry of the network****	**Relative effect*** **(95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** **(P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT$_3$ receptor antagonists							
Dolasetron (5 RCTs; 400 participants)	**0.56** (0.43 to 0.74)	300 per 1000[1]	168 per 1000	132 fewer per 1000 (171 fewer to 78 fewer)	⊕⊕⊖⊖ **Low** Due to study limitations, heterogeneity, incoherence[2]	**Rank 49** (0.2897) Rank 14 of 28 single drugs	**Dolasetron may reduce vomiting**
Granisetron (16 RCTs; 2270 participants)	**0.45** (0.38 to 0.54)	300 per 1000[1]	135 per 1000	165 fewer per 1000 (186 fewer to 138 fewer)	⊕⊕⊕⊕ **High** [3]	**Rank 38** (0.4234) Rank 6 of 28 single drugs	**Granisetron reduces vomiting**

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Ondansetron (77 RCTs; 14,435 participants)	**0.55** (0.51 to 0.60)	300 per 1000[1]	165 per 1000	135 fewer per 1000 (147 fewer to 120 fewer)	⊕⊕⊕⊕ **High** [3]	**Rank 48** (0.2974) Rank 13 of 28 single drugs	**Ondansetron reduces vomiting**
Palonosetron (6 RCTs; 1111 participants)	**0.62** (0.48 to 0.80)	300 per 1000[1]	186 per 1000	114 fewer per 1000 (156 fewer to 60 fewer)	⊕⊕⊕⊖ **Low** Due to study limitations, imprecision	**Rank 56** (0.2275) Rank 21 of 28 single drugs	**Palonosetron may reduce vomiting**
Ramosetron (6 RCTs; 618 participants)	**0.44** (0.32 to 0.59)	300 per 1000[1]	132 per 1000	168 fewer per 1000 (204 fewer to 123 fewer)	⊕⊕⊕⊕ **High**	**Rank 36** (0.4361) Rank 5 of 28 single drugs	**Ramosetron reduces vomiting**
Tropisetron (13 RCTs; 1275 participants)	**0.52** (0.43 to 0.63)	300 per 1000[1]	156 per 1000	144 fewer per 1000 (171 fewer to 111 fewer)	⊕⊕⊕⊖ **Low** Due to study limitations[4]	**Rank 42** (0.3334) Rank 9 of 28 single drugs	**Tropisetron may reduce vomiting**
D2 receptor antagonists							
Amisulpride (2 RCTs; 841 participants)	**0.71** (0.46 to 1.09)	300 per 1000[1]	213 per 1000	87 fewer per 1000 (162 fewer to 27 more)	⊕⊕⊕⊖ **Moderate** Due to imprecision, heterogeneity[5,6]	**Rank 59** (0.1769) Rank 23 of 28 single drugs	**Amisulpride probably reduces vomiting**
Droperidol (41 RCTs; 6156 participants)	**0.61** (0.54 to 0.69)	300 per 1000[1]	183 per 1000	117 fewer per 1000 (138 fewer to 93 fewer)	⊕⊕⊕⊖ **Moderate** Due to publication bias, heterogeneity[3,7]	**Rank 55** (0.2320) Rank 20 of 28 single drugs	**Droperidol probably reduces vomiting**

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Haloperidol (4 RCTs; 327 participants)	**0.61** (0.43 to 0.87)	300 per 1000[1]	183 per 1000	117 fewer per 1000 (171 fewer to 39 fewer)	⊕⊕⊖⊖ **Low** Due to imprecision, incoherence	**Rank 53** (0.2449) Rank 18 of 28 single drugs	**Haloperidol may reduce vomiting**
Metoclopramide (21 RCTs; 2134 participants)	**0.73** (0.63 to 0.86)	300 per 1000[1]	219 per 1000	81 fewer per 1000 (111 fewer to 42 fewer)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence	**Rank 62** (0.1445) Rank 26 of 28 single drugs	**We are uncertain whether metoclopramide reduces vomiting**
Perphenazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at vomiting**
NK1 receptor antagonists							
Aprepitant (1 RCT; 94 participants)	**0.26** (0.18 to 0.38)	300 per 1000[1]	78 per 1000	222 fewer per 1000 (246 fewer to 186 fewer)	⊕⊕⊕⊕ **High**	**Rank 20** (0.6760) Rank 3 of 28 single drugs	**Aprepitant reduces vomiting**
Casopitant (no direct evidence, indirect evidence only)	**0.16** (0.07 to 0.35)	300 per 1000[1]	48 per 1000	252 fewer per 1000 (279 fewer to 195 fewer)	⊕⊕⊖⊖ **Low** Due to study limitations, incoherence	**Rank 10** (0.8037) Rank 2 of 28 single drugs	**Casopitant may reduce vomiting**
Fosaprepitant (No direct evidence, indirect evidence only)	**0.06** (0.02 to 0.21)	300 per 1000[1]	18 per 1000	282 fewer per 1000 (294 fewer to 237 fewer)	⊕⊕⊕⊖ **Moderate** [8] Due to incoherence	**Rank 4** (0.9189) Rank 1 of 28 single drugs	**Fosaprepitant probably reduces vomiting**
Rolapitant (1 RCT; 515 participants)	**0.56** (0.34 to 0.92)	300 per 1000[1]	168 per 1000	132 fewer per 1000 (198 fewer to 24 fewer)	⊕⊖⊖⊖ **Very low**	**Rank 47** (0.2999)	**We are uncertain whether rolapitant reduces vomiting**

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					Due to study limitations, imprecision[9]	Rank 12 of 28 single drugs	
Corticosteroids							
Dexamethasone (43 RCTs; 4804 participants)	**0.51** (0.44 to 0.57)	300 per 1000[1]	153 per 1000	147 fewer per 1000 (168 fewer to 471 fewer)	⊕⊕⊕⊕ **High** [3]	**Rank 41** (0.3588) Rank 8 of 28 single drugs	**Dexamethasone reduces vomiting**
Methylprednisolone (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at vomiting**
Antihistamines							
Dimenhydrinate (1 RCT; 56 participants)	**0.55** (0.20 to 1.52)	300 per 1000[1]	165 per 1000	135 fewer per 1000 (240 fewer to 156 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence[10]	**Rank 43** (0.3225) Rank 10 of 28 single drugs	**We are uncertain whether dimenhydrinate reduces vomiting**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at vomiting**
Promethazine (3 RCTs; 210 participants)	**0.53** (0.33 to 0.86)	300 per 1000[1]	159 per 1000	141 fewer per 1000 (201 fewer to 42 fewer)	⊕⊕⊕⊖ **Moderate** Due to imprecision	**Rank 44** (0.3196) Rank 11 of 28 single drugs	**Promethazine probably reduces vomiting**
Anticholinergics							
Scopolamine (6 RCTs; 549 participants)	**0.61** (0.44 to 0.84)	300 per 1000[1]	183 per 1000	117 fewer per 1000 (168 fewer to 48 fewer)	⊕⊕⊖⊖ **Low**	**Rank 54** (0.2443) Rank 19 of 28 single drugs	**Scopolamine may reduce vomiting**

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					Due to study limitations, imprecision		
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 65** (0.0607)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 8 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-1-vomiting 24). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) obtained from the consensus guideline on postoperative nausea and vomiting (Gan-2014). The general incidence of vomiting after surgery is about 30%.

[2] Serious concerns for study limitations, heterogeneity, and incoherence. Heterogeneity and incoherence are overlapping domains for which we downgraded only once.

[3] Evidence only for recommended and high doses because low doses showed no clinically important effect.

[4] Very serious concerns for study limitations.

[5] Serious concerns for imprecision and heterogeneity. Imprecision and heterogeneity are overlapping domains for which we downgraded only once.

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[6] Poorly connected to the network. Only direct evidence available.

[7] Serious concerns for publication bias and heterogeneity. Publication bias and heterogeneity are overlapping domains for which we downgraded only once.

[8] Poorly connected to the network. Fosaprepitant was directly compared only to ondansetron.

[9] Very serious concerns for study limitations, serious concerns for imprecision.

[10] Very serious concerns for imprecision, serious concerns for study limitations and incoherence.

Summary of findings 3. Summary of findings (serious adverse events)

HARM

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: serious adverse events (SAEs)

Setting: inpatient and outpatient

Total studies: 28 RCTs **Total participants: 10,766** **Number of treatments: 22** **Geometry of the network****	**Relative effect***** **(95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** **(P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT3 receptor antagonists							
Dolasetron (3 RCTs; 1448 participants)	**0.31** (0.10 to 1.00)	14 per 1000[1]	4 per 1000	10 fewer per 1000 (13 fewer to 0 fewer)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision[2]	**Rank 1** (0.8229) Rank 14 of 13 single drugs	**Dolasetron may reduce SAEs**
Granisetron	**1.21**	14 per 1000[1]	17 per 1000	3 more per 1000	⊕⊖⊖⊖	**Rank 16**	**We are uncertain whether granisetron increases SAEs**

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(2 RCTs; 401 participants)	(0.11 to 13.15)			(12 fewer to 170 more)	**Very low** Due to study limitations, imprecision[3]	(0.4612) Rank 10 of 13 single drugs	
Ondansetron (3 RCTs; 833 participants)	**1.62** (0.32 to 8.10)	14 per 1000[1]	23 per 1000	9 more per 1000 (10 fewer to 99 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 20** (0.3708) Rank 12 of 13 single drugs	**We are uncertain whether ondansetron increases SAEs**
Palonosetron (3 RCTs; 1319 participants)	**0.71** (0.33 to 1.53)	14 per 1000[1]	10 per 1000	4 fewer per 1000 (9 fewer to 7 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2,3]	**Rank 3** (0.6255) Rank 3 of 13 single drugs	**We are uncertain whether palonosetron reduces SAEs**
Ramosetron (1 RCT; 236 participants)	**0.89** (0.05 to 15.74)	14 per 1000[1]	12 per 1000	2 fewer per 1000 (13 fewer to 206 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[4]	**Rank 8** (0.5366) Rank 7 of 13 single drugs	**We are uncertain whether ramosetron reduces SAEs**
Tropisetron (2 RCTs; 727 participants)	**0.58** (0.10 to 3.24)	14 per 1000[1]	8 per 1000	6 fewer per 1000 (13 fewer to 31 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 2** (0.6905) Rank 2 of 13 single drugs	**We are uncertain whether tropisetron reduces SAE**
D2 receptor antagonists							
Amisulpride (2 RCTs; 904 participants)	**0.86** (0.38 to 1.94)	14 per 1000[1]	12 per 1000	2 fewer per 1000 (9 fewer to 13 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2,5]	**Rank 6** (0.5579) Rank 5 of 13 single drugs	**Amisulpride may reduce SAEs**

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Droperidol (2 RCTs; 304 participants)	**0.88** (0.08 to 9.71)	14 per 1000[1]	12 per 1000	2 fewer per 1000 (13 fewer to 122 more)	⊕⊕⊖⊖ **Low** Due to imprecision[5]	**Rank 7** (0.5430) Rank 6 of 13 single drugs	**Droperidol may reduce SAEs**
Haloperidol (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**
Metoclopramide (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**
Perphenazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**
NK1 receptor antagonists							
Aprepitant (no direct evidence, indirect evidence only)	**1.39** (0.26 to 7.36)	14 per 1000[1]	19 per 1000	5 more per 1000 (10 fewer to 89 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence[6,7]	**Rank 17** (0.4421) Rank 11 of 13 single drugs	**We are uncertain whether aprepitant increases SAEs**
Casopitant (No direct evidence, indirect evidence only)	**3.64** (0.57 to 23.11)	14 per 1000[1]	51 per 1000	37 more per 1000 (6 fewer to 310 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence[6]	**Rank 22** (0.1498) Rank 13 of 13 single drugs	**We are uncertain whether casopitant increases SAEs**
Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**

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Corticosteroids							
Dexamethasone (3 RCTs; 376 participants)	**1.16** (0.28 to 4.85)	14 per 1000[1]	16 per 1000	2 more per 1000 (10 fewer to 54 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 15** (0.4632) Rank 9 of 13 single drugs	**We are uncertain whether dexamethasone increases SAEs**
Methylprednisolone (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**
Antihistamines							
Dimenhydrinate (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**
Promethazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at SAEs**
Anticholinergics							
Scopolamine (1 RCT; 174 participants)	**0.98** (0.02 to 48.71)	14 per 1000[1]	14 per 1000	0 fewer per 1000 (14 fewer to 668 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[4]	**Rank 12** (0.5101) Rank 8 of 13 single drugs	**We are uncertain whether scopolamine has no or minimal effect on SAEs**
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 14** (0.5020)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

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** Geometry of the network is presented in Figure 10 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-2-SAE). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome SAEs. The general incidence of SAEs after surgery with placebo is about 1.43%.

[2] Poorly connected to the network. Only direct evidence available.

[3] Serious concerns for study limitations and very serious concerns for imprecision.

[4] Very serious concerns for study limitations and imprecision.

[5] Very serious concerns for imprecision.

[6] Serious concerns for study limitations and incoherence, and very serious concerns for imprecision.

[7] Poorly connected to the network. Aprepitant was directly compared only to ondansetron.

Summary of findings 4. Summary of findings (any adverse event)

HARM
Patient or population: adults undergoing any type of surgery under general anaesthesia
Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

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Comparator (reference): placebo (or no treatment)

Outcome: any adverse event (AE)

Setting: inpatient and outpatient

Total studies: 61 RCTs **Total participants: 19,423** **Number of treatments: 27** **Geometry of the network****	**Relative effect*** **(95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** **(P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT3 receptor antagonists							
Dolasetron (1 RCT; 203 participants)	**0.86** (0.66 to 1.11)	377 per 1000[1]	324 per 1000	53 fewer per 1000 (128 fewer to 41 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, heterogeneity[2,3]	**Rank 8** (0.6383) Rank 4 of 15 single drugs	**We are uncertain whether dolasetron reduces any AE**
Granisetron (6 RCTs; 699 participants)	**0.92** (0.80 to 1.05)	377 per 1000[1]	347 per 1000	30 fewer per 1000 (75 fewer to 19 more)	⊕⊕⊕⊖ **Moderate** Due to imprecision	**Rank 11** (0.5436) Rank 7 of 15 single drugs	**Granisetron probably has little or no effect on any AE**
Ondansetron (12 RCTs; 4892 participants)	**0.95** (0.88 to 1.01)	377 per 1000[1]	358 per 1000	19 fewer per 1000 (45 fewer to 4 more)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision	**Rank 16** (0.4655) Rank 9 of 15 single drugs	**Ondansetron may have little or no effect on any AE**
Palonosetron (2 RCTs; 946 participants)	**0.95** (0.87 to 1.03)	377 per 1000[1]	358 per 1000	19 fewer per 1000 (49 fewer to 11 more)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision	**Rank 17** (0.4608) Rank 10 of 15 single drugs	**Palonosetron may have little or no effect on any AE**

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Ramosetron (2 RCTs; 173 participants)	**1.00** (0.65 to 1.54)	377 per 1000[1]	377 per 1000	0 fewer/more per 1000 (132 fewer to 204 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[4]	**Rank 18** (0.4159) Rank 11 of 15 single drugs	**We are uncertain whether ramosetron has little or no effect on any AE**
Tropisetron (3 RCTs; 1007 participants)	**1.00** (0.84 to 1.19)	377 per 1000[1]	377 per 1000	0 fewer/more per 1000 (60 fewer to 72 more)	⊕⊕⊖⊖ **Low** Due to imprecision[5]	**Rank 22** (0.3561) Rank 13 of 15 single drugs	**Tropisetron may have little or no effect on any AE**
D2 receptor antagonists							
Amisulpride (2 RCTs; 904 participants)	**0.97** (0.90 to 1.06)	377 per 1000[1]	366 per 1000	11 fewer per 1000 (38 fewer to 23 more)	⊕⊕⊕⊖ **Moderate** Due to imprecision[3]	**Rank 20** (0.3917) Rank 12 of 15 single drugs	**Amisulpride probably has little or no effect on any AE**
Droperidol (2 RCTs; 1622 participants)	**0.89** (0.81 to 0.98)	377 per 1000[1]	336 per 1000	41 fewer per 1000 (72 fewer to 8 fewer)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision	**Rank 10** (0.6164) Rank 6 of 15 single drugs	**Droperidol may reduce any AE**
Haloperidol (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at any AE**
Metoclopramide (3 RCTs; 853 participants)	**0.92** (0.83 to 1.03)	377 per 1000[1]	347 per 1000	30 fewer per 1000 (64 fewer to 11 more)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision	**Rank 12** (0.5302) Rank 8 of 15 single drugs	**Metoclopramide may have little or no effect on any AE**
Perphenazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at any AE**
NK1 receptor antagonists							

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Aprepitant (no direct evidence, indirect evidence only)	**0.87** (0.78 to 0.97)	377 per 1000[1]	328 per 1000	49 fewer per 1000 (83 fewer to 11 fewer)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence[6]	**Rank 6** (0.6589) Rank 3 of 15 single drugs	**We are uncertain whether aprepitant reduces any AE**
Casopitant (no direct evidence, indirect evidence only)	**0.88** (0.74 to 1.05)	377 per 1000[1]	332 per 1000	45 fewer per 1000 (98 fewer to 19 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence	**Rank 9** (0.6170) Rank 5 of 15 single drugs	**We are uncertain whether casopitant reduces any AE**
Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at any AE**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at any AE**
Corticosteroids							
Dexamethasone (6 RCTs; 1152 participants)	**0.77** (0.55 to 1.08)	377 per 1000[1]	290 per 1000	87 fewer per 1000 (170 fewer to 30 more)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision	**Rank 4** (0.7526) Rank 2 of 15 single drugs	**Dexamethasone may reduce any AE**
Methylprednisolone (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at any AE**
Antihistamines							
Dimenhydrinate (no direct evidence, indirect evidence only)	**5.70** (1.36 to 23.93)	377 per 1000[1]	1000 per 1000	1000 per 1000 (136 more to 623 more)	⊕⊕⊖⊖ **Low** Due to study limitations, incoherence[7]	**Rank 27** (0.0140) Rank 15 of 15 single drugs	**Dimenhydrinate may increase any AE**

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Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at any AE**
Promethazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at any AE**
Anticholinergics							
Scopolamine (3 RCTs; 273 participants)	**2.12** (1.71 to 2.64)	377 per 1000[1]	799 per 1000	422 more per 1000 (268 more to 618 more)	⊕⊕⊖⊖ **Low** Due to study limitations[3,8]	**Rank 26** (0.0500) Rank 14 of 15 single drugs	**Scopolamine may increase any AE**
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 23** (0.3129)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was only assessed for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 12 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-3-any AE). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

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Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome any AE. The general incidence of any AE after surgery with placebo is about 37.68%.

[2] Very serious concern for study limitations and serious concerns for imprecision and heterogeneity. Imprecision and heterogeneity are overlapping domains for which we downgraded only once.

[3] Poorly connected to the network. Only direct evidence available.

[4] Serious concerns for study limitations and very serious concerns for imprecision.

[5] Very serious concerns for imprecision.

[6] Poorly connected to the network. Aprepitant was directly compared only to ondansetron.

[7] Poorly connected to the network. Dimenhydrinate was directly compared only to ondansetron.

[8] Very serious concerns for study limitations.

Summary of findings 5. Summary of findings (headache)

HARM

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: headache within 7 days postoperatively

Setting: inpatient and outpatient

Total studies: 208 RCTs **Total participants: 42,445** **Number of treatments: 53** **Geometry of the network****	**Relative effect*** (95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** (P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			

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5-HT3 receptor antagonists							
Dolasetron (10 RCTs; 3990 participants)	**1.13** (0.93 to 1.36)	96 per 1000[1]	108 per 1000	12 more per 1000 (7 fewer to 35 more)	⊕⊕⊝⊝ **Low** Due to study limitations, imprecision	**Rank 39** (0.3426) Rank 15 of 23 single drugs	**Dolasetron may increase headache**
Granisetron (15 RCTs; 1639 participants)	**1.20** (1.01 to 1.42)	96 per 1000[1]	115 per 1000	19 more per 1000 (1 more to 40 more)	⊕⊝⊝⊝ **Very low** Due to study limitations, imprecision, incoherence	**Rank 45** (0.2914) Rank 19 of 23 single drugs	**We are uncertain whether granisetron increases headache**
Ondansetron (57 RCTs; 12260 participants)	**1.16** (1.06 to 1.28)	96 per 1000[1]	111 per 1000	15 more per 1000 (6 more to 27 more)	⊕⊕⊕⊝ **Moderate** Due to imprecision	**Rank 44** (0.3082) Rank 18 of 23 single drugs	**Ondansetron probably increases headache**
Palonosetron (7 RCTs; 1259 participants)	**1.15** (0.89 to 1.49)	96 per 1000[1]	110 per 1000	14 more per 1000 (11 fewer to 47 more)	⊕⊝⊝⊝ **Very low** Due to study limitations, imprecision[2]	**Rank 42** (0.3310) Rank 17 of 23 single drugs	**We are uncertain whether palonosetron increases headache**
Ramosetron (14 RCTs; 1529 participants)	**1.13** (0.93 to 1.37)	96 per 1000[1]	108 per 1000	12 more per 1000 (7 fewer to 36 more)	⊕⊕⊝⊝ **Low** Due to study limitations, imprecision	**Rank 40** (0.3416) Rank 16 of 23 single drugs	**Ramosetron may increase headache**
Tropisetron (10 RCTs; 1656 participants)	**1.09** (0.91 to 1.32)	96 per 1000[1]	104 per 1000	8 more per 1000 (9 fewer to 31 more)	⊕⊕⊝⊝ **Low** Due to study limitations, imprecision	**Rank 38** (0.3699) Rank 14 of 23 single drugs	**Tropisetron may have little or no effect on headache**
D2 receptor antagonists							

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Amisulpride (2 RCTs; 904 participants)	**1.59** (0.80 to 3.19)	96 per 1000[1]	153 per 1000	57 more per 1000 (19 fewer to 210 more)	⊕⊕⊖⊖ **Low** Due to imprecision[3,4]	**Rank 51** (0.2027) Rank 22 of 23 single drugs	**Amisulpride may increase headache**
Droperidol (22 RCTs; 3679 participants)	**0.76** (0.67 to 0.86)	96 per 1000[1]	73 per 1000	23 fewer per 1000 (32 fewer to 13 fewer)	⊕⊕⊕⊖ **Moderate** Due to study limitations	**Rank 13** (0.6563) Rank 5 of 23 single drugs	**Droperidol probably reduces headache**
Haloperidol (2 RCTs; 99 participants)	**0.54** (0.27 to 1.06)	96 per 1000[1]	52 per 1000	44 fewer per 1000 (70 fewer to 6 more)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision	**Rank 4** (0.7742) Rank 2 of 23 single drugs	**Haloperidol may reduce headache**
Metoclopramide (11 RCTs; 1313 participants)	**0.93** (0.76 to 1.13)	96 per 1000[1]	89 per 1000	7 fewer per 1000 (23 fewer to 12 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2]	**Rank 28** (0.5149) Rank 11 of 23 single drugs	**We are uncertain whether metoclopramide has little or no effect on headache**
Perphenazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at headache**
NK1 receptor antagonists							
Aprepitant (1 RCT; 120 participants)	**0.86** (0.35 to 2.11)	96 per 1000[1]	83 per 1000	13 fewer per 1000 (62 fewer to 107 more)	⊕⊕⊖⊖ **Low** Due to imprecision[3]	**Rank 24** (0.5349) Rank 10 of 23 single drugs	**Aprepitant may reduce headache**
Casopitant (no direct evidence, indirect evidence only)	**0.81** (0.49 to 1.34)	96 per 1000[1]	78 per 1000	18 fewer per 1000 (49 fewer to 33 more)	⊕⊖⊖⊖ **Very low** Due to imprecision, incoherence[5]	**Rank 18** (0.5927) Rank 7 of 23 single drugs	**We are uncertain whether casopitant reduces headache**

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Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at headache**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at headache**
Corticosteroids							
Dexamethasone (13 RCTs; 1678 participants)	**0.85** (0.63 to 1.13)	96 per 1000[1]	82 per 1000	14 fewer per 1000 (36 fewer to 12 more)	⊕⊕⊖⊖ **Low** Due to imprecision[3]	**Rank 19** (0.5806) Rank 8 of 23 single drugs	**Dexamethasone may reduce headache**
Methylprednisolone (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at headache**
Antihistamines							
Dimenhydrinate (1 RCT; 50 participants)	**1.23** (0.33 to 4.55)	96 per 1000[1]	118 per 1000	22 more per 1000 (64 fewer to 341 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2]	**Rank 37** (0.3709) Rank 13 of 23 single drugs	**We are uncertain whether dimenhydrinate increases headache**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at headache**
Promethazine (1 RCT; 50 participants)	**0.27** (0.01 to 4.83)	96 per 1000[1]	26 per 1000	70 fewer per 1000 (95 fewer to 368)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2]	**Rank 5** (0.7644) Rank 3 of 23 single drugs	**We are uncertain whether promethazine reduces headache**
Anticholinergics							
Scopolamine (4 RCTs; 447 participants)	**1.03** (0.55 to 1.94)	96 per 1000[1]	99 per 1000	3 more per 1000 (43 fewer to 90 more)	⊕⊖⊖⊖ **Very low**	**Rank 33** (0.4285)	**We are uncertain whether scopolamine has little or no effect on headache**

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					Due to study limitations, imprecision[4,6]	Rank 12 of 23 single drugs	
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 31** (0.4543)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 14 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-4-headache). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome headache. The general incidence of headache after surgery with placebo is about 9.56%.

[2] Serious concerns for study limitations and very serious concerns for imprecision.

[3] Very serious concerns for imprecision.

[4] Poorly connected to the network. Only direct evidence available.

[5] Very serious concerns for imprecision, serious concerns for incoherence.

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[6] Very serious concerns for study limitations and imprecision.

Summary of findings 6. Summary of findings (sedation)

HARM

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: sedation within 7 days postoperatively

Setting: inpatient and outpatient

Total studies: 117 RCTs **Total participants: 21,440** **Number of treatments: 44** **Geometry of the network****	**Relative effect*** **(95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** **(P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT$_3$ receptor antagonists							
Dolasetron (5 RCTs; 2402 participants)	**1.00** (0.88 to 1.13)	130 per 1000[1]	130 per 1000	0 fewer/more per 1000 (16 fewer to 17 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 23** (0.5028) Rank 14 of 24 single drugs	**Dolasetron may have little or no effect on sedation**
Granisetron (9 RCTs; 850 participants)	**1.00** (0.86 to 1.17)	130 per 1000[1]	130 per 1000	0 fewer/more per 1000 (18 fewer to 22 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 24** (0.4996) Rank 15 of 24 single drugs	**We are uncertain whether granisetron has little or no effect on sedation**

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Ondansetron (36 RCTs; 6092 participants)	**0.87** (0.79 to 0.96)	130 per 1000[1]	113 per 1000	17 fewer per 1000 (41 fewer to 5 fewer)	⊕⊕⊕⊖ **Moderate** Due to imprecision[4]	**Rank 9** (0.6623) Rank 5 of 24 single drugs	**Ondansetron probably reduces sedation**
Palonosetron (2 RCTs; 278 participants)	**1.16** (0.89 to 1.51)	130 per 1000[1]	151 per 1000	21 more per 1000 (14 fewer to 66 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 34** (0.3743) Rank 15 of 24 single drugs	**We are uncertain whether palonosetron increases sedation**
Ramosetron (5 RCTs; 581 participants)	**0.89** (0.72 to 1.10)	130 per 1000[1]	116 per 1000	14 fewer per 1000 (36 fewer to 13 more)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision	**Rank 13** (0.6263) Rank 8 of 24 single drugs	**Ramosetron may reduce sedation**
Tropisetron (2 RCTs; 98 participants)	**0.74** (0.54 to 1.00)	130 per 1000[1]	96 per 1000	34 fewer per 1000 (60 fewer to 0 fewer)	⊕⊕⊖⊖ **Low** Due to study limitations, imprecision	**Rank 7** (0.7327) Rank 4 of 24 single drugs	**Tropisetron may reduce sedation**
D2 receptor antagonists							
Amisulpride (1 RCT; 689 participants)	**1.00** (0.02 to 50.11)	130 per 1000[1]	130 per 1000	0 fewer/more per 1000 (127 fewer to 870 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2,5]	**Rank 21** (0.5105) Rank 13 of 24 single drugs	**Amisulpride may have little or no effect on sedation**
Droperidol (21 RCTs; 3739 participants)	**0.99** (0.96 to 1.01)	130 per 1000[1]	129 per 1000	1 fewer per 1000 (5 fewer to 1 more)	⊕⊕⊖⊖ **Low** Due to study limitations[6]	**Rank 18** (0.5152) Rank 11 of 24 single drugs	**Droperidol may have little or no effect on sedation**
Haloperidol	**0.95** (0.67 to 1.35)	130 per 1000[1]	124 per 1000	6 fewer per 1000 (43 fewer to 46 more)	⊕⊖⊖⊖ **Very low**	**Rank 15** (0.5487)	**We are uncertain whether haloperidol has little or no effect on sedation**

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(no direct evidence, indirect evidence only)					Due to study limitations, imprecision, incoherence[7]	Rank 9 of 24 single drugs	
Metoclopramide (15 RCTs; 1178 participants)	**0.97** (0.82 to 1.13)	130 per 1000[1]	126 per 1000	4 fewer per 1000 (23 fewer to 17 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence[7]	**Rank 17** (0.5412) Rank 10 of 24 single drugs	**We are uncertain whether metoclopramide has little or no effect on sedation**
Perphenazine (1 RCT; 115 participants)	**0.23** (0.03 to 1.73)	130 per 1000[1]	30 per 1000	100 fewer per 1000 (126 fewer to 95 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 3** (0.8469) Rank 1 of 24 single drugs	**We are uncertain whether perphenazine reduces sedation**
NK1 receptor antagonists							
Aprepitant (no direct evidence, indirect evidence only)	**0.43** (0.01 to 21.65)	130 per 1000[1]	56 per 1000	74 fewer per 1000 (129 fewer to 870 more)	⊕⊖⊖⊖ **Very low** Due to imprecision, incoherence[8]	**Rank 10** (0.6518) Rank 6 of 24 single drugs	**We are uncertain whether aprepitant reduces sedation**
Casopitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at sedation**
Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at sedation**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at sedation**
Corticosteroids							
Dexamethasone	**1.00**	130 per 1000[1]	130 per 1000	0 fewer/more per 1000	⊕⊕⊕⊕	**Rank 25**	**Dexamethasone has no effect on sedation**

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(9 RCTs; 1290 participants)	(0.91 to 1.09)			(12 fewer to 12 more)	**High**	(0.4982) Rank 16 of 24 single drugs	
Methylprednisolone (1 RCT; 112 participants)	**4.83** (0.24 to 98.29)	130 per 1000[1]	628 per 1000	498 more per 1000 (99 fewer to 870 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2,5]	**Rank 40** (0.2156) Rank 21 of 24 single drugs	**Methylprednisolone may increase sedation**
Antihistamines							
Dimenhydrinate (1 RCT; 50 participants)	**7.66** (3.10 to 18.94)	130 per 1000[1]	996 per 1000	866 more per 1000 (273 more to 870 more)	⊕⊕⊕⊖ **Moderate** Due to study limitations	**Rank 42** (0.0774) Rank 22 of 24 single drugs	**Dimenhydrinate probably increases sedation**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at sedation**
Promethazine (3 RCTs; 162 participants)	**1.06** (0.59 to 1.92)	130 per 1000[1]	138 per 1000	8 more per 1000 (53 fewer to 120 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 29** (0.4695) Rank 17 of 24 single drugs	**We are uncertain whether promethazine has no or minimal effect on sedation**
Anticholinergics							
Scopolamine (4 RCTs; 204 participants)	**1.47** (0.79 to 2.72)	130 per 1000[1]	191 per 1000	61 more per 1000 (27 fewer to 224 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 38** (0.3011) Rank 20 of 24 single drugs	**We are uncertain whether scopolamine increase sedation**
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 26** (0.4880)	**Reference comparator**

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NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 16 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-5-sedation). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome sedation. The general incidence of sedation after surgery with placebo is about 13%.

[2] Very serious concerns for imprecision.

[3] Serious concerns for study limitations and very serious concerns for imprecision.

[4] Evidence only for recommended and high doses.

[5] Poorly connected to the network. Only direct evidence available.

[6] Very serious concerns for study limitations.

[7] Serious concerns for study limitations and incoherence, and very serious concerns for imprecision.

[8] Serious concerns for incoherence and very serious concerns for imprecision.

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Summary of findings 7. Summary of findings (extrapyramidal symptoms)

HARM

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: extrapyramidal symptoms within 7 days postoperatively

Setting: inpatient and outpatient

Total studies: 64 RCTs **Total participants: 10,724** **Number of treatments: 30** **Geometry of the network****	**Relative effect*** **(95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** **(P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT3 receptor antagonists							
Dolasetron (3 RCTs; 288 participants)	**0.67** (0.10 to 4.38)	8 per 1000[1]	5 per 1000	3 fewer per 1000 (7 fewer to 27 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 5** (0.5860) Rank 3 of 16 single drugs	**Dolasetron may reduce extrapyramidal symptoms**
Granisetron (5 RCTs; 330 participants)	**0.90** (0.23 to 3.57)	8 per 1000[1]	7 per 1000	1 fewer per 1000 (6 fewer to 21 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 12** (0.5109) Rank 6 of 16 single drugs	**We are uncertain whether granisetron reduces extrapyramidal symptoms**
Ondansetron (7 RCTs; 751 participants)	**0.73** (0.39 to 1.38)	8 per 1000[1]	6 per 1000	2 fewer per 1000 (5 fewer to 3 more)	⊕⊖⊖⊖ **Very low**	**Rank 3** (0.6026) Rank 1 of 16 single drugs	**We are uncertain whether ondansetron reduces extrapyramidal symptoms**

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					Due to study limitations, imprecision[3]		
Palonosetron (1 RCT; 60 participants)	**1.00** (0.02 to 48.80)	8 per 1000[1]	8 per 1000	0 fewer/more per 1000 (8 fewer to 382 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3,4]	**Rank 18** (0.4885) Rank 8 of 16 single drugs	**We are uncertain whether palonosetron has no or minimal effect on extrapyramidal symptoms**
Ramosetron (no direct evidence, indirect evidence only)	**0.73** (0.01 to 37.44)	8 per 1000[1]	6 per 1000	2 fewer per 1000 (8 fewer to 292 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence[5]	**Rank 8** (0.5409) Rank 5 of 16 single drugs	**We are uncertain whether ramosetron reduces extrapyramidal symptoms**
Tropisetron (3 RCTs; 187 participants)	**0.82** (0.43 to 1.58)	8 per 1000[1]	7 per 1000	1 fewer per 1000 (5 fewer to 5 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[6]	**Rank 7** (0.5553) Rank 4 of 16 single drugs	**We are uncertain whether tropisetron reduces extrapyramidal symptoms**
D2 receptor antagonists							
Amisulpride (1 RCT; 689 participants)	**1.00** (0.02 to 50.11)	8 per 1000[1]	8 per 1000	0 fewer/more per 1000 (8 fewer to 393 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2,4]	**Rank 19** (0.4872) Rank 9 of 16 single drugs	**Amisulpride may have little or no effect on extrapyramidal symptoms**
Droperidol (22 RCTs; 3270 participants)	**1.36** (0.89 to 2.08)	8 per 1000[1]	11 per 1000	3 more per 1000 (1 fewer to 9 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 29** (0.3456) Rank 15 of 16 single drugs	**Droperidol may increase extrapyramidal symptoms**
Haloperidol	**1.18** (0.37 to 3.73)	8 per 1000[1]	9 per 1000	1 more per 1000	⊕⊕⊖⊖ **Low**	**Rank 27** (0.4202)	**Haloperidol may increase extrapyramidal symptoms**

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(5 RCTs; 437 participants)				(5 fewer to 22 more)	Due to imprecision[2]	Rank 14 of 16 single drugs	
Metoclopramide (12 RCTs; 855 participants)	**1.14** (0.59 to 2.20)	8 per 1000[1]	9 per 1000	1 fewer per 1000 (3 fewer to 10 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 26** (0.4257) Rank 13 of 16 single drugs	**Metoclopramide may increase extrapyramidal symptoms**
Perphenazine (1 RCT; 115 participants)	**1.03** (0.05 to 23.02)	8 per 1000[1]	8 per 1000	0 fewer/more per 1000 (8 fewer to 176 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 23** (0.4774) Rank 12 of 16 single drugs	**We are uncertain whether perphenazine has no or minimal effect on extrapyramidal symptoms**
NK1 receptor antagonists							
Aprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**
Casopitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**
Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**
Corticosteroids							
Dexamethasone (4 RCTs; 1031 participants)	**0.70** (0.17 to 2.80)	8 per 1000[1]	6 per 1000	2 fewer per 1000 (7 fewer to 14 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 4** (0.5865) Rank 2 of 16 single drugs	**Dexamethasone may reduce extrapyramidal symptoms**
Methylprednisolone	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**

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(0 RCTs; 0 participants)							
Antihistamines							
Dimenhydrinate (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**
Promethazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**
Anticholinergics							
Scopolamine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at extrapyramidal symptoms**
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 22** (0.4778)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 18 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-6-extrapyramidal symptoms). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

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Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome extrapyramidal symptoms. The general incidence of extrapyramidal symptoms after surgery with placebo is about 0.79%.

[2] Very serious concerns for imprecision.

[3] Serious concerns for study limitations and very serious concerns for imprecision.

[4] Poorly connected to the network. Only direct evidence available.

[5] Serious concerns for study limitations and incoherence, and very serious concerns for imprecision.

[6] Very serious concerns for study limitations and imprecision.

Summary of findings 8. Summary of findings (constipation)

HARM

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: constipation within 7 days postoperatively

Setting: inpatient and outpatient

Total studies: 43 RCTs **Total participants: 11,481** **Number of treatments: 23**	**Relative effect*** (95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** (P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			

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Geometry of the network**							
5-HT3 receptor antagonists							
Dolasetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Granisetron (3 RCTs; 230 participants)	**0.59** (0.21 to 1.63)	74 per 1000[1]	44 per 1000	30 fewer per 1000 (58 fewer to 47 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2]	**Rank 2** (0.7350) Rank 1 of 12 single drugs	**We are uncertain whether granisetron reduces constipation**
Ondansetron (8 RCTs; 1475 participants)	**1.02** (0.71 to 1.46)	74 per 1000[1]	75 per 1000	1 more per 1000 (21 fewer to 34 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2]	**Rank 13** (0.4677) Rank 6 of 12 single drugs	**We are uncertain whether ondansetron has no or minimal effect on constipation**
Palonosetron (3 RCTs; 1437 participants)	**1.06** (0.80 to 1.40)	74 per 1000[1]	78 per 1000	4 more per 1000 (15 fewer to 30 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2]	**Rank 15** (0.4406) Rank 8 of 12 single drugs	**We are uncertain whether palonosetron has no or minimal effect on constipation**
Ramosetron (2 RCTs; 280 participants)	**0.74** (0.39 to 1.40)	74 per 1000[1]	55 per 1000	19 fewer per 1000 (45 fewer to 30 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2]	**Rank 5** (0.6692) Rank 3 of 12 single drugs	**We are uncertain whether ramosetron reduces constipation**
Tropisetron (2 RCTs; 226 participants)	**1.25** (0.28 to 5.59)	74 per 1000[1]	93 per 1000	19 more per 1000 (53 fewer to 340 more)	⊕⊖⊖⊖ **Very low**	**Rank 17** (0.4130) Rank 10 of 12 single drugs	**We are uncertain whether tropisetron increases constipation**

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					Due to study limitations, imprecision[2]		
D2 receptor antagonists							
Amisulpride (2 RCTs; 904 participants)	**1.12** (0.71 to 1.75)	74 per 1000[1]	83 per 1000	9 more per 1000 (21 fewer to 56 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[2,3]	**Rank 18** (0.4124) Rank 11 of 12 single drugs	**We are uncertain whether amisulpride increases constipation**
Droperidol (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Haloperidol (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Metoclopramide (1 RCT; 80 participants)	**1.90** (0.34 to 10.68)	74 per 1000[1]	141 per 1000	67 fewer per 1000 (49 fewer to 716 more)	⊕⊕⊖⊖ **Low** Due to imprecision[5]	**Rank 21** (0.2869) Rank 12 of 12 single drugs	**Metoclopramide may increase constipation**
Perphenazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
NK1 receptor antagonists							
Aprepitant (no direct evidence, indirect evidence only)	**1.03** (0.59 to 1.80)	74 per 1000[1]	76 per 1000	2 more per 1000 (30 fewer to 129 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence[4]	**Rank 14** (0.4638) Rank 7 of 12 single drugs	**We are uncertain whether aprepitant has no or minimal effect on constipation**
Casopitant	**0.82** (0.42 to 1.62)	74 per 1000[1]	61 per 1000	13 fewer per 1000	⊕⊖⊖⊖ **Very low**	**Rank 6** (0.6111)	**We are uncertain whether casopitant reduces constipation**

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(no direct evidence, indirect evidence only)				(43 fewer to 46 more)	Due to study limitations, imprecision, incoherence[4]	Rank 4 of 12 single drugs	
Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Corticosteroids							
Dexamethasone (3 RCTs; 327 participants)	**0.83** (0.21 to 3.25)	74 per 1000[1]	61 per 1000	13 fewer per 1000 (58 fewer to 167 more)	⊕⊕⊖⊖ **Low** Due to imprecision[5]	**Rank 7** (0.5802) Rank 5 of 12 single drugs	**Dexamethasone may reduce constipation**
Methylprednisolone (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Antihistamines							
Dimenhydrinate (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Promethazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**
Anticholinergics							
Scopolamine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at constipation**

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Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 12** (0.4889)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 20 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-7-constipation). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome constipation. The general incidence of constipation after surgery with placebo is about 7.39%.

[2] Serious concerns for study limitations and very serious concerns for imprecision.

[3] Poorly connected to the network. Only direct evidence available.

[4] Serious concerns for study limitations and incoherence, and very serious concerns for imprecision.

[5] Very serious concerns for imprecision.

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Summary of findings 9. Summary of findings (postoperative wound infection)

HARM

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: wound infection within 7 days postoperatively

Setting: inpatient and outpatient

Total studies: 32 RCTs **Total participants: 4369** **Number of treatments: 10** **Geometry of the network****	**Relative effect*** (95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** (P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT3 receptor antagonists							
Dolasetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Granisetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Ondansetron (no direct evidence, indirect evidence only)	**1.28** (0.01 to 115.24)	4 per 1000[1]	5 per 1000	1 more per 1000 (4 fewer to 457 more)	⊕⊖⊖⊖ **Very low** Due to imprecision, incoherence[2]	**Rank 9** (0.3974) Rank 6 of 6 single drugs	**We are uncertain whether ondansetron increases wound infection**
Palonosetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Ramosetron	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**

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(0 RCTs; 0 participants)							
Tropisetron (1 RCT; 156 participants)	**0.42** (0.04 to 4.55)	4 per 1000[1]	2 per 1000	2 fewer per 1000 (4 fewer to 14 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 2** (0.6171) Rank 2 of 6 single drugs	**Tropisetron may reduce wound infection**
D_2 receptor antagonists							
Amisulpride (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Droperidol (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Haloperidol (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Metoclopramide (1 RCT; 104 participants)	**0.96** (0.04 to 21.33)	4 per 1000[1]	4 per 1000	0 fewer/more per 1000 (4 fewer to 81 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 5** (0.4360) Rank 3 of 6 single drugs	**We are uncertain whether metoclopramide has little or no effect on wound infection**
Perphenazine (0 RCT; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
NK1 receptor antagonists							
Aprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Casopitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Fosaprepitant	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**

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(0 RCTs; 0 participants)							
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Corticosteroids							
Dexamethasone (24 RCTs; 3199 participants)	**0.91** (0.45 to 1.87)	4 per 1000[1]	4 per 1000	0 fewer/more per 1000 (2 fewer to 3 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 8** (0.4272) Rank 5 of 6 single drugs	**We are uncertain whether dexamethasone has little or no effect on wound infection**
Methylprednisolone (1 RCT; 40 participants)	**1.00** (0.02 to 48.03)	4 per 1000[1]	4 per 1000	0 fewer/more per 1000 (4 fewer to 188 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3,4]	**Rank 5** (0.4360) Rank 3 of 6 single drugs	**We are uncertain whether methylprednisolone has little or no effect on wound infection**
Antihistamines							
Dimenhydrinate (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Promethazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Anticholinergics							
Scopolamine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at wound infection**
Comparator							

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Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 10** (0.3885)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 22 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-8-wound infection). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome wound infection. The general incidence of wound infection after surgery with placebo is about 0.44%.

[2] Very serious concerns for imprecision and serious concerns for incoherence.

[3] Serious concerns for study limitations and very serious concerns for imprecision.

[4] Poorly connected to the network. Only direct evidence available.

Summary of findings 10. Summary of findings (arrhythmia)

HARM

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Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: arrhythmia within 7 days postoperatively

Setting: inpatient and outpatient

Total studies: 25 RCTs **Total participants: 5067** **Number of treatments: 18** **Geometry of the network****	**Relative effect***** **(95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ****** **(P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT3 receptor antagonists							
Dolasetron (2 RCTs; 1184 participants)	**0.72** (0.39 to 1.34)	43 per 1000[1]	31 per 1000	12 fewer per 1000 (26 fewer to 15 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 4** (0.5944) Rank 1 of 12 single drugs	**Dolasetron may reduce arrhythmia**
Granisetron (1 RCT; 50 participants)	**0.95** (0.04 to 21.59)	43 per 1000[1]	41 per 1000	2 fewer per 1000 (41 fewer to 885 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 8** (0.4688) Rank 5 of 12 single drugs	**We are uncertain whether granisetron has little or no effect on arrhythmia**
Ondansetron (4 RCTs; 1643 participants)	**1.27** (0.47 to 3.43)	43 per 1000[1]	55 per 1000	12 more per 1000 (23 fewer to 104 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 17** (0.3492) Rank 11 of 12 single drugs	**We are uncertain whether ondansetron increases arrhythmia**
Palonosetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**

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Ramosetron (1 RCT; 140 participants)	**1.30** (0.80 to 2.10)	43 per 1000[1]	56 per 1000	13 more per 1000 (9 fewer to 47 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2,4]	**Rank 18** (0.0.3138) Rank 12 of 12 single drugs	**Ramosetron may increase arrhythmia**
Tropisetron (1 RCT; 50 participants)	**0.95** (0.04 to 21.59)	43 per 1000[1]	41 per 1000	2 fewer per 1000 (41 fewer to 885 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 9** (0.4688) Rank 6 of 12 single drugs	**We are uncertain whether tropisetron has little or no effect on arrhythmia**
D2 receptor antagonists							
Amisulpride (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**
Droperidol (7 RCTs; 659 participants)	**0.88** (0.31 to 2.48)	43 per 1000[1]	39 per 1000	4 fewer per 1000 (20 fewer to 64 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 7** (0.4981) Rank 4 of 12 single drugs	**We are uncertain whether droperidol reduces arrhythmia**
Haloperidol (2 RCTs; 99 participants)	**1.14** (0.13 to 10.14)	43 per 1000[1]	49 per 1000	6 more per 1000 (37 fewer to 393 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 14** (0.4170) Rank 9 of 12 single drugs	**We are uncertain whether haloperidol increases arrhythmia**
Metoclopramide (3 RCTs; 150 participants)	**1.13** (0.17 to 7.57)	43 per 1000[1]	49 per 1000	6 more per 1000 (36 fewer to 283 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 16** (0.4070) Rank 10 of 12 single drugs	**We are uncertain whether metoclopramide increases arrhythmia**
Perphenazine	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**

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(0 RCTs 0 participants)							
NK1 receptor antagonists							
Aprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**
Casopitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**
Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**
Corticosteroids							
Dexamethasone (3 RCTs; 189 participants)	**0.81** (0.44 to 1.51)	43 per 1000[1]	35 per 1000	8 fewer per 1000 (24 fewer to 22 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 6** (0.5380) Rank 3 of 12 single drugs	**Dexamethasone may reduce arrhythmia**
Methylprednisolone (1 RCT; 96 participants)	**0.96** (0.06 to 14.90)	43 per 1000[1]	41 per 1000	2 fewer per 1000 (40 fewer to 598 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[4,5]	**Rank 10** (0.4655) Rank 7 of 12 single drugs	**We are uncertain whether methylprednisolone has little or no effect on arrhythmia**
Antihistamines							
Dimenhydrinate (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**

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Promethazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**
Anticholinergics							
Scopolamine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at arrhythmia**
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 13** (0.4400)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 24 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between risk of the intervention group and risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-9-arrhythmia). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome arrhythmia. The general incidence of arrhythmia after surgery with placebo is about 4.25%.

[2] Very serious concerns for imprecision.

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[3] Serious concerns for study limitations and very serious concerns for imprecision.

[4] Poorly connected to the network. Only direct evidence available.

[5] Very serious concerns for study limitations and imprecision.

Summary of findings 11. Summary of findings (visual disturbances)

HARM

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: visual disturbances within 7 days postoperatively

Setting: inpatient and outpatient

Total studies: 21 RCTs **Total participants: 3634** **Number of treatments: 12** **Geometry of the network****	**Relative effect*** (95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** (P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT3 receptor antagonists							
Dolasetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Granisetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Ondansetron (3 RCTs; 506 participants)	**1.29** (0.73 to 2.27)	75 per 1000[1]	97 per 1000	22 more per 1000 (20 fewer to 95 more)	⊕⊕⊖⊖ **Low**	**Rank 10** (0.3694)	**Ondansetron may increase visual disturbances**

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					Due to imprecision[2]	Rank 9 of 10 single drugs	
Palonosetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Ramosetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Tropisetron (1 RCT; 97 participants)	**0.90** (0.35 to 2.29)	75 per 1000[1]	68 per 1000	8 fewer per 1000 (49 fewer to 97 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 6** (0.5558) Rank 6 of 10 single drugs	**We are uncertain whether tropisetron reduces visual disturbances**
D2 receptor antagonists							
Amisulpride (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Droperidol (5 RCTs; 682 participants)	**0.66** (0.36 to 1.22)	75 per 1000[1]	50 per 1000	25 fewer per 1000 (48 fewer to 17 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[4]	**Rank 3** (0.7073) Rank 3 of 10 single drugs	**We are uncertain whether droperidol reduces visual disturbances**
Haloperidol (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Metoclopramide (1 RCT; 100 participants)	**1.29** (0.58 to 2.88)	75 per 1000[1]	97 per 1000	22 more per 1000 (32 fewer to 141 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 9** (0.3759) Rank 8 of 10 single drugs	**Metoclopramide may increase visual disturbances**
Perphenazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**

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NK1 receptor antagonists							
Aprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Casopitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Corticosteroids							
Dexamethasone (1 RCT; 40 participants)	**0.83** (0.27 to 2.54)	75 per 1000[1]	62 per 1000	13 fewer per 1000 (55 fewer to 116 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2,5]	**Rank 5** (0.5737) Rank 5 of 10 single drugs	**Dexamethasone may reduce visual disturbances**
Methylprednisolone (1 RCT; 96 participants)	**0.32** (0.01 to 7.92)	75 per 1000[1]	24 per 1000	51 fewer per 1000 (74 fewer to 519 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3,5]	**Rank 2** (0.7236) Rank 2 of 10 single drugs	**We are uncertain whether methylprednisolone reduces visual disturbances**
Antihistamines							
Dimenhydrinate (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**
Promethazine	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at visual disturbances**

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(0 RCTs; 0 participants)							
Anticholinergics							
Scopolamine (8 RCTs; 683 participants)	**2.01** (1.28 to 3.17)	75 per 1000[1]	151 per 1000	76 more per 1000 (21 more to 163 more)	⊕⊕⊖⊖ **Low** Due to study limitations, heterogeneity	**Rank 11** (0.1890) Rank 10 of 10 single drugs	**Scopolamine may increase visual disturbances**
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 7** (0.5098)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 26 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between the risk of the intervention group and the risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-10-visual disturbances). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome visual disturbances. The general incidence of visual disturbances after surgery with placebo is about 7.46%.

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[2] Very serious concerns for imprecision.

[3] Very serious concerns for study limitations and imprecision.

[4] Serious concerns for study limitations and very serious concerns for imprecision.

[5] Poorly connected to the network. Only direct evidence available.

Summary of findings 12. Summary of findings (QT prolongation)

HARM

Patient or population: adults undergoing any type of surgery under general anaesthesia

Interventions: antiemetic drugs (monoprophylaxis and combination prophylaxis)*

Comparator (reference): placebo (or no treatment)

Outcome: QT prolongation within 7 days postoperatively

Setting: inpatient and outpatient

Total studies: 18 RCTs **Total participants: 4440** **Number of treatments: 13** **Geometry of the network****	**Relative effect*** (95% CI)**	**Anticipated absolute effect **** (95% CI)**			**Certainty of evidence**	**Ranking ***** (P score)**	**Interpretation of findings**
		Without intervention	With intervention	Difference			
5-HT3 receptor antagonists							
Dolasetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Granisetron (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Ondansetron (1 RCT; 60 participants)	**0.93** (0.18 to 4.76)	21 per 1000[1]	20 per 1000	1 fewer per 1000	⊕⊕⊖⊖ **Low**	**Rank 5** (0.4773)	**Ondansetron may have no or minimal effect on QT prolongation**

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				(17 fewer to 79 more)	Due to imprecision[2]	Rank 4 of 8 single drugs	
Palonosetron (1 RCT; 546 participants)	**0.16** (0.02 to 1.39)	21 per 1000[1]	3 per 1000	18 fewer per 1000 (21 fewer to 8 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 1** (0.8896) Rank 1 of 8 single drugs	**We are uncertain whether palonosetron reduces QT prolongation**
Ramosetron (no direct evidence, indirect evidence only)	**0.62** (0.08 to 4.76)	21 per 1000[1]	13 per 1000	8 fewer per 1000 (19 fewer to 79 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision, incoherence[4]	**Rank 3** (0.6133) Rank 2 of 8 single drugs	**We are uncertain whether ramosetron reduces QT prolongation**
Tropisetron (1 RCT; 385 participants)	**1.01** (0.04 to 24.68)	21 per 1000[1]	21 per 1000	0 fewer/more per 1000 (20 fewer to 497 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3,5]	**Rank 8** (0.4548) Rank 5 of 8 single drugs	**We are uncertain whether tropisetron has no or minimal effect on QT prolongation**
D2 receptor antagonists							
Amisulpride (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Droperidol (3 RCTs; 303 participants)	**1.29** (0.71 to 2.34)	21 per 1000[1]	27 per 1000	6 more per 1000 (6 fewer to 28 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 12** (0.3348) Rank 8 of 8 single drugs	**Droperidol may increase QT prolongation**
Haloperidol (4 RCTs; 338 participants)	**0.98** (0.20 to 4.87)	21 per 1000[1]	21 per 1000	0 fewer/more per 1000 (17 fewer to 81 more)	⊕⊕⊖⊖ **Low** Due to imprecision[2]	**Rank 11** (0.4261) Rank 7 of 8 single drugs	**Haloperidol may have no or minimal effect on QT prolongation**

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Metoclopramide (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Perphenazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
NK1 receptor antagonists							
Aprepitant (nNo direct evidence, indirect evidence only)	**0.96** (0.19 to 4.92)	21 per 1000[1]	20 per 1000	1 fewer per 1000 (17 fewer to 82 more)	⊕⊖⊖⊖ **Very low** Due to imprecision, incoherence[6]	**Rank 10** (0.4264) Rank 6 of 8 single drugs	**We are uncertain whether aprepitant have no or minimal effect on QT prolongation**
Casopitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Fosaprepitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Rolapitant (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Corticosteroids							
Dexamethasone (1 RCT; 149 participants)	**0.75** (0.05 to 12.06)	21 per 1000[1]	16 per 1000	5 fewer per 1000 (20 fewer to 232 more)	⊕⊖⊖⊖ **Very low** Due to study limitations, imprecision[3]	**Rank 4** (0.5370) Rank 3 of 8 single drugs	**We are uncertain whether dexamethasone reduces QT prolongation**
Methylprednisolone (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Antihistamines							

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Dimenhydrinate (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Meclizine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Promethazine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Anticholinergics							
Scopolamine (0 RCTs; 0 participants)	**NA**	NA	NA	NA	**NA**	**NA**	**No studies were found that looked at QT prolongation**
Comparator							
Placebo	**Reference comparator**	Not estimable	Not estimable	Not estimable	**Reference comparator**	**Rank 7** (0.4552)	**Reference comparator**

NMA-SoF table definitions:

* Certainty of evidence was assessed only for single antiemetic drugs of direct interest.

** Geometry of the network is presented in Figure 28 (netgraph).

*** Network estimates are reported as risk ratio (RR) with confidence interval (CI).

**** Anticipated absolute effects. The anticipated absolute effect compares two risks by calculating the difference between the risk of the intervention group and the risk of the control group.

***** Ranking of treatments includes all single drugs and combinations of drugs and is based on the P score (a value on a continuous 0 to 1 scale), which measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Supplementary Files-11-QT prolongation). Larger P scores indicate better treatments. In addition, the rank of the treatment out of all single drugs is indicated.

GRADE working group grades of evidence (or certainty of the evidence).

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect.

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Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Explanatory footnotes:

[1] Baseline risks (assumed control risk) are based on the total events of all placebo groups included in the outcome QT prolongation. The general incidence of QT prolongation after surgery with placebo is about 2.12%.

[2] Very serious concerns for imprecision.

[3] Serious concerns for study limitations and very serious concerns for imprecision.

[4] Serious concerns for study limitations and incoherence, and very serious concerns for imprecision.

[5] Poorly connected to the network. Only direct evidence available.

[6] Very serious concerns for imprecision and serious concerns for incoherence.

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BACKGROUND

Description of the condition

Postoperative nausea and vomiting (PONV) is one of the major and most frequently observed problems anaesthetists and patients have to face after surgical procedures. In the majority of cases, PONV occurs during the first 24 hours postoperatively with a peak in the immediate postoperative hours (Apfel 2002). About 30% of all patients undergoing anaesthesia using volatile anaesthetics without prior prophylaxis are affected by PONV after surgery (Apfel 1999). In 1998, Apfel and colleagues developed a simplified score that helps to predict individual risk for the occurrence of PONV in adults. The four risk factors included are female gender, non-smoker status, history of PONV or motion sickness, and expected postoperative opioid use (Doleman 2018). Apfel suggests that the likelihood of PONV ranges from 10% (no risk factors present) to 79% (all four risk factors present) (Apfel 1999). The incidence of PONV varies with a number of other factors,including hydration status (Jewer 2019), type of anaesthetic (intravenous versus inhalational (Miller 2018)) and possibly depth of anaesthesia (Lewis 2019). The use of opioids can be avoided or minimised through the use of regional anaesthetic techniques (Weinstein 2018) or systemic, non-opioid analgesics such as lidocaine (Weibel 2018).

Rarely described but serious consequences of PONV that are usually secondary to vomiting include aspiration pneumonia, Boerhaave's syndrome, and severe subcutaneous emphysema (Attalah 2004; Baric 2000; Kranke 2011; Reddy 2008; Schumann 1999). However, PONV is itself an unpleasant and uncomfortable feeling and a burdensome side effect for patients receiving anaesthesia (Kranke 2011). It is subjectively rated to be as serious as postoperative pain and has an important influence on the quality of recovery (Hocking 2013; Kranke 2011). Moreover, PONV can lead to a prolonged or unexpected hospital stay, or even to re-admission. It also interferes with early postoperative recovery (Kranke 2011).

Description of the intervention

A large variety of antiemetic drugs—grouped into six different drug classes—are available for prevention of PONV (Gan 2007a; Gan 2014; Horn 2014; Wiesmann 2015): 5-HT_3 receptor antagonists (e.g. ondansetron, dolasetron, granisetron, tropisetron, ramosetron, palonosetron); D_2 receptor antagonists (e.g. droperidol, haloperidol, metoclopramide, perphenazine, amisulpride, alizapride, chlorpromazine, domperidone, prochlorperazine, sulpiride, trimethobenzamide); NK_1 receptor antagonists (e.g. aprepitant, casopitant, rolapitant, fosaprepitant, CP-122,721, vestipitant); corticosteroids (e.g. dexamethasone, methylprednisolone, betamethasone); antihistamines (e.g. dimenhydrinate, meclizine, promethazine, cyclizine); and anticholinergics (i.e. scopolamine).

The six different substance classes are characterized by varying adverse effects: 5-HT_3 receptor antagonists (e.g. headache, constipation), D_2 receptor antagonists (e.g. extrapyramidal symptoms, sedation, arrhythmia, QT prolongation), corticosteroids (e.g. hyperglycaemia, immunosuppression, wound healing deficits), antihistamines (e.g. drowsiness, xerostomia, urinary tract difficulties), and anticholinergics (e.g. dry mouth, visual disturbances) (Gan 2014; Horn 2014; Wiesmann 2015). Currently limited evidence is available on adverse effects arising from NK_1 receptor antagonists. However, increased dizziness or headache was described by individual studies (Diemunsch 2009).

Drugs with different mechanisms of action should be used in combination to optimize efficacy (Gan 2007b). For example, the 5-HT_3 antagonists, which have better anti-vomiting than anti-nausea efficacy (although associated with headache), can be used in combination with droperidol, which has greater anti-nausea efficacy and a protective effect against headache (Gan 2007b).

In addition to drugs with direct antiemetic action, several other strategies for PONV prophylaxis are available such as use of drugs with indirect opioid-sparing effects (e.g. gabapentin; Grant 2016), or strategies such as reducing the emetic potency of the anaesthesia itself (e.g. by using propofol; Apfel 2004), or non-pharmacologic prophylaxis strategies (e.g. stimulation of the wrist acupuncture point PC6; Lee 2015). These strategies are not within the focus of the current review.

Gan 2014 in its 'Consensus guidelines for the management of postoperative nausea and vomiting' provides information about current options for prevention and treatment of PONV including both pharmacologic and non-pharmacologic regimens comprising the most commonly used antiemetic drugs, doses, and timing of application. With adequate prophylaxis, one antiemetic agent can reduce the likelihood (relative reduction) of PONV by 25% (Gan 2014). This evidence-based guideline currently recommends one to two interventions for PONV prophylaxis for patients at moderate risk (Gan 2014).

It is important to provide adequate prophylaxis with regard to the type and time of application. Intravenous or parenteral application of antiemetics in accordance with their pharmacokinetic profile may be appropriate for mitigating the risk of the varying duration of surgery and the need for a reasonably effective drug level at the 'time of risk' in the postoperative setting. A large majority of antiemetic drugs are usually administered by a slow intravenous push or as an infusion administered over a short time. Although some 'alternative' therapies are available (e.g. aromatherapy (Hines 2018)), this review does not include such substances.

How the intervention might work

Five of the six substance classes with direct antiemetic effects differ mostly in their antagonistic action against different emetogenic substances at specific receptors, for example, in the area postrema or on the free nerve endings of the vagus nerve (Gan 2007a; Gan 2014; Horn 2014; Wiesmann 2015).

- 5-HT_3 receptor antagonists: high levels of the neurotransmitter serotonin (5-hydroxytryptamine, 5-HT) induce nausea and vomiting by activating specific receptors in the gut and central nervous system. Drugs belonging to this substance class inhibit serotonin receptors centrally and peripherally.
- D_2 receptor antagonists: dopamine antagonists work as antiemetics in small dosages by blocking central dopamine receptors.
- NK_1 receptor antagonists: the neurotransmitter substance P binds to the neurokinin 1-receptor in the area postrema and thereby induces nausea and vomiting. NK_1 receptor antagonists block these receptors and inhibit this pathway.
- Antihistamines (histamine 1 receptor antagonists): the tissue hormone histamine induces nausea and vomiting

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by activating central H_1-receptors. Antihistamines for PONV prevention predominantly block these receptors but also have anticholinergic effects.

- Anticholinergics: anticholinergic agents have a parasympatholytic effect by inhibiting binding between the neurotransmitter acetylcholine and the muscarinic receptor centrally.

A sixth group of antiemetics with direct antiemetic effects consists of corticosteroids. It is not known with any certainty how corticosteroids exert their antiemetic effects. Some theories assume that the anti-inflammatory impact and the decrease in arachidonic acid release reduce the occurrence of PONV.

Why it is important to do this review

Preventing PONV is important for the well-being of patients and is a major factor influencing patients' satisfaction with anaesthesia. It is therefore important for patients to be provided with sufficient antiemetic prophylaxis. PONV is also a major contributor to direct and indirect healthcare costs (Eberhart 2014; Hirsch 1994). Amongst others, these include costs for prolonged stays in recovery rooms and costs of extra nursing time (Hirsch 1994; Smith 2012). In times when healthcare resources are scarce and the healthcare workforce is decreasing, the correct prophylaxis offers an advantage. Many antiemetics have proven efficacy for clinical use. Unfortunately, the use of prophylactic antiemetics for patients at risk is not part of the daily routine of all anaesthetists due to inadequate implementation of the risk-adapted approach in some clinical departments (Franck 2010). Moreover, risk–benefit issues remain a topic of debate in the anaesthesia community, and the fear of possible adverse effects (Weibel 2018) may be another reason for restraint (Kranke 2011).

Many studies have investigated not only monotherapies but also combinations of antiemetics to reduce the likelihood of developing PONV. Trials examining different doses or dose ranges of one or more drugs administered in various ways (intravenous, intramuscular, oral, or transdermal) create a wide spectrum of information that is difficult to assess by simple direct comparisons.

In 2006, Carlisle and Stevenson performed a systematic review that assessed all available drugs with antiemetic action for preventing PONV in adults and children in terms of efficacy and side effects. This review included more than 700 studies with over 100,000 participants (Carlisle 2006a). All trials reporting PONV as an outcome and comparing a drug with placebo, no treatment, or another drug, or comparing different dosing or timing of administration, were included. This review contained a large number of direct comparisons, as no restrictions regarding study population or type of intervention were defined.

Tricco and colleagues published a systematic review with network meta-analysis (NMA) of the efficacy and safety of serotonin receptor antagonists compared to each other, compared to placebo, and in combination with other antiemetic agents for PONV prevention (Tricco 2015a; Tricco 2015b). However, these review authors examined no other substance classes.

Despite the continuing flow of clinical trials on PONV prophylaxis, there is still no current overview of all relevant substance classes. There is a shortage of direct comparisons of frequently used antiemetics, and a clinically useful ranking of all antiemetic drugs with respect to both efficacy and safety is lacking. The Carlisle review of PONV needs to be updated (Carlisle 2006a). However, the original review was withdrawn in 2017, in part because several studies that had been included were retracted since publication (Carlisle 2017). Another reason for withdrawal was that the literature is now so large and complex that a very large series of direct comparisons—as performed in the Carlisle review of PONV—would create an overwhelmingly burdensome task and would be very difficult to comprehend. Therefore, a new and more efficient approach was needed to allow readers to appreciate readily the best-quality evidence available. For the current review, we performed an NMA that allows comparison of antiemetic drugs in a direct and indirect manner (see Methods). The aim of this review is to generate a clinically useful ranking of antiemetic drugs (monotherapy and combination prophylaxis). This review also seeks to provide clear information for patients and physicians to guide clinical decisions that enhance treatment efficacy and reduce the occurrence of side effects. To enhance the feasibility, we made a pre hoc decision to focus on the six clinically relevant drug classes with direct antiemetic action currently used or under investigation. Drugs such as gabapentin, which exert an antiemetic effect in an indirect way via an opioid-sparing effect (Grant 2016), as well as non-pharmacologic interventions (Lee 2015), are not within the scope of this review. This systematic review is deliberately designed to address some of the questions raised by the current PONV guideline (Gan 2014), with the aim of providing an evidence-based basis for future updates to this guideline.

OBJECTIVES

- To compare the efficacy and safety of different prophylactic pharmacologic interventions (antiemetic drugs) against no treatment, against placebo, or against each other (as monotherapy or combination prophylaxis) for prevention of postoperative nausea and vomiting in adults undergoing any type of surgery under general anaesthesia
- To generate a clinically useful ranking of antiemetic drugs (monotherapy and combination prophylaxis) based on efficacy and safety
- To identify the best dose or dose range of antiemetic drugs in terms of efficacy and safety

METHODS

Criteria for considering studies for this review

Types of studies

In this review, we included randomized controlled trials (RCTs) that compare one or more antiemetics for prevention of PONV against no treatment, placebo, or another antiemetic drug. We excluded quasi-randomized trials (i.e. trials in which treatment allocation is achieved by date of birth, alternation, or similar predictable methods), cluster-randomized trials, and cross-over studies.

We included trials in which allocation to treatment may not have been adequately concealed, but we considered trial methodological quality in data analyses and interpretation.

We did not restrict inclusion of studies based on language of publication.

Retracted studies and studies authored by Fujii and colleagues were not included in the review (Kranke 2000; Tramer 2013).

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Eligible studies must have been reported as full-text journal publications or comprehensive study reports. Because we expected to identify more than 1000 full-text studies, we excluded studies published in abstract form only to reduce the workload and to enhance the feasibility of completing the review in a reasonable time frame.

Types of participants

We included only trials that analysed adult participants (i.e. the majority of participants over 18 years of age) undergoing any type of surgery under general anaesthesia. We did not include studies using regional or sedative anaesthetic techniques.

Types of interventions

We included studies that compared any pharmacologic intervention(s) with antiemetic action belonging to one of the following drug classes versus each other or versus no treatment, or versus placebo.

- 5-HT_3 receptor antagonists.
- D_2 receptor antagonists.
- NK_1 receptor antagonists.
- Corticosteroids.
- Antihistamines (histamine 1 receptor antagonists).
- Anticholinergics.

For future updates, we may include emerging drugs from other drug classes if it has been demonstrated that they exert a direct antiemetic action.

We also included trials that analysed combinations of antiemetic drugs, whereby each combination represents a separate intervention of interest and therefore a separate node in the NMA (splitting). In the run-up to the NMA, we assessed the geometry of the network (all interventions (monotherapy and combination prophylaxis) versus monoprophylaxis alone). We aimed to examine all possible combination prophylaxis treatments in cases where the geometry of the network allowed this holistic approach. All networks in the current review were well connected.

Different doses of drugs were combined into one node (lumping). Dose effects were analysed in subgroup analyses, especially in cases of heterogeneity or inconsistency.

Not all eligible interventions from the various drug classes were of direct (primary) interest. All drugs of direct interest for the review with highest clinical relevance are listed in the section "Interventions of direct interest". Eligible interventions not of direct interest were included in the network to increase the amount of available (indirect) information in the analysis (see "Inclusion of additional interventions to supplement the analysis") (Ades 2013; Protocol Template 2014).

For inclusion, the antiemetic drug(s) had to have been administered before the onset of PONV. These drug(s) could have been given preoperatively, at induction of anaesthesia, or during anaesthesia.

Participants in all treatment arms within a study must have been subject to the same anaesthesia regimen with comparable dosing because the anaesthesia management itself may have an influence on the incidence of PONV. For studies that reported results separately for varying baseline anaesthesia regimens, the different regimens were not combined but were considered as sub-studies.

We assumed that, in principle, any participant meeting the inclusion criteria could be selected at random for one of the eligible interventions.

Interventions of direct interest

Antiemetic drugs of direct interest in the current review include those recommended in the "Consensus guidelines for the management of postoperative nausea and vomiting" (Gan 2014), as well as promising and emerging substances such as fosaprepitant and amisulpride. We planned to consider any other drug as an 'intervention of direct interest' if it was investigated in more than two studies with more than 400 participants and was published in the last five years before the search date (2017). In the current review, none of the antiemetics not currently listed in the "Interventions of direct interest" section fulfilled these criteria. Therefore, all other drugs were analysed as 'additional interventions to supplement the analysis'. The current review includes the following 'interventions of direct interest'.

- 5-HT_3 receptor antagonists: dolasetron (dola), granisetron (gran), ondansetron (onda), palonosetron (palo), ramosetron (ramo), and tropisetron (trop).
- D_2 receptor antagonists: amisulpride (amis), droperidol (drop), haloperidol (halo), metoclopramide (meto), and perphenazine (perp).
- NK_1 receptor antagonists: aprepitant (apre), casopitant (caso), fosaprepitant (fosa), and rolapitant (rola).
- Corticosteroids: dexamethasone (dexa) and methylprednisolone (meth).
- Antihistamines (histamine 1 receptor antagonists): dimenhydrinate (dime), meclizine (mecl), and promethazine (prom).
- Anticholinergics: scopolamine (scop).

We restricted all exploratory analyses and assessment of the certainty of evidence to the 'interventions of direct interest' and reported the findings in detail in this review.

Additional interventions to supplement the analysis

Eligible interventions not of direct interest were included in the network to increase the amount of available information included in the analysis. The following antiemetic drugs were considered as 'additional interventions to supplement the analysis'.

- 5-HT_3 receptor antagonists: azasetron (aza).
- D_2 receptor antagonists: alizapride (aliz), buspirone (busp), chlorpromazine (chlo), domperidone (domp), levomepromazine (levo), olanzapine (olan), prochlorperazine (proc), sulpiride (sulp), thiethylperazine (thie), and trimethobenzamide (trim).
- NK_1 receptor antagonists: CP-122,721 (cp12) and vestipitant (vest).
- Corticosteroids: betamethasone (beta) and prednisolone (pred).
- Antihistamines (histamine 1 receptor antagonists): benzquinamide (benz), cetrizine (cetr), cyclizine (cycl), dixyrazine (dixy), and doxylamine/diclectin (doxy).

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- Anticholinergics: diphenidol (diph), oxybutynin (oxyb), and penehyclidine (pene).

Types of outcome measures

Studies must have reported at least one of the following primary or secondary outcomes to be fully eligible for and to be included in the review. Reporting of outcomes of interest was an essential eligibility criterion to enhance the feasibility of the review workload.

Primary outcomes

We estimated the relative effects of competing interventions according to the following primary outcomes.

- Vomiting (or dry retching) within 24 hours: number of participants with events within 0 to 24 hours (± 6 hours) postoperatively.
- Serious adverse events (SAEs): number of participants with at least one SAE (as defined in the study) in the observation period (up to seven days).
- Any adverse event (AE): number of participants with at least one AE (as defined in the study) in the observation period (up to seven days).

Secondary outcomes

We estimated the relative effects of competing interventions according to the following secondary outcomes.

Substance class-specific side effects

- Headache: number of participants with headache in the observation period (up to seven days)
- Sedation/drowsiness: number of participants with sedation/drowsiness in the observation period (up to seven days)
- Extrapyramidal symptoms: number of participants with extrapyramidal symptoms (e.g. dystonia, dyskinesia, akathisia, bradykinesia, tremor) in the observation period (up to seven days)
- Constipation: number of participants with constipation in the observation period (up to seven days)
- Postoperative wound infection: number of participants with postoperative wound infection in the observation period (up to seven days)
- Arrhythmia: number of participants with an arrhythmia (as defined by triallists) in the observation period (up to seven days)
- Visual disturbances: number of participants with visual disturbances (e.g. blurred vision) in the observation period (up to seven days)
- QT prolongation: number of participants with a QT prolongation (as defined by triallists) in the observation period (up to seven days)

Other secondary outcomes

- Mortality: number of participants who have died in the observation period (up to seven days)
- Early postoperative vomiting (or dry retching): number of participants with events within an observation period starting immediately after anaesthesia and ending two to six hours later (or defined as occurring in the postanaesthesia care unit (PACU))
- Late postoperative vomiting (or dry retching): number of participants with events within an observation period within the range of two to 24 hours postoperatively. If studies have recorded the outcome during different periods of the two to 24 hour postoperative period but have not reported the risk for the complete observation period (two to 24 hours), we reported the risk of the outcome once for each study using the risk for the period in which the outcome was most common (all groups combined)
- Nausea within 24 hours postoperatively (0 to 24 hours ± 6 hours): studies that have reported the combined endpoint PONV only (and not nausea separately) were considered as nausea. We did not include in the analysis continuous data on nausea (such as grades of nausea measured on appropriate scales)
- Complete response: number of participants without vomiting, nausea, or any need for rescue treatment within 24 hours postoperatively

Search methods for identification of studies

We searched for all kinds of comparisons involving the research question.

Electronic searches

We identified RCTs through literature searching designed to identify relevant trials, as outlined in Chapter 4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2019). We did not apply language restrictions.

We searched the following databases for relevant trials (first search 2017 November 6, update search 2020 April 23).

- Cochrane Central Register of Controlled Trials (CENTRAL; 2020, Issue 4).
- MEDLINE (Ovid SP, 1946 to 2020 April 20).
- Embase (Ovid SP, 1974 to 2020 April 20).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO host (1982 to 2020 April 20).

We developed a draft search strategy for MEDLINE, which we used as the basis for the search strategies applied in the other databases listed. These search strategies can be found in Appendix 1.
We scanned the following trials registries for study reports and protocols, and for ongoing and unpublished trials.

- ClinicalTrials.gov (2 November 2017).
- World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (3 November 2017).

In the updated search in 2020, the study registries were not searched. Records of the ClinicalTrial.gov and WHO ICTRP databases were systematically added to CENTRAL, starting in August 2017 and April 2019. These records are therefore covered in the updated CENTRAL search. The WHO ICTRP trial register was closed at the date of the update search because of COVID-19. Therefore, the WHO ICTRP search is currently not complete.

All included trials have been checked against the Retraction Watch database (November 2018).

Searching other resources

We scanned the reference lists of relevant systematic reviews for additional trials (Carlisle 2006a; De Oliveira 2013; Liu 2015; Tricco 2015a; Tricco 2015b).

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Data collection and analysis

Selection of studies

We used Covidence, a web-based software platform (Covidence), for the process of study selection. All records identified by the search strategy described above were imported into Covidence. The following review authors participated in the screening of records: SW, DM, MR, HH, AH, PKr, IB, DR, LE, MS, and TS. In each case, two of them independently screened the title and abstract of an individual record for eligibility using a pre-defined eligibility checklist (Appendix 2). For all potentially relevant records, we retrieved the full texts before making the final decision about which studies satisfied the inclusion criteria. When necessary, we contacted trial authors for missing information (18 requests sent to authors; none answered). All full texts were reviewed by two independent review authors. We resolved any discrepancies in judgement by discussion with a third review author (SW, PKr).

Data extraction and management

Two independent review authors extracted the data using a pre-defined data extraction form in the Covidence environment (Appendix 3; Covidence). Extracted data included data on outcomes and potential effect modifiers, along with other data. The following review authors participated in data extraction: SW, DM, MR, HH, AH, PKr, IB, DR, LE, and MS. A third review author (SW) checked all data extraction forms and resolved any discrepancies. When necessary, we contacted trial authors to request missing information (17 requests sent to authors; seven provided data). We exported data from Covidence into Review Manager software and Excel spreadsheets, and we checked them for accuracy (SW, OJ) (Review Manager 2014).

Basic study characteristics

We extracted from each included study data on the following additional information.

- Identification (year of publication; journal; first author (with contact information); location of study conduct; number of centres; duration of study; and trial registry number).
- Methods (study design and groups).
- Population details (inclusion and exclusion criteria with group differences; and participant flow (number of participants assessed for eligibility, number randomized, number that received treatment, and number analysed)).
- Prognostic variables (population and baseline characteristics, risk factors for PONV: gender; smoking status; history of PONV/motion sickness; type of surgery; type of anaesthesia; duration of anaesthesia; and use of perioperative opioids).

Outcome data

We extracted from each included study all data relevant to the primary and secondary outcomes listed in the section Types of outcome measures.

We extracted the following characteristics associated with monitoring and reporting of (severe) adverse events in each primary study.

- Type of monitoring for SAEs/AEs (active or passive).
- Types of AEs (defined AEs or any AEs).
- Use of an accepted international classification for SAEs (e.g. according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines).
- Number of SAEs reported (yes or no).

Data on potential effect modifiers

From each included study, we extracted data on the following potential effect modifiers.

- Intervention (dose; time point of administration (early versus late (after incision)); and route of administration).
- Risk of bias (sequence generation; blinding of participant, personnel, and outcome assessors; and incomplete outcome data).
- Funding source (sponsorship source and involvement).

Assessment of risk of bias in included studies

We assessed the risk of bias for each included study by using the Cochrane 'Risk of bias' assessment tool 1.0 (Higgins 2011). Standard items include random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and any other bias. We judged each item as being at 'low risk of bias', 'high risk of bias', or 'unclear risk of bias'. We included a 'Risk of bias' table as part of the Characteristics of included studies table and the 'Risk of bias summary'/'Risk of bias graph' figures, which detailed all of the judgements made for all studies included in the review.

We also assessed the characteristics associated with monitoring and reporting of severe and any adverse events in each primary study and reported this information in an additional table—"Assessment of adverse event monitoring"—along with a judgement on the risk of bias as described by Tramacere and colleagues (Tramacere 2015).

Two review authors independently performed study quality assessment using a pre-defined critical appraisal form in the Covidence environment (Appendix 4). We resolved any disagreements by discussion with a third review author (SW).

Random sequence generation

We considered sequence generation as adequate if it was generated by a random system (i.e. a computer, a random number table algorithm, or tossing of a coin). We considered sequence generation inadequate if a non-random system was used (i.e. names or dates). We excluded quasi-randomized trials. We assessed the study as having 'unclear risk of bias' if the only information on randomization was a statement that the study was randomized.

Allocation concealment

We considered concealment adequate if an acceptable method was used to ensure that group assignment was not revealed to patient recruiters, investigators, or participants before final allocation into the respective group. Acceptable methods included a central allocation system, sequentially numbered sealed opaque envelopes (SNOSEs), or an on-site locked computer. We considered concealment to be inadequate if it allowed patient recruiters, investigators, or participants to know the treatment allocation in advance. We assessed the study as having 'unclear risk of bias' if

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the concealment procedure was not reported or was not sufficiently reported.

Blinding of participants and personnel outcome assessors

We considered blinding adequate if all participants and personnel (e.g. anaesthetists) were blinded to the intervention. We considered blinding inadequate if participants and personnel were not blinded to the intervention. We assessed the study as having 'unclear risk of bias' if study authors stated only that the study was blinded and if it remained unclear who was blinded.

Blinding of outcome assessors

We considered blinding adequate if all outcome assessors were blinded to the intervention. We considered blinding inadequate if outcome assessors were not blinded to the intervention. We assessed the study as having 'unclear risk of bias' if study authors stated only that the study was blinded and if it remained unclear who was blinded.

Incomplete outcome data

We considered the domain 'incomplete outcome data' as adequate if the number of dropouts was 15% or less and was balanced between arms, and if the reasons for dropout were reported and appeared to be unrelated to the studied outcomes. We considered outcome data as incomplete if the number of dropouts was greater than 15% or was significantly imbalanced between groups, or if the reasons for dropout were not reported or appeared to be related to outcomes of interest in the study. We assessed the study as having 'unclear risk of bias' if details on the number of dropouts and reasons for dropout were not sufficiently reported.

Selective outcome reporting

We assessed selective outcome reporting by comparing the type and order of outcomes (primary versus secondary) reported in the study protocol, along with the published outcomes. We considered outcome reporting as adequate if a prospectively registered study protocol was available, and if all primary and secondary outcomes were also reported in the published study as prespecified in the protocol. We judged selective outcome reporting as having 'high risk of bias' if the pre-defined primary outcomes in the registered protocol differed from those in the published study report. If no prospectively registered study protocol was available, we assessed selective outcome reporting as having 'unclear risk of bias'.

Other sources of bias

Other potential risks of bias included baseline imbalance in population characteristics and risk factors for PONV (prognostic variables) within studies that are strongly related to outcome measures and therefore may cause bias in the intervention effect estimate. An imbalance was defined as either a 20% difference between groups or $P < 0.05$ for a difference between two groups, if reported in the study. We assessed the study as having 'unclear risk of other bias' if details on baseline characteristics or risk factors for PONV were not sufficiently reported.

Overall risk of bias summary

We summarized the risk of bias for each study by referring to judgements for the most important domains 'sequence generation', 'blinding of participant, personnel, and outcome assessors', and 'incomplete outcome data'. We did not include in the overall risk of bias summary the domains 'allocation concealment' (for explanation, see Differences between protocol and review), 'selective outcome reporting', and 'other sources of bias'. The review included studies published over a time span of 50 years, and judgements on the domains 'selective outcome reporting' and 'other sources of bias' strongly depend on the year the study was conducted. Older studies (before 2000) were not registered in trial registries, and risk factors for PONV were not specified at older dates. We performed sensitivity analyses with information from the domain 'other sources of bias'.

We classified each study as having 'low risk of overall bias' when we judged all relevant domains as having 'low risk of bias'. If we judged at least one domain as having 'high risk of bias' or all domains as having 'unclear risk of bias', we classified overall risk of bias for the study as 'high risk of overall bias'. In the remaining cases, we classified the study as having 'unclear risk of overall bias'. We used information from the 'overall risk of bias summary' when performing sensitivity analyses.

Assessment of adverse event monitoring

The way of monitoring adverse events may introduce bias to the relevant adverse outcomes. Therefore, we assessed the risk of bias associated with monitoring for adverse events. We evaluated the methods of monitoring for adverse events in each primary study on the basis of the following questions as described by Tramacere and colleagues with some modifications (Tramacere 2015).

- Any AE.
  - Did the authors pro-actively monitor for any AE?
  - Did the authors simply provide spontaneous reporting (passively) of AEs by participants?
  - Did the authors report all relevant (class-specific) AEs?
- SAEs.
  - Did the authors define SAEs according to an accepted international classification?

We did not include this information in the 'Risk of bias' table. We reported this information in an additional table 'Monitoring and reporting of any (severe) adverse events', along with a judgement of the risk of bias (Tramacere 2015).

We used information from the assessment of adverse event monitoring to test the robustness of effect estimates for the primary outcomes 'SAEs' and 'any AE' by sensitivity analyses (exclusion of 'high and unclear risk of bias' studies for adverse event monitoring).

Review of network geometry

We graphically evaluated the geometry of the whole network including interventions of direct interest (monotherapy and combination prophylaxis) and any other intervention in which we were not directly interested (see 'Additional interventions to supplement the analysis') using the function netgraph of the R package netmeta (Rücker 2016; netmeta). We used the information from the network geometry to determine whether a network meta-analysis was feasible for all interventions or only for sub-networks (e.g. monoprophylaxis). The network is laid out in the plane as a circle, where the nodes in the graph layout correspond to the treatments and edges display the observed (direct) treatment comparisons. The thickness of the edges is proportionate to the number of included studies comparing two treatments.

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Measures of treatment effect

Relative treatment effects

We estimated the pair-wise relative treatment effects of competing interventions using the risk ratio (RR) with 95% confidence intervals (95% CIs) for each outcome.

Results from network meta-analyses were presented as summary relative effects (RR) for each possible pair of treatments.

Relative treatment ranking

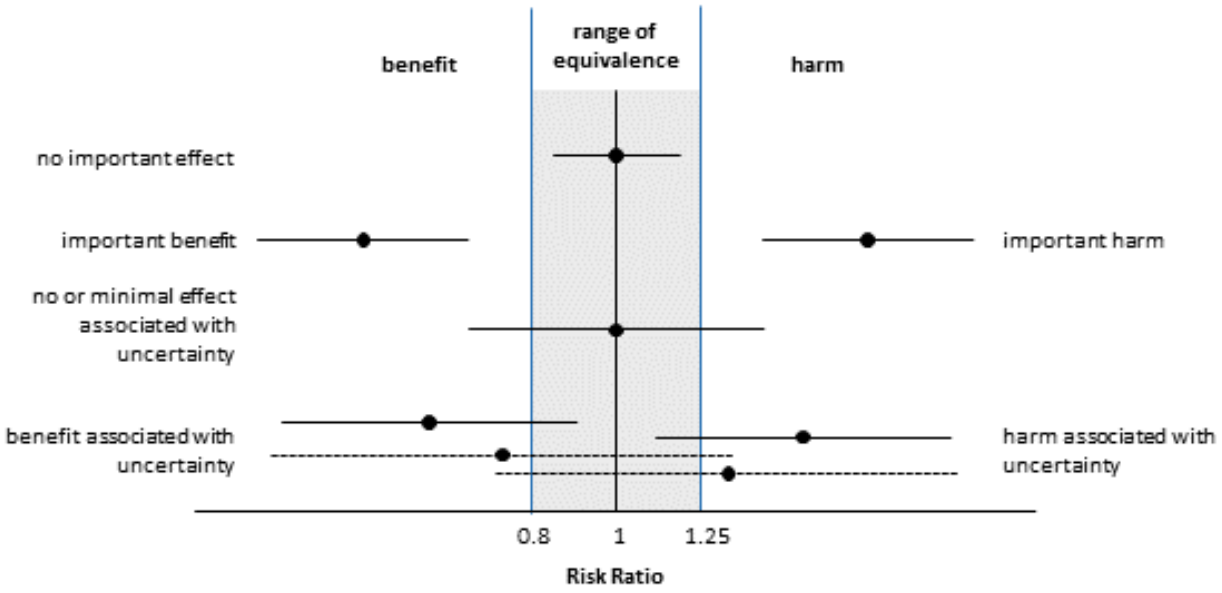
We ranked competing treatments by P scores (Rücker 2015), using the function netrank of the R package netmeta (netmeta). We used this method to measure the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Rücker 2015). P scores should not be confused with P values. P scores are the frequentist analogue and are numerically similar to Bayesian surface under the cumulative ranking curve (SUCRA) values (Rücker 2015). P scores are ranking numbers between 0 and 1 that are derived from the P values of all pair-wise comparisons. Treatments are ranked from best to worst according to decreasing P scores for all outcomes with the exception of complete response (increasing P scores).

We looked at comparative efficacies between antiemetic drugs and expressed this finding using placebo as the reference intervention and presented the results in forest plots. We ranked treatment effects in forest plots according to P scores in decreasing order (the most effective intervention is presented at the top).

Size of effects

We used clinically relevant size of effects rather than statistical significance to describe network meta-analysis estimates (Nikolakopoulou 2019 Wasserstein 2019). For efficacy outcomes such as prevention of vomiting or nausea, we defined the clinically important size of benefit as RR of 0.80 and the reciprocal as clinically important harm (RR 1.25). Effects lower than 0.80 and larger than 1.25 were considered to be clinically important. The range between 0.8 and 1.25 was termed the 'range of equivalence', which included unimportant treatment effects (Nikolakopoulou 2019). The relative position of the point estimates indicated the direction of the effect as 'benefit', 'no or minimal effect', or 'harm' (Figure 1). The extent of the 95% CI indicated the certainty of the estimated effect as 'important' or as 'associated with uncertainty' (Figure 1).

Figure 1. Magnitude-based inferences to describe effect estimates, CIs, and clinical relevance for efficacy outcomes. The range of equivalence is defined as a risk ratio of 0.8 to 1.25.



For safety outcomes such as any SAE, any AE, and all class-specific side effects, we defined the clinically important size of benefit as RR of 0.90 and the reciprocal as clinically important harm (RR 1.11) with a 'range of equivalence' of 0.9 to 1.11 (Figure 2). Effects lower than 0.90 and larger than 1.11 were considered to be clinically important.

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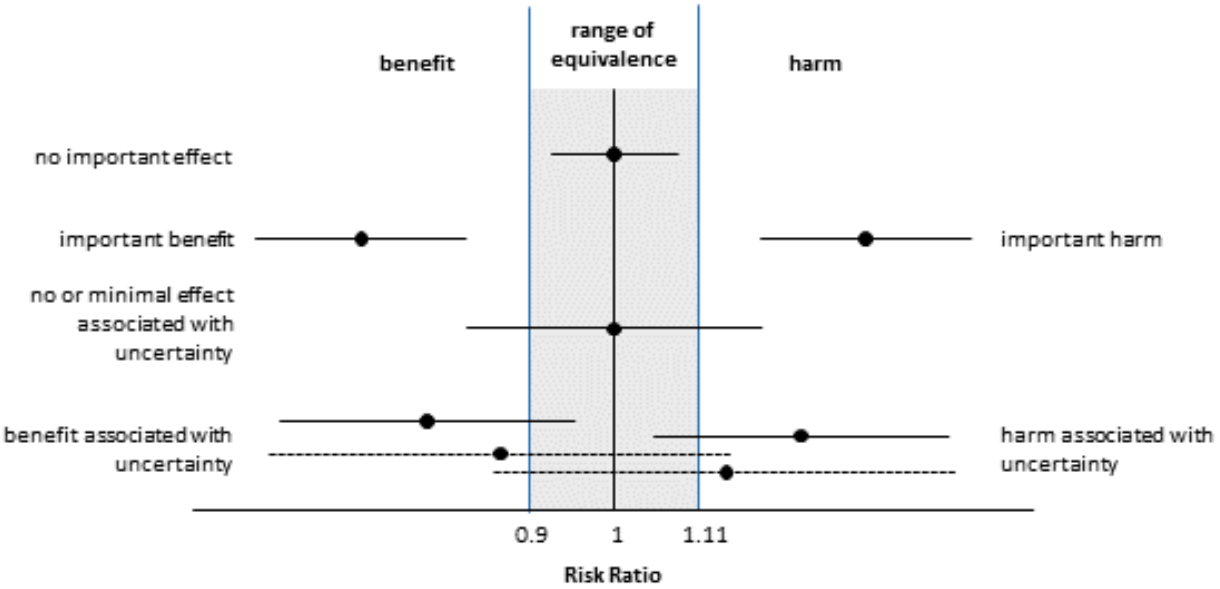
Figure 2. Magnitude-based inferences to describe effect estimates, CIs, and clinical relevance for safety outcomes. The range of equivalence is defined as a risk ratio of 0.9 to 1.11.



The 'range of equivalence' is presented in all forest plots and is indicated by blue border lines crossing RR 0.8/0.9 and RR 1.25/1.11 (efficacy/safety outcomes). We used the function forest of the R package netmeta version 1.0-1 for analysis and for visualization of the 'range of equivalence' (netmeta; Rücker 2019).

Unit of analysis issues

Cluster-randomized trials

We did not include cluster-randomized trials.

Cross-over trials

We did not include trials with cross-over design.

Studies with multiple treatment groups

We included multi-arm studies in the data set as a series of two-arm comparisons. To reflect the fact that comparisons within multi-arm studies are correlated, we adjusted the standard error of each two-arm comparison from a multi-arm study. We used the method proposed by Rücker and Schwarzer, which uses back-calculated standard errors in the weighted least-square estimator to reflect the within-study correlation (Rücker 2012; Rücker 2014; Rücker 2015).

Studies with zero events

We included in the analysis studies with zero events in one or more arms. We applied the constant continuity correction approach (continuity correction 0.5) as described by Sweeting 2004, using the R package netmeta version 1.0-1 for analysis (netmeta).

Dealing with missing data

We noted levels of attrition for included studies in the 'Risk of bias' table as part of the Characteristics of included studies. We did not request from trial authors missing participant outcome data to reduce the workload and to enhance the feasibility of the review being completed in a reasonable time frame.

We carried out analyses for efficacy outcomes, as far as possible, on an intention-to-treat (ITT) basis. For the analysis of safety, we carried out as-treated analysis as far as possible (and we were ready to accept if the randomization was broken).

In cases of missing data, we used an 'available-case analysis' by excluding from the analysis all participants for whom the outcome is missing.

Assessment of heterogeneity

Assessment of clinical and methodological heterogeneity within treatment comparisons

We planned to use descriptive statistics of parameters reported in the Characteristics of included studies table to assess whether the studies within each pair-wise comparison are homogenous enough with respect to potential effect modifiers (such as risk of bias, intervention details, and funding source), so that the assumption of homogeneity might be plausible. For the effect modifiers 'risk of bias' and 'dose of intervention', we accepted heterogeneity (see inclusion criteria of this review) and assessed the impact of these effect modifiers via sensitivity analysis for 'risk of bias' and subgroup analysis for 'dose of intervention'. Due to the quantity of data and the lack of information for the effect modifier 'funding source' in many studies, an objective and reliable assessment of the distribution of this effect modifier within all comparisons was not possible. In general, we assumed that for all included studies, the study populations, interventions, outcomes, and study settings matched the inclusion criteria of the current systematic review.

Assessment of transitivity across treatment comparisons

We planned to assess the assumption of transitivity by comparing the distribution of potential effect modifiers (see Appendix 3: 'Potential effect modifiers') across the different pair-wise comparisons. In the case of intransitivity (e.g. substantially imbalanced distribution of effect modifiers among comparisons),

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we planned to not perform NMA. For the effect modifiers 'risk of bias' and 'dose of intervention', we accepted differences in the distribution of these effect modifiers across treatment comparisons (see inclusion criteria of this review) and assessed the impact of these effect modifiers via sensitivity analysis for 'risk of bias' and subgroup analysis for 'dose of intervention'. Due to the quantity of data and the lack of information for the effect modifier 'funding source' in many studies, an objective and reliable assessment of the distribution of this effect modifier within all comparisons was not possible. In general, we assumed that for all included studies, the study populations, interventions, outcomes, and study settings matched the inclusion criteria of the current systematic review.

Assessment of reporting biases

When we identified 10 or more relevant studies, we investigated risk of bias across studies (such as publication bias) in pair-wise meta-analyses ('Interventions of direct interest', primary outcomes) using funnel plots. If funnel plot asymmetry was suggested by a visual assessment, we performed exploratory analyses (e.g. Rücker's arcsine test for dichotomous data, contour-enhanced funnel plots, trim and fill sensitivity analyses) to further investigate funnel plot asymmetry. We analysed reporting bias using the R package meta version 4.9-7 (meta).

Data synthesis

We used standard pair-wise meta-analysis and NMA for synthesizing information from numerous studies addressing the same outcomes but involving different interventions.

Methods for pair-wise meta-analyses and network meta-analyses

We performed standard pair-wise meta-analyses for all primary outcomes and substance class-specific side effects using a random-effects model (inverse variance weighting) in RevMan for each treatment comparison (drugs of primary interest versus placebo) with at least two studies. We reported the results in the Data and analyses section. We did not report the results in the Effects of interventions section to reduce the amount of information presented.

For NMAs, we used a frequentist approach based on the graph-theoretical method of Rücker et al (Rücker 2012). We performed random-effects NMAs for all outcomes in R using the package netmeta version 1.0-1 (netmeta; Rücker 2014). We separated mixed treatment evidence into direct and indirect evidence using the function netsplit from this package.

We reported all NMA, direct, and indirect estimates of all outcomes in supplementary files to reduce the amount of information provided in the text. In the Effects of interventions section, we presented only the following selection of NMA estimates of the primary analyses on the outcome level. First, we summarized the range of NMA effects for both drug combinations and single drugs with important clinical effects. Second, we summarized the range of NMA effects of all drug combinations and all single drugs (independent of the direction of effects). In the range of effects, we specified the most effective and the least effective drug or drug combination.

Methods for analysing additive effects of drug combinations

The primary NMA treated all single drugs and all combination prophylaxes as different nodes in the network. We performed a second analysis based on the assumption that the effects of combined treatments (e.g. A + B, A + B + C, B + C) are additive sums of their components. This assumption, together with the network structure, leads to a statistical model that allows decomposing the observed relative effects into the single components and estimating the effects of the components. The hypothesis of additivity can be tested by comparing estimates from this model with those from the primary analysis (Mills 2012). We used the function netcomb of the R package netmeta version 1.0-1 for analysis (netmeta; Rücker 2019).

Subgroup analysis and investigation of heterogeneity

Assessment of statistical heterogeneity

Assumptions when estimating the heterogeneity

In NMA, we assumed the same heterogeneity across the different comparisons. In standard pair-wise meta-analyses, we assumed the common heterogeneity variance estimated from the NMA for each pair-wise comparison.

Measures and tests for heterogeneity

We assessed heterogeneity by the common between-trial variance measure (tau^2), the Q-statistics, the I^2 statistic, and the 95% prediction interval (95% PI). The 95% PI shows where the true effect of a new study similar to the existing studies is expected to lie (Riley 2011). For interpretation of heterogeneity, we compared the 95% PI and the 95% CI of the NMA treatment estimate with respect to the range of clinically relevant effect sizes and the range of equivalence.

Assessment of statistical inconsistency (incoherence)

Inconsistency (incoherence) is the statistical manifestation of intransitivity that occurs when the direct and indirect estimates in a network of treatments do not agree. The distinction between intransitivity and inconsistency (incoherence) is analogous to the distinction between clinical (or methodological) heterogeneity and statistical heterogeneity in standard pair-wise meta-analysis (Cipriani 2013).

At a global level, we assessed heterogeneity and inconsistency (incoherence) of the whole network by decomposing the Q-statistic into variation of the effect estimates within designs (heterogeneity) and between designs (inconsistency) (Higgins 2012; Krahn 2013). A design is each combination of treatments within a study in a network meta-analysis (e.g. for treatments A, B, and C, possible designs are A:B, A:C, B:C, and A:B:C). In addition, we used the full random-effects design-by-treatment interaction model to assess whether all interventions behave similarly in all comparisons. We used the R package netmeta for Q decomposition and for calculation of the full random-effects design-by-treatment interaction model (netmeta).

At a local level, we assessed differences between direct and indirect effect estimates of specific comparisons (incoherence) using descriptive Z-tests and clinical relevance of the effect estimates. However, only clinically relevant incoherence based on different clinical conclusions of the 95% CI of direct and indirect treatment effect estimates with respect to the range of equivalence was used for interpretation of incoherence.

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Investigation of heterogeneity

In cases of statistical heterogeneity (Q-test with P < 0.05, 95% PI compared to 95% CI) within treatment comparisons, we explored possible sources (Higgins 2019). We restricted these explorative analyses to primary and GRADE-relevant secondary outcomes and to the effect modifier 'dose of the intervention' as potential sources of heterogeneity. For pair-wise comparisons (drugs of direct interest versus placebo), we performed subgroup analyses in RevMan. For the network, we used the R package netmeta to carry out separate analyses for the subgroups (netmeta).

Different treatment regimens—subgroup analysis of doses

Because it is of interest for clinicians and patients to know the optimal dose of antiemetic drugs with respect to efficacy and safety, we performed subgroup analyses.

We excluded combinations of drugs from the subgroup analysis because we cannot be sure whether some combinations can affect the dose effects. We performed the subgroup analysis of doses in the network with single drugs only (see 'Sensitivity analysis—Single drugs only') if the effect estimates remained robust compared to the primary analysis.

We separated different doses of the same drug into low, recommended, and high doses (Table 1). We restricted splitting of doses to single drugs of direct interest. The recommended doses or dose ranges for drugs are based on those reported in the 'consensus guidelines for the management of postoperative nausea and vomiting' (Gan 2014). For emerging substances, we used doses or dose ranges based on dose-finding studies (e.g. for amisulpride, see Kranke 2013; no data are available for fosaprepritant).

We categorized the spectrum of available fixed doses into low, recommended, and high doses according to the following algorithm.

- If a single dose X is recommended (Gan 2014), we defined X as the 'recommended dose'; 'low dose' as < X; 'high dose' as > X (lower and upper limits are defined only if reported in Gan 2014).
- If a dose range X to Y is recommended (Gan 2014), we defined X to Y as 'recommended dose range'; 'low dose' as < X; 'high dose' as > Y (lower and upper limits are defined only if reported in Gan 2014).

If flexible doses (e.g. mg/kg) were reported, we transformed flexible doses into fixed doses by multiplying the flexible dose by the mean/median weight of participants reported in the published study (if the weight was not reported, we assumed 70 kg).

Drugs without any dose recommendation according to Table 1 (fosaprepitant, scopolamine) and drugs not of direct interest were included in the analysis. In these cases, all doses of the same drug were lumped together in a dose category 'NA'.

If there were studies that used drugs of direct interest that were not attributable to any dose category in Gan 2014 (e.g. using different application routes), we excluded these studies from the subgroup analysis. Exclusion of these studies was necessary for subsequent analyses of additive dose effects (see 'Methods for analysing additive dose effects') because additional categories that could not assigned to the additive concept may interfere with the analysis.

We used the R package netmeta to carry out network meta-analyses with subgroups (netmeta). Network effect estimates were used for interpretation of subgroup analyses in this review. In addition, studies were divided into subgroups in pair-wise meta-analyses of primary and GRADE-relevant secondary outcomes, and these were reported in the Data and analyses section. We did not report these pair-wise subgroup analyses in the Effects of interventions section to reduce the amount of information provided in review text.

We performed this explorative analysis for all primary and for all secondary outcomes while considering side effects to answer this specific question about effects of the 'dose of the intervention' on effect estimates (Higgins 2019).

We summarized the most commonly used dosages, routes, and time points of administration of single drugs of direct interest for the primary outcome vomiting and reported this information in the Effects of interventions section.

Methods for analysing additive dose effects

We used the subgroup analysis of dose with splitting of drugs into the dose categories low, recommended, and high doses (see 'Different treatment regimens—subgroup analysis dose') as primary NMA. We performed a second analysis based on the assumption that the effects of combined categories (e.g. low + recommended, low + recommended + high, recommended + high) are additive sums of their individual categories. This assumption, together with the network structure, leads to a statistical model that allows decomposing of observed relative effects into single dose categories and estimating the effects of the dose categories. The hypothesis of additivity can be tested by comparing estimates from this model with those from the primary analysis (subgroup analysis dose) (Mills 2012). We used the function netcomb of the R package netmeta version 1.0-1 for analysis (netmeta; Rücker 2019).

Sensitivity analysis

We analysed the robustness of the effect estimates by performing the following sensitivity analyses.

- Risk of bias: including only trials at low risk of bias in the overall risk of bias summary (see 'overall risk of bias summary') and excluding all trials with high or unclear risk of bias in the overall risk of bias summary.
- Imbalance in baseline details: Including only trials with a balanced distribution of baseline details in the study arms and excluding all studies with imbalance in baseline details in the study arms.
- Primary PONV-related outcome: including only trials with a primary PONV-related outcome and excluding trials that analysed the outcomes vomiting and nausea not as primary endpoints.
- Funding source 'industry': including only trials funded by industry and excluding all other studies.
- Funding source 'non-industry': including only trials funded by non-industry resources and excluding all other studies.
- Single drugs only: including only study arms investigating single drugs and excluding study arms investigating combinations of drugs. This analysis compared the robustness of network effect estimates of the primary network meta-analysis and the sensitivity analysis including single drugs only (which is the basic analysis for the subgroup analysis dose).

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- Comparability of drug doses within studies: there is a possibility that some trials compare one drug at the upper limit of its therapeutic range (e.g. high dose) with another drug at the lower limit of its therapeutic range (e.g. low dose) within the same study. This can lead to an overestimation of the drug used in higher doses. We captured this study characteristic by adding a dichotomous variable indicating whether the dosages are comparable (yes = 1) or not (no = 2) and used this information for sensitivity analysis (Cipriani 2009). Comparable dose categories were low-low, recommended-recommended, and high-high (for definitions of dose categories of individual drugs, see Table 1). In the sensitivity analysis, we included only studies that investigated comparable dose categories of different drugs. This sensitivity analysis was restricted to single drugs only.
- Adverse event monitoring: we used the information on adverse event monitoring of studies to test the robustness of effect estimates for the primary outcomes 'SAE' and 'any AE' by sensitivity analyses. We included only studies with low risk of bias for adverse event monitoring and excluded high and unclear risk of bias studies for adverse event monitoring.

We restricted sensitivity analyses to primary outcomes with the exceptions of 'Risk of bias' and 'Comparability of drug doses within studies', which were relevant for all side effects (GRADE-relevant secondary outcomes).

We reported effect estimates of the sensitivity analyses of drugs of direct interest in the section Effects of interventions if the effect estimates differed from the primary analysis regarding clinical interpretation of the effect (non-robust effect estimates).

Summary of findings and assessment of the certainty of the evidence

We presented the main results of the review in 'Summary of findings' (SoF) tables including a rating of the certainty of evidence as suggested for network meta-analysis by Yepes-Nuñez 2019. The certainty rating was based on the principles of the GRADE Working Group and was assessed by an alternative system developed by Salanti et al (termed CINeMA, Confidence in Network Meta-Analysis, Salanti 2014).

We created one primary and eleven secondary SoF tables. In the primary SoF table, single antiemetic drugs of direct interest (see 'Interventions of direct interest') with important beneficial effect and with high or moderate certainty of evidence for the primary outcome (vomiting) were presented together with all relevant substance class-specific adverse events. For the secondary SoF tables, one table for each outcome (primary outcomes and drug-class important adverse effects) was created, comparing all single drugs of direct interest to placebo.

In the SoF tables we presented NMA relative treatment effects, anticipated absolute effects, ranking of treatments using P scores, and the certainty of evidence.

The quality of the body of the NMA evidence was assessed by two independent reviewers (SW, OJ) and reflects within-study risk of bias (study limitations), across-studies bias (publication bias), indirectness, imprecision, heterogeneity (variability between studies within each comparison), and incoherence (variability between direct and indirect evidence). We have only appraised the certainty of evidence for relative treatment effects and not for treatment rankings.

The clinically important size of effect and not the statistical significance of NMA relative treatment effects was relevant for assessing the certainty of evidence. We defined for efficacy and safety outcomes, a range of relative treatment effects around the line of no effect that do not indicate important clinical difference between the interventions, which is termed the 'range of equivalence'.

- Efficacy outcomes (vomiting 0 to 24 hours): a relevant effect is defined as RR 0.8 (range of equivalence: 0.8 to 1.25)
- Safety outcomes (SAE, any AE, headache, sedation, extrapyramidal symptoms, constipation, postoperative wound infection, arrhythmia, visual disturbances, and QT prolongation): a relevant effect is defined as RR 0.9 (range of equivalence: 0.9 to 1.11)

We GRADEd each network estimate according to the following criteria (details are described in the Appendix 5):

- Within-study risk of bias (study limitations)
- Across-studies bias (publication bias)
- Indirectness
- Imprecision
- Heterogeneity
- Incoherence

The GRADE assessment resulted in one of four levels of certainty and these express our confidence in the estimate of effect (Balshem 2011).

- High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
- Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Certainty of evidence for effect estimates can vary greatly across comparisons within a network, and can range from high to very low certainty. In making inferences regarding the choice of an intervention recognizing the certainty of each comparison is far more valuable than ranking efficacy alone (Puhan 2014).

Reporting guidelines

This review is reported based on the PRISMA Extension Statement for NMA (Hutton 2015) and on the 'Protocol template for a Cochrane Intervention review that compares multiple interventions' from the Cochrane Comparing Multiple Interventions Methods Group (Protocol Template 2014).

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RESULTS

Description of studies

Results of the search

The results of our search are displayed in a PRISMA flow chart (Figure 3). The first search was performed in November 2017. The search was updated in April 2020.

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Figure 3. Study flow diagram.

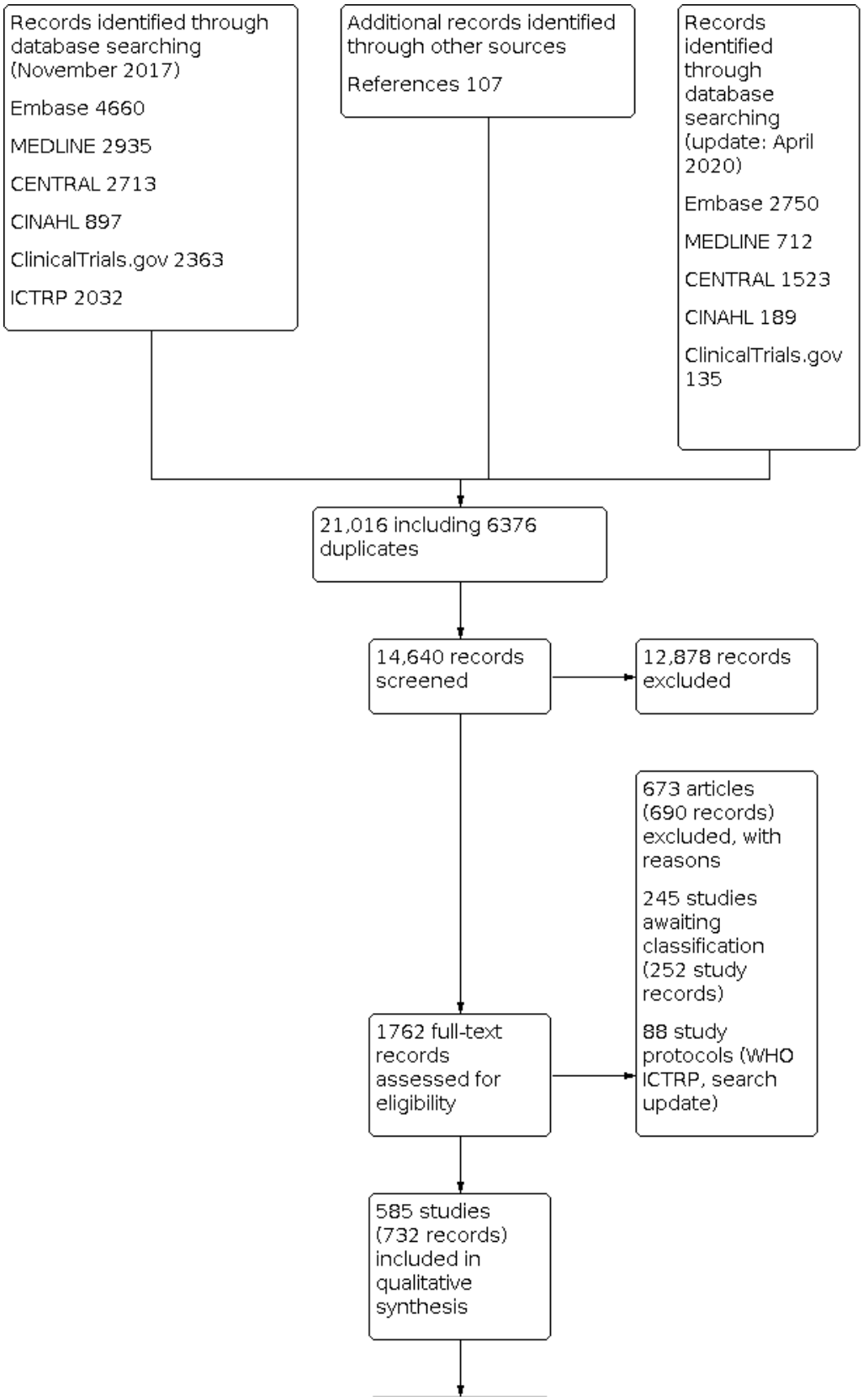

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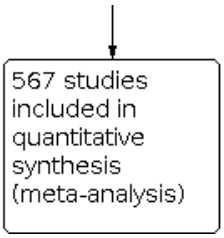
Figure 3. (Continued)



In the first search, we identified 15,600 records through database searching and another 107 by handsearching of reference lists of meta-analyses in the field. In the search update, we identified another 5309 records. In total, 14,640 records remained after duplicates had been removed. These were screened independently by 11 review authors (SW, DM, MR, HMS, AH, DR, ILB, MSS, LHJE, PKr, TS) regarding title and abstract. A total of 1762 remaining records were selected and assessed for eligibility by reviewing the full texts and protocols; 690 records did not fulfil the eligibility criteria and had to be excluded. A total of 245 studies (252 records) were awaiting classification. Of these, 206 studies were awaiting classification due to missing information in the study reports or study protocols, and 39 were identified as potentially eligible studies after the first search date (these studies will be fully included in the next review update). An additional 88 study protocols of the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) database identified in the search update were awaiting classification (until the next review update) because the database was closed at the time of the search update. All protocols were listed in a supplementary file (Supplementary File_ICTRP-protocols). Finally, 732 records (full-text primary and secondary study reports, abstracts, and protocols), which could be allocated to 585 studies, were included in the qualitative synthesis, and 567 of these studies were used to perform the pair-wise and network meta-analyses. Eighteen studies could not be used for analysis, although they reported outcomes of interest for this review. These studies did not report data in a way that could be used for analysis.

Eighty-three of 585 studies (14%) were not published in English. Twenty-seven studies were published in Korean (Ahn 2002; Choi 1999; Choi 2008; Joe 2009; Kil 1999; Kim 1992; Kim 1999; Kim 2000; Kim 2001; Kim 2005a; Kim 2005b; Kim 2007; Kim 2012; Kim JE 2005; Koo 2001; Lee 2008b; Lee HS 2004; Lee SY 2001; Lee YC 2009; Moon 2010; Park 2006; Rho 2001-1; Ryu 2007; Seo 2003; Suh 2007; Yoon 2009; Yoon 2016), 14 in German (Alon 1982; Biedler 1998; Eberhart 1999b; Heinke 1996-1; Lutz 1969; Morin 1999; Muller 2003; Piper 2003; Ploner 1997; Rusch 1999; Rusch 2002; Schuh 1987; Tolksdorf 1986; Triem 1999), 11 in Turkish (Akin 2005; Akkaya 2001; Altunkaya 2003; Cekmen 2003; Cubukcu 2007; Guldogus 1994; Karabayirli 2003; Kaya 2000; Ozdamar 2006; Ozunlu 2005; Tezcan 1993), eight in Spanish (Agamez Medina 2015; Alonso Damian 2012; Cabrera 1997; Delas Ramirez 2001; Perez Ascencio 1992; Perez Garcia 2000; Pertusa 1996; Sanduende 2007), seven in Chinese (Jin 2013; Li 2015-1; Liu 2011; Quan 2007; Quan 2011; Wang 1995; Zhu 2010), three in Italian (Pascucci 1996; Rettori 2011; Stefani 1995), three in Persian (Heidari 2015b; Hemmati 2014; Safae 2011), two in French (Badaoui 1998; Badaoui 1999), two in Russian (Gallinger 2007; Ionescu 2007), and one each in Bulgarian (Dimov 2004), Danish (Jespersen 1989), Dutch (Gijzels 2006), Greek (Kanakoudis 1985), Japanese (Seki 2005), and Portuguese (Martins 1995).

We did not include in our systematic review any abstracts lacking a published full-text study report. We included six studies that were not published in a journal but were presented as publicly available study reports with results (NCT00888329; NKO101287; NKT102245; NKT102260; NKT102552; PALO-04-07).

Included studies

We included 585 studies (733 records) in this systematic review. Three publications included two different studies (Gesztesi 2000-1; Gesztesi 2000-2; White 2005-1; White 2005-2; White 2007-1; White 2007-2). Six studies included two different anaesthesia regimens (inhalational and propofol anaesthesia), and we divided the participant population into several sub-studies for analysis only (Apfel 2004-1; Apfel 2004-2; Heinke 1996-1; Heinke 1996-2; Li 2015-1; Li 2015-2; Rho 2001-1; Rho 2001-2; Voigt 2011-1; Voigt 2011-2; Zhang 2013-1; Zhang 2013-2). We could allocate 83 study protocols to 75 included studies. Forty-five studies were published more than once. A total of 64 records were multiple publications of clinical studies in abstract format or as a journal publication.

The included studies were published between 1965 (Khanna 1965) and 2017 (Bang 2017; Bjerregaard 2018; Corcoran 2017; Cortes Flores 2018; Gan 2017; Hu 2017; Kizilcik 2017; Koyuncu 2017; Monohar 2017; Mujoo 2017; Satomoto 2017; Song 2017; Yang 2017). A majority of included studies (71%) were published in the last two decades between 2000 and 2017. The number of RCTs increased over time, reaching a peak of publications in 2007 with 36 (36/585; 6%) published trials (Figure 4). From 1996 to 2016, more than 15 trials were published annually (Figure 4).

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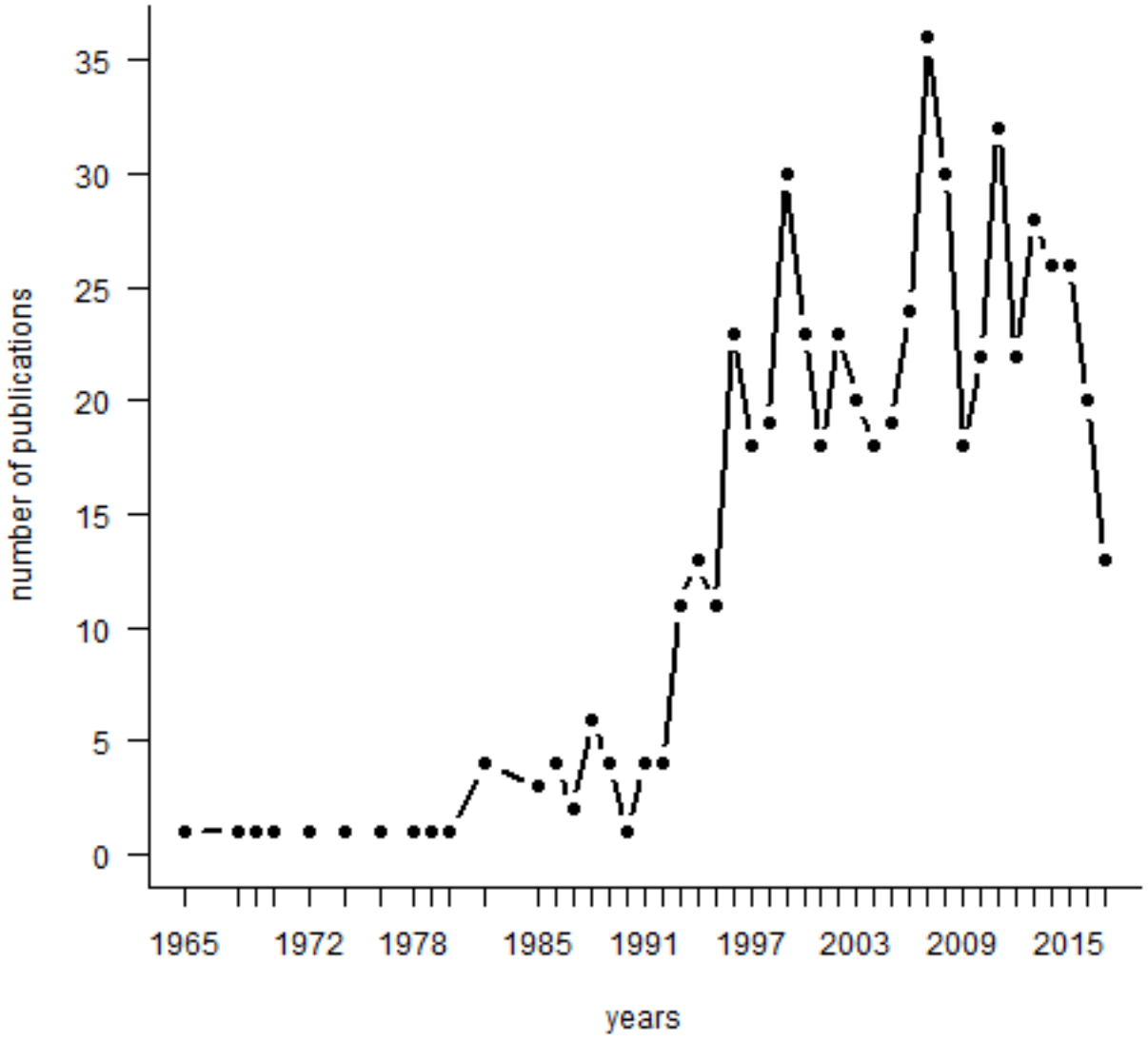
Figure 4. Number of annual publications (included studies, n = 585) from 1965 to 2017 (first search).



The included studies provide data on 97,516 randomized participants, of which data on 93,211 were analysed. A detailed description of the trials can be found under Characteristics of included studies.

Comparators

This review compared 21 single interventions of direct interest and 23 additional single interventions to supplement the analysis. All interventions are listed in Types of interventions. Of 585 included studies, 541 studies (93%) investigated drugs of direct interest, 19 studies investigated drugs not of direct interest, and 25 studies investigated both types of interventions.

A total of 384 studies (66%) included an inactive control arm (placebo or no treatment) in the study design. Active interventions only were compared in 201 studies (34%). The number of eligible study arms in included trials ranged between two and 16. In summary, 310 studies (53%) investigated two groups, 160 studies (27%) three groups, 77 studies (13%) four groups, 23 studies (4%) five groups, 11 studies (2%) six groups, two studies (0.3%) seven groups, and two studies more than seven groups (Apfel 2004-1; Apfel 2004-2; Beattie 1993).

A total of 423 studies (72%) investigated only single drugs, 31 studies (5%) compared only combinations of drugs, and 131 studies (23%) compared both single drugs and combinations of drugs.

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The top 10 of the most investigated antiemetic drugs administered as single prophylaxis for prevention of PONV in this review were ondansetron (246 studies), dexamethasone (120 studies), droperidol (97 studies), metoclopramide (76 studies), granisetron (51 studies), ramosetron (38 studies), palonosetron (35 studies), tropisetron (32 studies), dolasetron (20 studies), and scopolamine (18 studies). Thus, the 5-HT_3 receptor antagonists are the most widely studied substance class in this review. Other drugs of direct interest administered as single interventions were much less studied, with 10 studies for haloperidol, seven studies for aprepitant and promethazine, five studies for dimenhydrinate and methylprednisolone, three studies for fosaprepitant, two studies for amisulpride, casopitant, and perphenazine, and one study for rolapitant. No eligible study was found that investigated meclizine as a single intervention.

Among the combinations of drugs, two-fold combinations were investigated in 159 studies, three-fold combinations in eight studies (Apfel 2004-1; Benevides 2013; Bergese 2016; DeOliveira 2011; Gallinger 2007; Liu 2011; Long 2014; Tang 2003), and one four-fold combination in one study (Hammas 2002). Forty-three different two-fold combinations were used in the included studies. Four of these two-fold drug combinations were used in 10 or more studies (54 times: dexamethasone-ondansetron, 20 times: dexamethasone-granisetron, 15 times: droperidol-ondansetron, 10 times: dexamethasone-metoclopramide). A total of seven different three-fold drug combinations were investigated, of which dexamethasone-droperidol-ondansetron was used most often in four of eight studies (Apfel 2004-1; Gallinger 2007; Liu 2011; Tang 2003). The other six three-fold combinations were investigated once each (aprepitant-dexamethasone-ondansetron, aprepitant-dexamethasone-promethazine, dexamethasone-dolasetron-droperidol, dexamethasone-haloperidol-ondansetron, dexamethasone-metoclopramide-ondansetron, dexamethasone-ondansetron-promethazine). The only investigated four-fold drug combination was dexamethasone-droperidol-metoclopramide-ondansetron.

Details of interventions

We recorded doses, administration time points, and application routes for all interventions administered as single drugs. We categorized doses of drugs that are of direct interest into low, recommended, and high doses according to Table 1. We categorized time points of administration into before anaesthesia, at induction of anaesthesia, during surgery, and at end of surgery. We differentiated between intravenous, oral, intramuscular, and other routes of administration (e.g. epidural, intranasal).

Eighty studies (14%) investigated different doses of the same antiemetic drug, 12 studies (2%) different administration time points, and nine studies (2%) different routes of application.

5-HT_3 receptor antagonists

Dolasetron (20 studies) was administered intravenously or per oral at doses of 12.5 to 100 mg (recommended to high) and 25 to 200 mg (no dose recommendation available), respectively. Most of the study arms (56%) investigating intravenous dolasetron used high doses (> 12.5 mg). Intravenously administered dolasetron was given at induction of anaesthesia (22%) or at end of surgery (78%). Oral dolasetron was administered before anaesthesia.

Granisetron (51 studies) was mainly administered via the intravenous route at doses of 0.1 to 4 mg (low to high). Most of the study arms (84%) investigating intravenous granisetron used recommended doses (0.35 to 3 mg). Intravenous granisetron was given at all different time points ranging from before anaesthesia to end of surgery. Granisetron was administered orally before anaesthesia at doses of 2 mg in one study (Bhatnagar 2007).

Ondansetron (246 studies) was administered via the intravenous or oral route at doses of 1 to 16 mg (low to high) and 4 to 16 mg (low to high), respectively. In most of the study arms (71%) investigating intravenous ondansetron, recommended doses were used. Low and high doses of intravenous ondansetron were used in 9% and 25% of study arms, respectively. Intravenous ondansetron was administered most often at induction of anaesthesia (69%) and at end of surgery (26%). Oral ondansetron given before anaesthesia was investigated in 32% of study arms at low doses, in 47% at recommended doses, and in 21% at high doses.

Palonosetron (35 studies) was administered only via the intravenous route at doses of 0.007 to 2.169 mg (low to high). In most of the study arms, palonosetron was used at recommended doses (69%), followed by study arms using low doses (21%). Administration at induction of anaesthesia was used most often (69%), followed by administration at end of surgery (28%).

Ramosetron (38 studies) was administered intravenously or per oral at doses of 0.1 to 0.45 mg (low to high) and 0.1 mg (no dose recommendation available), respectively. Most study arms (89%) investigating intravenous ramosetron used recommended doses. Administration of intravenous ramosetron at end of surgery was used most often (67%), followed by administration at induction of anaesthesia (28%). Oral ramosetron (three studies) was administered before anaesthesia.

Tropisetron (32 studies) was administered intravenously or per oral at doses of 0.5 to 7.25 mg (low to high) and 5 mg (no dose recommendation available), respectively. Most study arms investigating intravenous tropisetron used high doses (69%), followed by recommended doses (25%). Administration of intravenous tropisetron at induction of anaesthesia was used most often (75%), followed by administration at end of surgery (19%). Oral tropisetron (three studies) was administered before anaesthesia.

D_2 receptor antagonists

Amisulpride (two studies) was administered only via the intravenous route at induction of anaesthesia at doses of 1 to 20 mg (low to high).

Droperidol (97 studies) was administered mainly intravenously at doses of 0.25 to 7.5 mg (low to high). In addition, intramuscular (Rothenberg 1991; Tezcan 1993; Verhasselt 1988), epidural (Lee 2000; Lee IH 2007), and acupoint injection—Jin 2013; Zhu 2010—were tested at doses of 2.5 to 5 mg (no dose recommendation available). Patton 1974 injected droperidol via intravenous (1.25 mg) and intramuscular routes (3.75 mg) shortly after the start of surgery. Two studies did not report the route of administration (Nesek Adam 2004; Prescott 1976). Most study arms investigating intravenous droperidol used recommended doses (57%), followed by high doses (37%). Intravenous low-dose droperidol was investigated in 6% of study arms. Intravenous droperidol was given at all different time points ranging from before anaesthesia to end

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of surgery. However, administration at induction of anaesthesia of intravenous droperidol was used most often (73%), followed by administration at end of surgery (18%). Intramuscular droperidol was administered before anaesthesia or at end of surgery. Epidural droperidol was administered at end of surgery. Droperidol injected into the acupoint was administered before or at induction of anaesthesia.

Haloperidol (10 studies) was administered mainly intravenously at doses of 1 to 2 mg (recommended to high). In addition, one study investigated intramuscular injection of 2 mg haloperidol at end of surgery (Feng 2009), and another study did not report the route and time point of administration (Judkins 1982). Most study arms investigating intravenous haloperidol used high doses (63%), followed by recommended doses (37%). Administration of intravenous haloperidol at induction of anaesthesia was used most often (75%), followed by administration at end of surgery (25%).

Metoclopramide (76 studies) was administered mainly intravenously at doses of 7 to 38.4 mg (low to recommended). In most study arms, intravenous metoclopramide was used at low doses (97%). Two studies used intravenous metoclopramide at recommended doses (Derbent 2005; Talesh 2011). In addition, intramuscular—Huseyinoglu 2016—and intranasal injections —Wagner 1996—were tested at doses of 10 and 20 mg (no dose recommendation available), respectively. One study did not report the route of administration (Nesek Adam 2004). Administration of intravenous metoclopramide at induction of anaesthesia was used most often (60%), followed by administration at end of surgery (35%). Oral metoclopramide was given before anaesthesia.

Perphenazine (two studies) was administered only via the intravenous route at induction of anaesthesia at the recommended dose of 5 mg (Desilva 1995; Steinbrook 1998).

NK_1 receptor antagonists

Aprepitant (seven studies) was administered only via the oral route before surgery at doses of 40 to 125 mg (recommended to high). In most of the study arms (66%), aprepitant was used at high doses, followed by study arms using recommended doses (33%).

Casopitant (two studies) was administered only via the oral route before surgery at the recommended dose of 150 mg.

Fosaprepitant (three studies) was administered only via the intravenous route at induction of anaesthesia at doses of 150 mg (no dose recommendation available).

Rolapitant (one study) was administered only via the oral route before surgery at doses of 5 to 200 mg (low to recommended).

Corticosteroids

Dexamethasone (120 studies) was administered mainly intravenously at doses of 1.25 to 35 mg (low to high). In addition, oral administration (Eberhart 2006; Ozdamar 2006), epidural injection (Hefni 2014; Khafagy 2010), and perineural injection—Tomar 2017—were tested at doses of 4 to 8 mg (no dose recommendation available). One study did not report the route of administration (Heidari 2015b). Most study arms investigating intravenous dexamethasone used high doses (69%), followed by recommended doses (27%). Intravenous low-dose dexamethasone was investigated in 4% of study arms. Intravenous dexamethasone was given at all different time points ranging from before anaesthesia to end of surgery. However, administration at induction of anaesthesia was used most often (77%), followed by administration before anaesthesia (13%) and at end of surgery (8%). Epidural and perineural dexamethasone were administered at induction of anaesthesia; oral dexamethasone was given before anaesthesia.

Methylprednisolone (five studies) was administered intravenously at doses of 40 to 125 mg (recommended to high), intramuscularly at doses of 40 mg (no dose recommendation available), and interarticularly at doses of 40 mg (no dose recommendation available). Intravenous injection was administered at induction of anaesthesia, intramuscular injection was administered at induction of anaesthesia or at end of surgery, and intra-articular injection occurred during surgery.

Antihistamines

Dimenhydrinate (five studies) was administered intravenously at doses of 50 mg (low), intramuscularly at doses of 50 mg (no dose recommendation available), and per oral at doses of 75 mg (no dose recommendation available). Intravenous injection was administered at induction of anaesthesia; intramuscular injection and oral application were performed before anaesthesia.

Promethazine (seven studies) was administered intravenously at doses of 5.6 to 56.5 mg (low and high), intramuscularly at doses of 25 mg (no dose recommendation available), and per oral at doses of 20 mg (no dose recommendation available). Intravenous injection was administered at induction of anaesthesia or at end of surgery, intramuscular promethazine was administered at end of surgery, and oral application was performed before anaesthesia.

No eligible study was found that investigated meclizine as a single intervention.

Anticholinergics

Scopolamine (18 studies) was administered mainly via a transdermal patch before anaesthesia at doses of 0.5 to 1.5 mg (recommended to high). Five studies did not report the dose of transdermally administered scopolamine (Schuh 1987; Semple 1992; Stromberg 1991; Tolksdorf 1986; Wilkinson 1989). In addition, one study investigated an intramuscular injection of 0.46 mg scopolamine before anaesthesia (Larsson 1988), and two studies investigated the oral route of scopolamine at doses of 0.3 to 0.6 mg (Baxendale 1993; Simpson 1988). Two studies did not report the route of administration (Heidari 2015b; Shah 1972).

Anaesthesia and surgical procedures

In 515 studies (88%), participants were anaesthetized through inhalational anaesthesia techniques based on volatiles alone (sevoflurane, isoflurane, desflurane, etc.), a balanced anaesthesia regimen (volatile with opioid), or a combined regimen (volatile with propofol). Total intravenous anaesthesia (TIVA) was used in 56 studies (10%). Six studies used both inhalational anaesthesia and TIVA in the study design, and we divided participant populations into sub-studies for analysis according to the anaesthesia regimen used (Apfel 2004-1; Apfel 2004-2; Heinke 1996-1; Heinke 1996-2; Li 2015-1; Li 2015-2; Rho 2001-1; Rho 2001-2; Voigt 2011-1; Voigt 2011-2; Zhang 2013-1; Zhang 2013-2). Eight studies did not specify which type of anaesthesia was used, but it was reported that anaesthesia was standardized for all participants within the individual studies (Alia 2015; Backes 2013; Barrow 1994; Gesztesi

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2000-1; Gesztesi 2000-2; Khan 2006; Kumar 2013; NCT00888329; Thimmasettaiah 2012). The overall mean duration of anaesthesia for all studies was 108 minutes. The overall median duration of anaesthesia was 101 minutes with an interquartile range of 68 to 140 minutes. The shortest mean duration of anaesthesia reported in a study was 1.72 minutes (Ali Melkkila 1996), and the longest mean duration of anaesthesia was 486 minutes (Tsutsumi 2014).

In 189 studies (32%), gynaecological procedures were most common, followed by gastrointestinal (19%) and miscellaneous procedures (18%). The latter included unspecified abdominal surgery, unspecified plastic surgery, and multiple surgery types within individual studies. Participants were undergoing otolaryngological procedures in 36 studies (6%), endocrine surgery including thyroidectomy in 35 studies (6%), breast surgery including plastic breast surgery in 24 studies (4%), any unspecified laparoscopic procedure in 19 studies (3%), ocular surgery in 13 studies (2%), neurological procedures including spine surgery in 13 studies (2%), orthopaedic surgery in 11 studies (2%), dental procedures in nine studies (2%), cardiovascular and thoracic procedures in four studies (1%), and urological surgery in three studies (1%). In 10 studies (2%), the surgical procedure was not specified.

Population baseline details

The overall mean age of populations in all included studies in this review was 42.4 years, and the median age was 42.5 years. Thirty-four studies (6%) reported a low mean age between 18 and 29 years, and 15 studies (3%) reported a high mean age of more than 60 years. Thirty studies (5%) did not report the mean age of the study population. Most of the included participants were women (83%). In 412 studies (70%), included participants were healthy individuals (American Society of Anesthesiologists (ASA) 1 and 2). In 100 studies (17%), participants were eligible with substantial physical and functional limitations (ASA > 2). In 73 studies (12%), ASA physical health status was not reported.

We collected study population data on the four risk factors for PONV according to Apfel (female gender, non-smoker status, history of PONV or motion sickness, postoperative opioid use). Females only were included in 292 studies (50%), whereas four studies (< 1%) included only males. In 93 studies (16%), a balanced gender distribution with 40% to 60% females was reported. Twenty-seven studies (5%) did not report the gender distribution. A non-smoking status of 100% in the study population was reported in 55 studies (9%). Only active smoking participants were included in one study (Jo 2012). In 399 studies (68%), the smoking status of the study population was not reported. A history of PONV or motion sickness in 100% of the study population was reported in five—Altorjay 2011; Dagtekin 2009; Kim SH 2013; Koivuranta 1999; Pan 2008—and four studies—Altorjay 2011; Dagtekin 2009; Kim SH 2013; Pan 2008—respectively. Exclusion of participants with history of PONV or motion sickness was reported in 100 (17%) and 104 (18%) studies, respectively. In 266 (45%) and 299 studies (51%), respectively, no details on participant history of PONV and motion sickness were reported. In 514 studies (88%), participants received perioperative opioids. In 15 studies (3%), no perioperative opioids were used. For 153 studies (26%), data were provided for all four risk factors. High-risk populations with participants having three and four risk factors at 100% (inclusion criteria) were studied in five—Altorjay 2011; Dagtekin 2009; Kim SH 2013; NKT102552; Pan 2008—and 31 studies, respectively—a total of 6% of all studies. Two risk factors at 100% (inclusion criteria) were reported in 242 studies (41%).

Study conduct (location, setting, funding)

A total of 298 studies (51%) were conducted in Asia, followed by Europe with 148 studies (25%) and North America with 96 studies (16%). Eleven studies (2%) were conducted in South America, nine studies (2%) in Africa, and seven studies (1%) in Australia/Oceania. Sixteen studies (3%) were carried out in several countries.

A total of 489 studies (84%) were conducted at a single centre, and 60 studies (10%) were conducted at multi-centres. The largest multi-centre study (with 58 study centres) was Morris 1998. In 36 studies (6%), the number of involved studies centres was not reported.

Inpatient participants were included in 409 studies (70%), and outpatient participants were included in 103 studies (18%). Twenty-one studies included both inpatient and outpatient participants, and 52 studies (9%) did not report this study setting.

A total of 97 studies (17%) have reported that they were funded by industry, and 104 studies (18%) have reported that they were funded by non-industrial resources. A majority of studies with a total of 384 studies (66%) have not declared any details on funding of the study.

Sample size

The mean sample size of all studies was 167 participants, and the median sample size was 100, with an interquartile range of 70 to 160 participants. The smallest sample size reported in a study was 20 participants with two study groups (Seki 2005), and the largest randomized sample size was 5199 participants with 16 study arms (Apfel 2004-1; Apfel 2004-2). A total of seven studies included more than 1000 participants (Apfel 2004-1; Fortney 1998; Hechler 2001; Morris 1998; Pearman 1994; Philip 2000; Scuderi 2001).

Study focus and reported outcomes

The titles of the studies indicated that 516 studies (88%) had a focus on PONV research. The titles of 69 studies (12%) did suggest a focus other than PONV research. Most of these studies (33%) investigated dexamethasone on postoperative recovery.

A total of 309 studies (53%) explicitly specified a primary study outcome(s) or provided a sample size calculation for one specific outcome. A total of 86% of these primary outcomes were PONV, nausea, or vomiting, and 14% were not PONV-related. A total of 276 studies (47%) have not specified which reported outcome was the primary outcome and did not provide any sample calculation.

A total of 522 studies (89%) investigated relevant efficacy outcomes for this review. In 327 studies (56%), relevant safety outcomes were reported. Eighteen studies (3%) did not report numerical data that can be used in meta-analyses for this review (Aasboe 1998; Altunkaya 2003; Asadollah 2014; Barros 2013; Barrow 1994; Cubukcu 2007; Derbent 2005; Forrester 2007; Gupta 2011; Judkins 1982; Khanna 1965; Kim WJ 2013; Mohammadi 2007; Ozdamar 2006; Ploner 1997; Sniadach 1997; Turner 2004; Vale 2011). These studies provided general statements on relevant safety outcomes.

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Excluded studies

We excluded 673 articles (690 records) after reviewing the full texts. Reasons for exclusion are listed under Characteristics of excluded studies. The most common reason for exclusion was a wrong administration time point of the interventions (after the occurrence of PONV, therapeutic not prophylactic intention) with a total of 136 studies (19%), followed by abstracts with 89 studies (13), non-clinical study reports (editorials, commentaries, narrative reviews) with 80 studies (12%), wrong outcomes with 76 studies (11%), paediatric or mixed populations (adults and children) with 68 studies (10%), regional or sedative anaesthesia with 57 studies (8%), wrong study design with 48 studies (7%), wrong or no eligible comparator with 42 studies (6%), different baseline anaesthesia regimens in study arms with 31 studies (5%), wrong intervention with 29 studies (4%), wrong population with seven studies (1%), retracted studies (e.g. authored by Fujii) or notes to retracted studies with six studies (1%), and meta-analysis with four studies (1%).

Studies awaiting classification

A total of 245 studies (252 records) are awaiting classification. Of these, 185 studies were identified during the first search in 2017, with 86 studies reported as full-text journal publications and 99 as study protocols posted on either ClinicalTrials.gov or WHO ICTRP. The other 60 studies were identified after the first search or during the search update in 2020. Thirty-nine of these 60 studies will be fully included in the next review update, and 21 studies are awaiting classification due to missing study information. Details on studies awaiting classification are listed in the Characteristics of studies awaiting classification tables.

Of the 86 studies identified in the first search and reported as journal publications, no full text was available for 29 studies. Amongst the missing information of studies with full text were lack of population age (19 studies), details on the anaesthesia regimen (11 studies), randomization details (eight studies), study design (eight studies), outcome details (six studies), and time point of drug administration (one study). Two studies from an author for whom several publications were currently retracted or listed in the retraction watch database are awaiting classification until resolution of concerns (Schietroma 2010; Schietroma 2013). Two other studies seem to share identical study arms without co-referencing each other (Isazadehfar 2016; Isazadehfar 2017). Requests for missing information were sent to all authors who reported contact email addresses in the journal publication. Requests regarding 18 studies remained unanswered.

Of the 99 study protocols retrieved in the first search, three protocols posted results on ClinicalTrials.gov (NCT00231777; NCT01149616; NCT01612702). Due to missing contact email addresses, missing information on the anaesthesia regimen or the time point of administration could not be clarified. The status of 25 studies was 'not yet recruiting' or 'recruitment' at the time of the search. The status of 71 studies was 'closed', 'completed', 'terminated', or 'unknown', and none of the protocols could be allocated to one of the included or excluded studies of the current review. Missing information for individual studies that are allocated to awaiting classification is provided under Characteristics of studies awaiting classification.

Risk of bias in included studies

The risk of bias of each included study was rated, and details on judgements are described in the Characteristics of included studies section. All judgements about each risk of bias item for each included study are graphically presented in Figure 5 (higher-resolution image is available online: Supplementary File_Summary of Risk of bias). Judgements about each risk of bias item presented as percentages across all included studies are graphically presented in Figure 6. About half of all studies were rated as low risk of bias for random sequence generation (48%), blinding of participants and personnel (46%), and blinding of outcome assessors (61%). Incomplete reporting of outcome data was a minor problem in this review, as 90% of studies have been assessed as having low risk of attrition bias. Major problems were unclear risk of selection bias due to insufficient information on allocation concealment and unclear risk of reporting bias due to lack of registered study protocols. Only 12% of all studies were assessed as having low risk of allocation concealment, and only 2% of all studies were assessed as having low risk of selective outcome reporting. The item 'other bias' captures the risk of baseline imbalance, and 12% of all studies were assessed as having low risk due to reporting on all relevant population details and prognostic variables, without any imbalance in these data.

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Figure 5. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. Higher-resolution image is available online (Supplementary File_Summary of Risk of bias).

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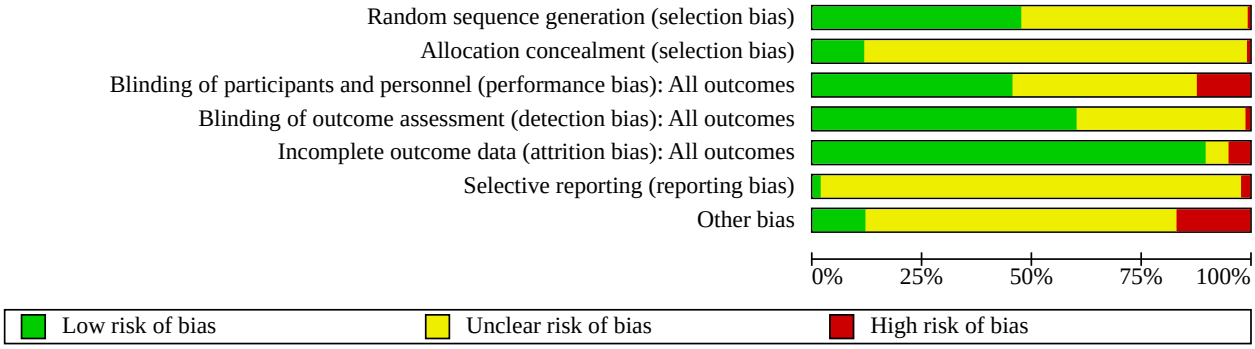
Figure 5. (Continued)

Figure 6. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Three studies were assessed as having low risk of bias for all seven risk of bias items (NKT102245; NKT102552; Tolver 2012).

We assessed the overall risk of bias by summarizing risk of bias for the items 'sequence generation', 'blinding of participant,

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personnel, and outcome assessors', and 'incomplete outcome data'. A total of 157 studies (27%) were assessed as having overall low risk of bias, 101 studies (17%) as having overall high risk of bias, and 327 studies (56%) as having overall unclear risk of bias.

Allocation

Random sequence generation

A total of 282 studies (48%) have reported adequate methods for sequence generation such as random number tables or computer-generated random numbers. These 282 studies were assessed as having low risk of bias. One randomized study was assessed as having high risk of selection bias according to a statement on the potential threat due to selection bias reported in the results section without further description of the study protocol (NCT00888329). All of the other 302 studies (52%) have not reported sufficient information on the method used for random sequence generation. Most often, these studies have stated only that the study was randomized without describing the method; therefore we assessed them as having unclear risk of bias.

Allocation concealment

Sixty-nine studies (12%) were judged to have low risk of bias because allocation concealment was achieved by using central allocation or sequentially numbered opaque sealed envelopes (SNOSE). Two studies were assessed as having high risk of bias (NCT00888329; Olajumoke 2013). NCT00888329 reported the risk of selection bias as a limitation in the study protocol. Olajumoke 2013 was judged as having high risk because there was a high possibility that assignments could be foreseen by using an open random allocation schedule. A total of 514 studies (88%) did not describe any method used for allocation concealment, or it was not clear from the description whether SNOSE was correctly applied to cover allocation. These studies were assessed as having unclear risk of bias.

Blinding

Blinding of participants and personnel

In 271 studies (46%), it was reported that participants and personnel were blinded. Sixty-seven studies (12%) had an unblinded study design. Most often, anaesthesiologists responsible for intraoperative management were not blinded to the treatment. In 247 studies (42%), there was no or insufficient information on blinding of participants or personnel, and statements such as 'blinded study' or 'double-blind study' were used. These studies were assessed as having unclear risk of bias.

Blinding of outcome assessment

In 355 studies (61%), it was reported that outcome assessors were blinded. Four studies (< 1%) had an unblinded study design (Dsouza 2011; Laha 2013; Lee WS 2015; Wattwil 2003). In 226 studies (39%), there was no or insufficient information on blinding of outcome assessors, and statements such as 'blinded study' or 'double-blind study' were used. These studies were assessed as having unclear risk of bias.

Incomplete outcome data

A total of 528 studies (90%) were judged as having low risk of attrition bias, 27 studies (5%) high risk, and 30 studies (5%) unclear risk.

Selective reporting

The risk of selective outcome reporting bias can be reliably assessed only if a study protocol was prospectively registered. A total of 510 studies (87%) have not published a study protocol available on the ClinicalTrials.gov or WHO ICTRP database. All of these studies were at unclear risk of reporting bias. Of the other 75 studies with registered study protocols, 58 studies have referenced the study protocol in the journal publication, six studies without a full-text journal publication have reported study results in the study protocol or the study report (NCT00888329; NKO101287; NKT102245; NKT102260; NKT102552; PALO-04-07), and 11 studies have not referenced their registered study protocols in the published journal report, and vice versa (Agarkar 2015; Alghanem 2010; Bang 2017; Blitz 2012; Choi 2016; Jung 2013; Kakuta 2011; Kim SH 2013; Kizilcik 2017; Ryoo 2015; Sanchez Rodriguez 2010). The 11 corresponding study protocols were retrieved in our search of the ClinicalTrials.gov or WHO ICTRP database, and we could allocate the protocols to the published journal reports based on corresponding study details.

Of the 75 studies (13%) with registered study protocols, 27 studies (5% of all 585 studies) were prospectively registered, 47 (8%) were retrospectively registered, and one could not be assessed due to different study dates in the protocol and in the report (Kim 2015). Of the 27 studies with prospectively registered protocols, 11 studies (2% of all 585 studies) were assessed as having low risk of selective outcme reporting bias (Altorjay 2011; Bjerregaard 2018; Gan 2011; Kranke 2012; Kranke 2013; NKO101287; NKT102245; NKT102552; PALO-04-07; Tarantino 2015; Tolver 2012), 10 studies (2%) were assessed as having high risk of selective outcome reporting bias (DeOliveira 2011; Fahlenkamp 2016; Green 2012; Hu 2017; Kim SH 2013; Sinha 2014; Soga 2015; Vallejo 2012; Yang 2017; Zhou 2012), and six studies were assessed as having unclear risk of selective outcome reporting bias (Corcoran 2017; Dewinter 2016; Kakuta 2011; Kakuta 2015; Segelman 2016; Tsutsumi 2014). All retrospectively registered studies were assessed as having unclear risk of reporting bias.

Other potential sources of bias

A total of 71 studies (12%) have had no baseline imbalance in population characteristics or risk factors for PONV between study arms and were judged as having low risk of other bias. Ninety-seven studies (17%) showed an imbalance and were judged as having high risk of other bias. In 417 studies (71%), information on relevant population characteristics or risk factors for PONV was missing, and we judged these studies as having unclear risk of other bias.

Assessment of adverse events monitoring

Sixty-one studies (10%) reported data on the outcome 'any AE'. We assessed the ways of definition and monitoring of any AE (Table 2). Eleven studies were judged as having low risk of bias because any adverse events were actively monitored (active survey) and all relevant substance class-specific AEs were included and reported (Ahn 2002; Bailey 1990; Diemunsch 2007; Gan 2007; Green 2012; Helmers 1993; Lee SY 2002; Murphy 2011a; NKT102245; NKT102260; NKT102552). Twenty-seven studies were judged as having high risk of bias because substance class-specific adverse events were not included or reported under the composite outcome AE, and there were no details on monitoring of AEs reported, or AEs were not actively monitored. Twenty-three studies provided no details on monitoring of AEs reported nor on all relevant substance class-

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specific AEs included and reported. These studies were judged as having unclear risk of bias.

Twenty-nine studies (5%) reported data on the outcome 'SAE'. We assessed whether SAEs were defined according to an internationally accepted classification system (Table 2). Five studies defined SAEs according to the ICH guideline for good clinical practice and were assessed as having low risk of bias (Hanaoka 2004; NKT102245; NKT102260; NKT102552; Tarantino 2015). All of the other 24 studies did not define SAEs in the study report and were assessed as having high risk of bias.

Effects of interventions

See: **Summary of findings 1** Primary summary of findings; **Summary of findings 2** Summary of findings (vomiting within 24 hours postoperatively); **Summary of findings 3** Summary of findings (serious adverse events); **Summary of findings 4** Summary of findings (any adverse event); **Summary of findings 5** Summary of findings (headache); **Summary of findings 6** Summary of findings (sedation); **Summary of findings 7** Summary of findings (extrapyramidal symptoms); **Summary of findings 8** Summary of findings (constipation); **Summary of findings 9** Summary of findings (postoperative wound infection); **Summary of findings 10** Summary of findings (arrhythmia); **Summary of findings 11** Summary of findings (visual disturbances); **Summary of findings 12** Summary of findings (QT prolongation)

Summary of findings tables

Summaries of findings are presented in one primary Summary of findings (SoF) table and 11 secondary SoF tables.

The primary SoF table includes a selection of interventions according to the following criteria: single antiemetic drugs of direct interest (compared to placebo) with important beneficial effect and with high or moderate certainty of evidence for the primary outcome (vomiting) along with all relevant side effects.

- Primary SoF (Summary of findings 1)

Secondary SoF tables are outcome-specific and include all single drugs of direct interest compared to placebo.

- Vomiting (or dry retching) within 24 hours postoperatively (Summary of findings 2).
- Serious adverse events (SAEs) (Summary of findings 3).
- Any adverse event (any AE) (Summary of findings 4).
- Headache (Summary of findings 5).
- Sedation/drowsiness (Summary of findings 6).
- Extrapyramidal symptoms (Summary of findings 7).
- Constipation (Summary of findings 8).
- Postoperative wound infection (Summary of findings 9).
- Arrhythmia (Summary of findings 10).
- Visual disturbances (Summary of findings 11).
- QT prolongation (Summary of findings 12).

To get an overview about all GRADE-relevant outcomes and all single drugs of direct interest (compared to placebo), we summarized the direction of network effect estimates and the level of certainty of evidence in Figure 7 (Supplementary File_Summary of results).

Figure 7. Direction of network effect estimates (colour code) of single drugs of direct interest compared to placebo with certainty levels of evidence (high, moderate, low, very low) for all GRADE-relevant, pre-defined outcomes.

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Colour code: important benefit (green), uncertain benefit (light green), no important effect (yellow), uncertain minimal (or no) effect (light yellow), uncertain harm (orange), important harm (red), no studies available (NA).

Outcomes	Any AE	Headache	Constipation	Extrapyramidal symptoms	Sedation	Arrhythmia	QT prolongation	Wound infection	Visual disturbances
	very low	low	NA	low	low	low	NA	NA	NA
	moderate	very low	very low	very low	very low	very low	NA	NA	NA
	low	moderate	very low	very low	moderate*	very low	low	very low	low
	low	very low	very low	very low	very low	NA	very low	NA	NA
	very low	low	very low	very low	low	low	very low	NA	NA
	low	low	very low	very low	low	very low	very low	low	very low
	moderate	low	very low	low	low	NA	NA	NA	NA
	low	moderate	NA	low	low	very low	low	NA	very low
	NA	low	NA	low	very low	very low	low	NA	NA
	low	very low	low	low	very low	very low	NA	very low	low
	NA	NA	NA	very low	very low	NA	NA	NA	NA
	very low	low	very low	NA	very low	NA	very low	NA	NA
	very low	very low	very low	NA	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA	NA	NA	NA	NA
	low	low	low	low	high	low	very low	very low	low
	NA	NA	NA	NA	low	very low	NA	very low	very low
	low	very low	NA	NA	moderate	NA	NA	NA	NA
	NA	NA	NA	NA	NA	NA	NA	NA	NA
	NA	very low	NA	NA	very low	NA	NA	NA	NA
	low	very low	NA	NA	very low	NA	NA	NA	low

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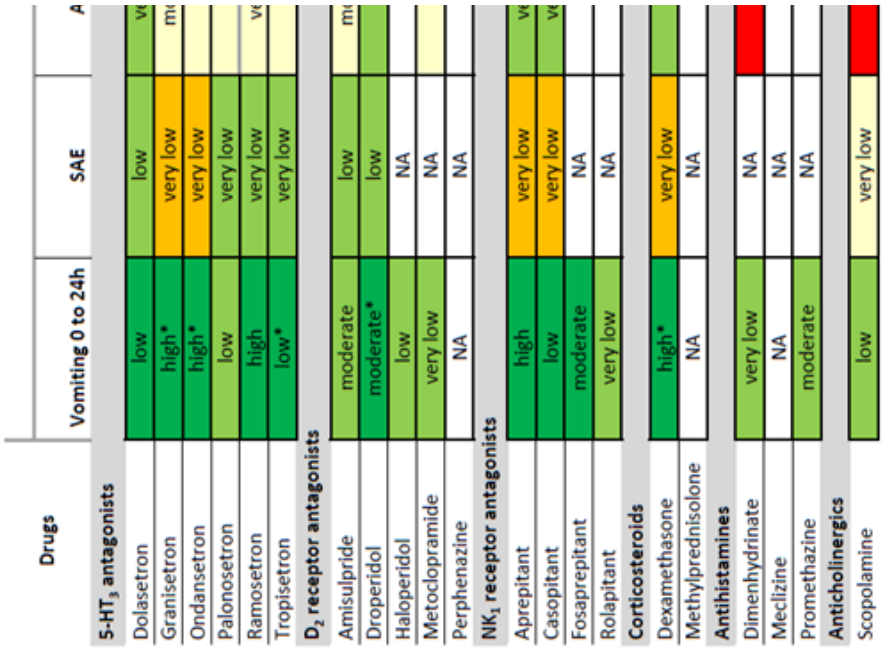
Figure 7. (Continued)



Primary outcomes

Vomiting within 24 hours postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of vomiting

Pairwise meta-analyses for vomiting comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for amisulpride (Analysis 1.1), aprepitant (Analysis 2.1), dexamethasone (Analysis 3.1), dimenhydrinate (Analysis 4.1), dolasetron (Analysis 5.1), droperidol (Analysis 6.1), granisetron (Analysis 7.1), haloperidol (Analysis 8.1), metoclopramide (Analysis 10.1), ondansetron (Analysis 11.1), palonosetron (Analysis 12.1), promethazine (Analysis 14.1), ramosetron (Analysis 15.1), rolapitant (Analysis 16.1), scopolamine (Analysis 17.1), and tropisetron (Analysis 18.1). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, not applicable (NA)).

Primary analysis of vomiting: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome vomiting (24 hours) are available in an online repository (Supplementary Files-1-vomiting 24 *; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

In total, 283 RCTs including 50,907 participants were eligible for the network meta-analysis of vomiting within 24 hours postoperatively. Three studies (1%) have reported zero events in all study arms. One study was not connected to the network and was excluded from the following analyses: Bergese 2016—comparison: aprepitant-dexamethasone-promethazine versus ondansetron-dexamethasone-promethazine. The network geometry of the remaining 282 studies including 50,812 participants with 572 pairwise comparisons due to multi-arm studies included 65 different treatments (nodes) (Figure 8). Of the 65 treatments, 36 were drug combinations (32 times: a two-fold combination; three times: three-fold; once: four-fold), 28 were single drugs, and one was placebo or no treatment. The most commonly studied comparisons included ondansetron (k = 77, with k = number of studies), dexamethasone (k = 43), droperidol (k = 41), metoclopramide (k = 21), and granisetron (k = 16), all compared to placebo. Of all single drugs of direct interest included in the network of vomiting, two drugs, namely, fosaprepitant (k = 3) and amisulpride (k = 2), were connected only to ondansetron and placebo, respectively.

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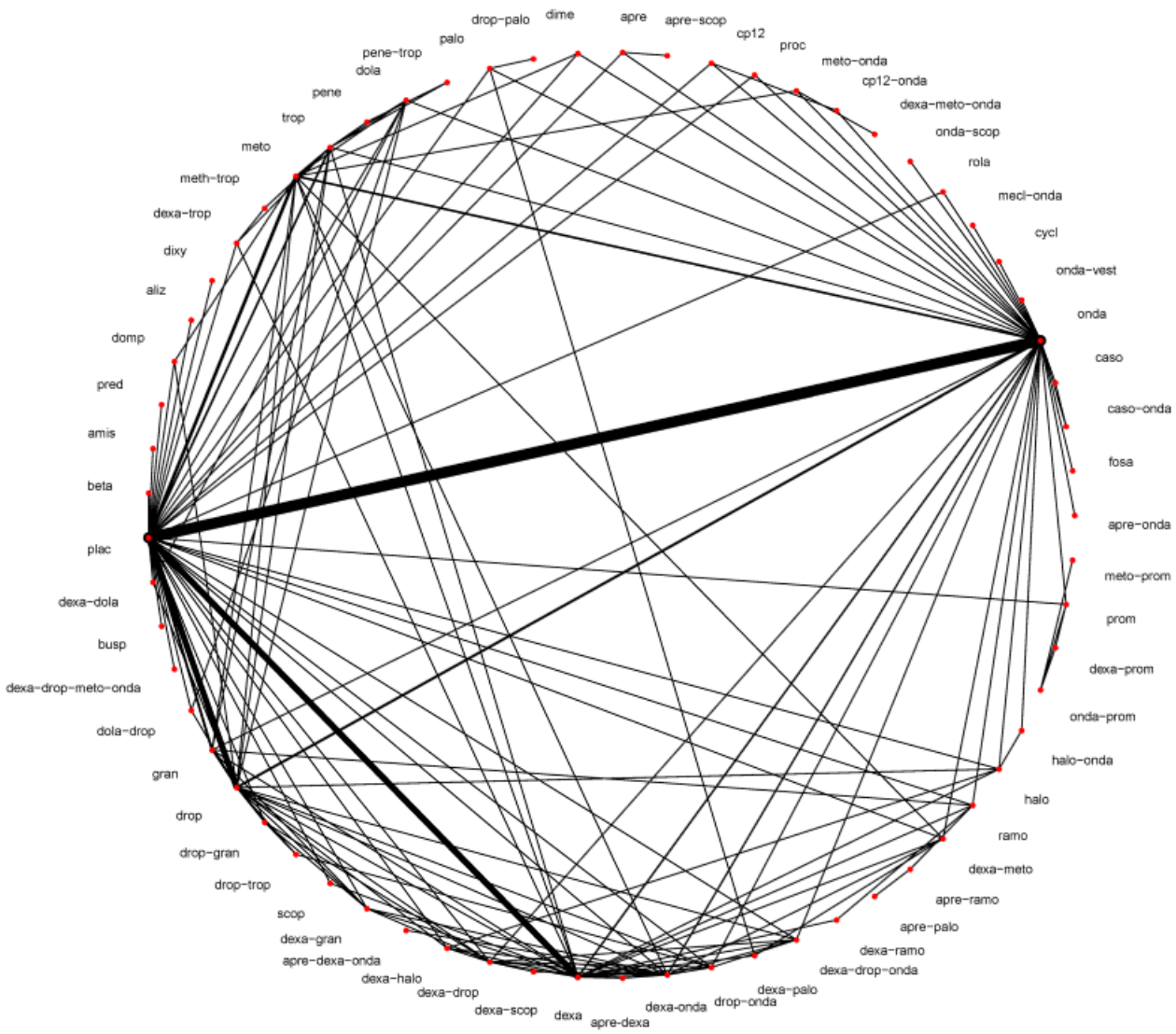
Figure 8. Network geometry of eligible comparisons for postoperative vomiting within 24 hours after surgery. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 65 different treatments, 2080 comparisons are possible, and the results of all network estimates are available in the online repository. For 130 of 2080 comparisons, direct and indirect evidence was available, whereas for 27 comparisons, only direct evidence was available, and for 1923 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio (RR) with 95% confidence interval (CI)) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 9. In terms of preventing vomiting within 24 hours, 10 out of 28 single drugs showed important benefit (95% CI upper boundary < 0.8) compared to placebo, with RRs ranging between 0.06 (95% CI 0.02 to 0.21) for fosaprepitant and 0.61 (95% CI 0.54 to 0.69) for droperidol. Amongst the most effective single drugs of direct interest with important benefit for preventing vomiting compared to placebo in decreasing order according to P scores were fosaprepitant, casopitant, aprepitant, ramosetron, granisetron, dexamethasone, tropisetron, ondansetron, dolasetron, and droperidol. Fosaprepitant, the most effective drug in the network meta-analysis, was poorly connected to the network, with only three studies comparing fosaprepitant to ondansetron. Fourteen single drugs (CP-122,721, alizapride, dimenhydrinate,

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promethazine, rolapitant, prednisolone, prochlorperazine, dixyrazine, haloperidol, scopolamine, palonosetron, amisulpride, penehyclidine, metoclopramide) showed benefit, and four drugs (cyclizine, betamethasone, domperidone, buspirone) showed no or minimal effect; all treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs compared to placebo ranged between RR 0.06 (95% CI 0.02 to 0.21) for fosaprepitant and RR 1.08 (95% CI 0.54 to 2.15) for buspirone. Of the drug combinations, 29 out of 36 drug combinations showed important benefit compared to placebo (95% CI upper boundary < 0.8), with RRs ranging between 0.01 (95% CI 0.00 to 0.19) for aprepitant-palonosetron and 0.47 (95% CI 0.28 to 0.78) for ondansetron-scopolamine. Six drug combinations showed benefit associated with uncertainty compared to placebo, and one combination (metoclopramide-promethazine) showed no or minimal effect associated with uncertainty. Treatment effects of drug combinations compared to placebo ranged between RR 0.01 (95% CI 0.00 to 0.19) for aprepitant-palonosetron and RR 1.04 (95% CI 0.17 to 6.45) for metoclopramide-promethazine.

Figure 9. Forest plot of network meta-analysis of all trials for postoperative vomiting within 24 hours after surgery. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of

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equivalence (RR = 0.8 to 1.25). Treatments are ranked according to efficacy based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.

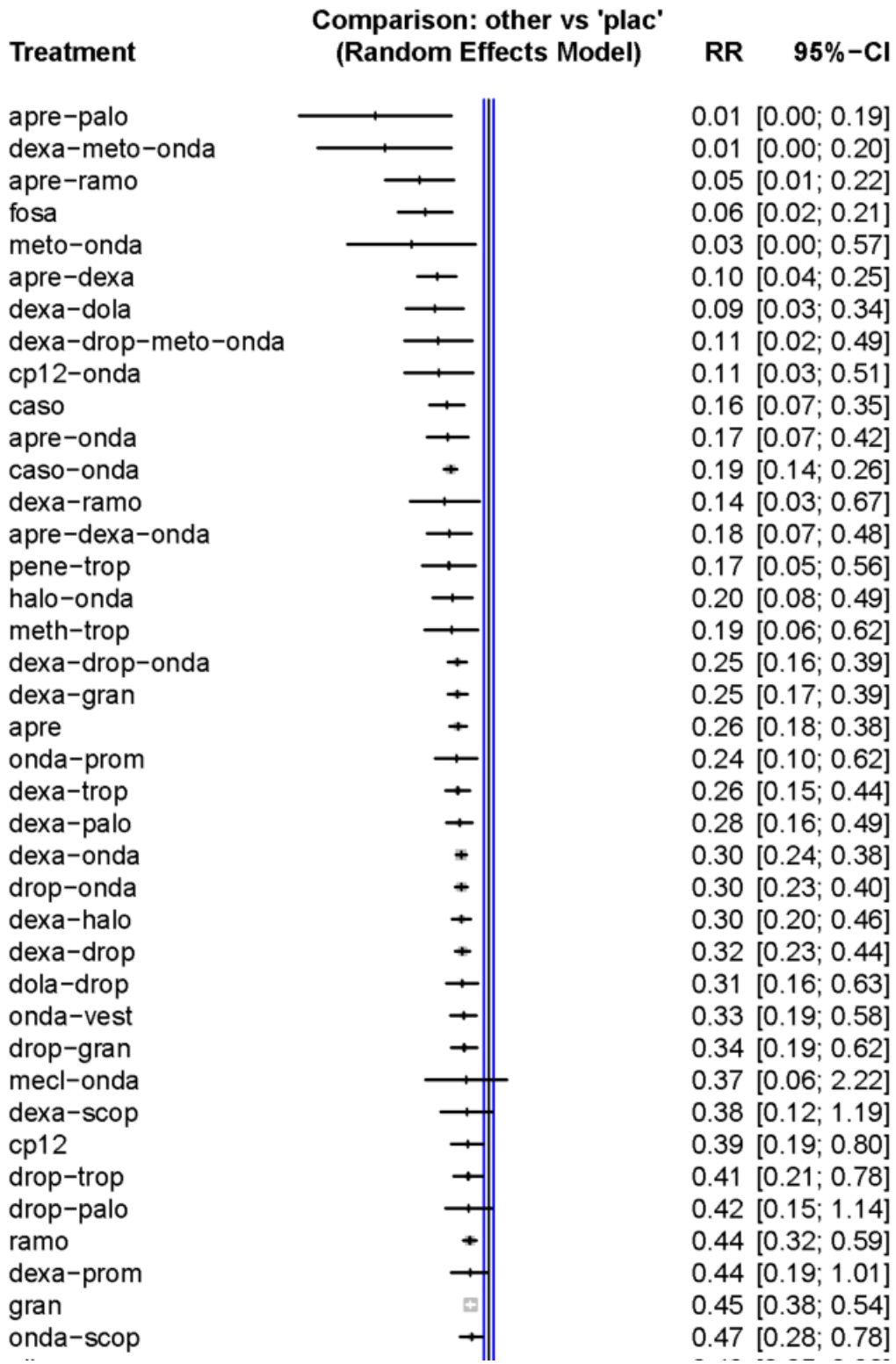

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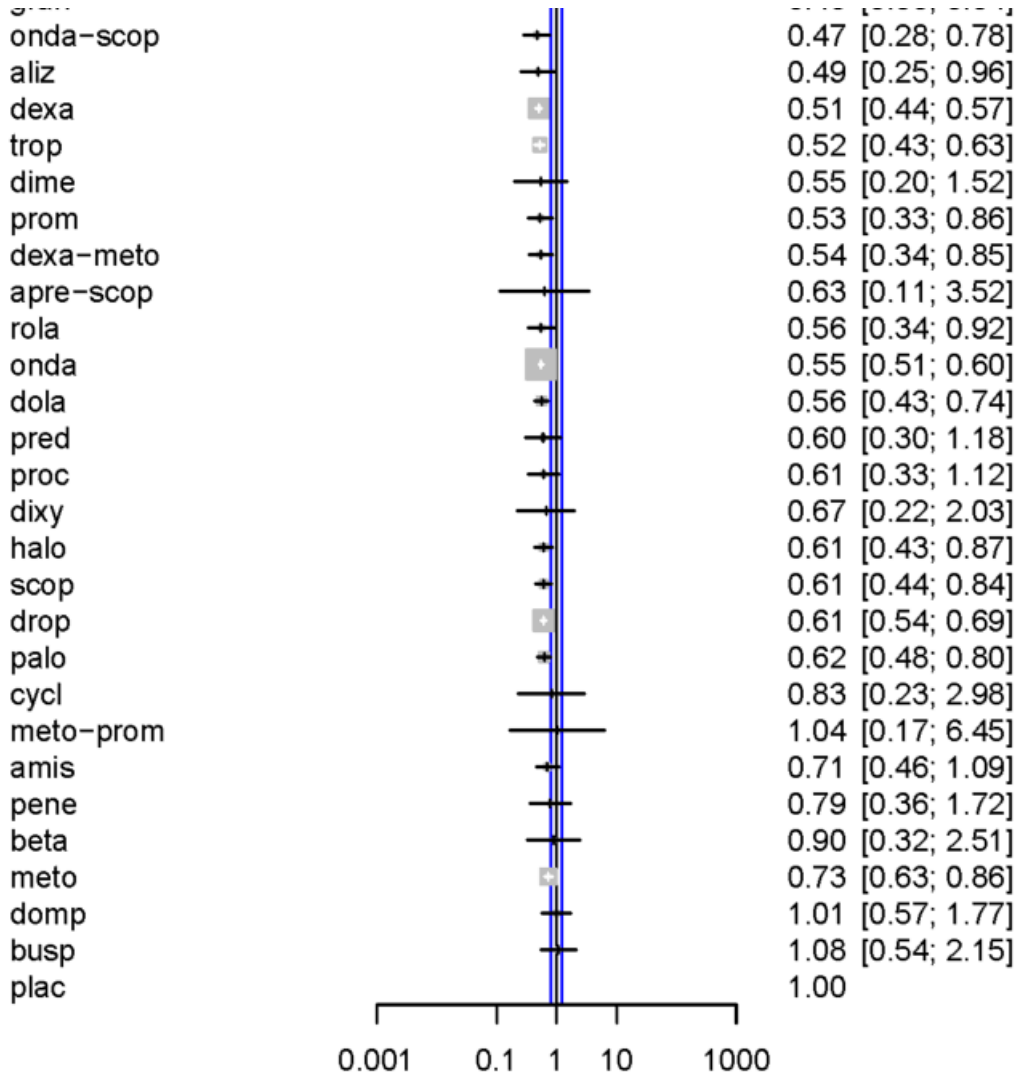
Figure 9. (Continued)



The estimated value of between-study variance for the network meta-analysis of vomiting was 0.061 (tau²) (I^2 = 45.3%). For the random-effects model, there was both large heterogeneity within designs (Q = 347.44, 179 degrees of freedom (df), P < 0.0001) and inconsistency between designs (Q = 262.98, df = 155, P < 0.0001). When the full random-effects design-by-treatment interaction model was used, there was no evidence of residual statistical inconsistency, which means that differences in treatment effects between designs are sufficient to explain all inconsistency (Q = 162.45, df = 155, P = 0.33). Clinically relevant heterogeneity for relevant comparisons (single drugs of direct interest compared to placebo) was detected for ondansetron, tropisetron, dolasetron, droperidol, amisulpride, and dexamethasone. In these cases, 95% prediction intervals (PIs) of treatment estimates included different clinical implications compared to 95% CIs. Splitting direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed disagreement (direct versus indirect) for two out of 130 comparisons, namely, dexamethasone versus ondansetron (P = 0.044) and dexamethasone-ondansetron versus placebo (P = 0.02). Clinically relevant incoherence for direct and indirect treatment estimates of single drugs of direct interest compared to placebo was found for dolasetron, haloperidol, metoclopramide, and dimenhydrinate.

Sensitivity analyses of vomiting

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of vomiting: risk of bias

For vomiting 0 to 24 hours, 44 (16%) of 282 studies were rated as high risk of overall bias, 153 (54%) studies as unclear, and 85 (30%) as low. The sensitivity network meta-analysis including only studies at low risk of bias revealed a connected network with 83 studies, excluding Dabbous 1998 (ondansetron-promethazine versus metoclopramide-

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promethazine) and DeOliveira 2011 (metoclopramide-ondansetron versus dexamethasone-metoclopramide-ondansetron) due to lack of connection, with a total of 39 treatments including placebo. Eighteen out of 39 treatments were single drugs, with seven showing important benefit compared to placebo, including the following drugs in decreasing order according to P scores: fosaprepitant (RR 0.07, 95% CI 0.02 to 0.26); and aprepitant, ramosetron, dexamethasone, granisetron, droperidol, and ondansetron (RR 0.58, 95% CI 0.47 to 0.73). Of the single drugs of direct interest included in the primary network meta-analysis, casopitant, rolapitant, dimenhydrinate, and scopolamine were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. In contrast to the treatment effects in the primary network meta-analysis, the benefit of tropisetron (RR 0.73, 95% CI 0.38 to 1.40) and dolasetron (RR 0.46, 95% CI 0.26 to 0.82) was uncertain, and uncertainty of the benefit of palonosetron (RR 0.84, 95% CI 0.38 to 1.88) and metoclopramide (RR 0.87, 95% CI 0.58 to 1.30) was increased further. The estimated value of between-study variance for the sensitivity network meta-analysis of vomiting was 0.089 (tau^2) (I^2 = 40.3%).

Sensitivity analysis of vomiting: imbalance in baseline details and/or risk factors for PONV in study participants

We assessed studies with imbalance in baseline details and/or risk factors for PONV between study arms as having high risk of other bias. For vomiting 0 to 24 hours, 38 (13%) of 282 studies were rated as high risk of other bias, 200 (71%) studies as unclear risk of other bias, and 44 (16%) as low risk of other bias. The network graph and the forest plot of the sensitivity meta-analysis including studies at low risk of other bias are shown in the online repository with 29 treatments, including placebo. Thirteen treatments were single drugs, with five showing important benefit compared to placebo: fosaprepitant (RR 0.06, 95% CI 0.01 to 0.25); and granisetron, ramosetron, tropisetron, and ondansetron (RR 0.52, 95% CI 0.35 to 0.76). In contrast to the treatment effects of the primary network meta-analysis, the benefit of dolasetron (RR 0.44, 95% CI 0.24 to 0.83), droperidol (RR 0.56, 95% CI 0.32 to 0.97), and dexamethasone (RR 0.64, 95% CI 0.45 to 0.90) was uncertain, and uncertainty of the benefit of palonosetron (RR 0.67, 95% CI 0.31 to 1.45), metoclopramide (RR 0.53, 95% CI 0.22 to 1.28), and haloperidol (RR 0.68, 95% CI 0.28 to 1.65) was increased further. Amisulpride, aprepitant, casopitant, dimenhydrinate, promethazine, and scopolamine were not included in the sensitivity network meta-analysis due to lack of studies with low risk of other bias. The estimated value of between-study variance for this sensitivity network meta-analysis of vomiting was 0.113 (tau^2) (I^2 = 44.1%).

Sensitivity analysis of vomiting: studies with PONV-related primary outcome(s)

In total, 150 (54%) of 282 studies have defined a PONV-related primary outcome in their published study report. The network of this sensitivity analysis consisted of 53 treatments including placebo, with 23 single-drug treatments. Ten single drugs compared to placebo showed important benefits in this sensitivity analysis, which were robust compared to those of the primary analysis. Promethazine was not included in the sensitivity analysis. The estimated value of between-study variance for this sensitivity network meta-analysis of vomiting was 0.0295 (tau^2) (I^2 = 36.8%).

Sensitivity analysis of vomiting: funding source

Fifty-five (20%) of 282 studies were reported to be funded by industry sources, 46 (16%) studies were funded by non-industrial resources, and 181 (64%) studies provided no information on funding source. Two sensitivity analyses—one for industry-funded and one for non-industry-funded studies—were performed. The network of the sensitivity analysis including only industry-funded studies consisted of 32 treatments including 17 single drugs and placebo. Compared to the primary analysis, treatment effects for five out of 17 single drugs (granisetron, droperidol, dolasetron, dexamethasone, metoclopramide) were not robust. Granisetron (RR 0.57, 95% CI 0.34 to 0.94), droperidol (RR 0.64, 95% CI 0.48 to 0.86), dolasetron (RR 0.66, 95% CI 0.38 to 1.13), and dexamethasone (RR 0.73, 95% CI 0.53 to 0.99) showed benefit associated with uncertainty compared to placebo. Metoclopramide (RR 1.06, 95% CI 0.62 to 1.81) showed no or minimal effect associated with uncertainty compared to placebo. The network of the sensitivity analysis including only non-industry-funded studies consisted of 25 treatments including 13 single drugs and placebo. Compared to the primary analysis, treatment effects of eight out of 13 single drugs (promethazine, palonosetron, tropisetron, dolasetron, granisetron, aprepitant, droperidol, ramosetron) in the sensitivity analysis were not robust. Promethazine (RR 0.26, 95% CI 0.09 to 0.78) and palonosetron (RR 0.37, 95% CI 0.19 to 0.72) showed important benefit compared to placebo. Tropisetron (RR 0.52, 95% CI 0.21 to 1.29), dolasetron (RR 0.54, 95% CI 0.32 to 0.88), granisetron (RR 0.56, 95% CI 0.34 to 0.93), aprepitant (RR 0.59, 95% CI 0.23 to 1.55) and droperidol (RR 0.66, 95% CI 0.51 to 0.85) showed benefit associated with uncertainty compared to placebo. Ramosetron (RR 0.81, 95% CI 0.36 to 1.83) showed no or minimal effect associated with uncertainty compared to placebo.

Casopitant, scopolamine, rolapitant, and amisulpride were represented only in the sensitivity analysis including industry-funded studies, and fosaprepitant, promethazine, haloperidol, and ramosetron only in the sensitivity analysis including non-industry-funded studies, respectively. Nine single drugs were included in both sensitivity analyses, with no differences in treatment effects for granisetron, ondansetron, dolasetron, and droperidol; more favourable results for aprepitant and tropisetron in industry-funded studies; and more favourable results for dexamethasone, palonosetron, and metoclopramide in non-industry-funded studies. For studies investigating dimenhydrinate, the funding source was not specified.

Reporting bias (vomiting)

Ten direct pair-wise comparisons included 10 or more studies for which small-study effects such as reporting or publication bias were investigated: ondansetron, dexamethasone, droperidol, metoclopramide, granisetron, and tropisetron were compared to placebo; and droperidol, metoclopramide, dexamethasone, and dexamethasone-ondansetron were compared to ondansetron. For all comparisons, funnel plots with interpretation, results of the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. According to explorative analyses, we suspected publication bias for the comparisons droperidol versus placebo (P = 0.005) and metoclopramide versus ondansetron (P = 0.01). Small P values when the arcsine test was used to detect funnel plot asymmetry were also found for ondansetron versus placebo (P = 0.01), dexamethasone versus placebo (P =0.0164), and dexamethasone

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versus ondansetron (P = 0.06). Contour-enhanced funnel plots suggested asymmetry for dexamethasone, granisetron, and ondansetron versus placebo. However, we did not suspect relevant publication bias for these comparisons because trim and fill sensitivity analysis did not change the conclusion with respect to the range of equivalence. Asymmetry may have been due to other factors such as heterogeneity (see "Certainty of evidence: vomiting").

Subgroup analysis of vomiting: dose effects

To account for the treatment effect modifier dose, we performed a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. We restricted splitting of doses to single drugs.

First, we conducted a network meta-analysis including single drugs only (and excluding combination treatments) with 230 RCTs and 29 treatments including placebo. The network was well connected, and effect estimates as well as the ranking order of drugs with placebo as comparator were comparable to the primary analysis, including combination prophylaxis. The estimated value of between-study variance for the network meta-analysis of single drugs for vomiting was 0.061 (tau^2) (I^2 = 48.3%).

Second, we conducted the subgroup analysis on dose for the network of single drugs only. We split the following drugs into dose categories: amisulpride, aprepitant, dexamethasone, dolasetron, droperidol, granisetron, haloperidol, ondansetron, palonosetron, promethazine, ramosetron, rolapitant, and tropisetron. For casopitant, dimenhydrinate, and metoclopramide, only one dose category (low, recommended, or high) was available for the subgroup analysis. Drugs without any dose recommendation according to Table 1 (fosaprepitant, scopolamine) and drugs not of direct interest (alizapride, betamethasone, buspirone, CP-122,721, cyclizine, dixyrazine, domperidone, penehyclidine, prednisolone, prochlorperazine) were included in the analysis and were lumped together, irrespective of the doses being analysed, in a category labelled 'NA'. We excluded six studies from the subgroup analysis because they were not attributable to one of the three dose categories (Eberhart 2006; Heidari 2015b; Huseyinoglu 2016; Jakobsson 1999; Phillips 1993; Verhasselt 1988). We split the subgroup network meta-analysis with 224 studies and 29 treatments including placebo into 50 nodes with dose categories, and this is presented in the online repository. In ranking of drugs according to efficacy with placebo as the comparator for higher or recommended doses of drugs ranked higher than lower doses, however, most of the 95% CIs were overlapping between different dose categories of the same drug. For dexamethasone, droperidol, granisetron, ondansetron, rolapitant, and tropisetron, the 95% CIs of the low doses showed uncertain benefit in contrast to recommended and/or high doses of the same drug.

We have summarized the most commonly used dosages, routes, and time points of administration of single drugs of direct interest for the primary outcome vomiting in Table 3.

Additivity of dose categories (vomiting)

A network meta-analysis with the assumption of additivity of dose categories revealed similar results as the standard network meta-analysis model when point estimates and 95% CIs were compared, suggesting additive dose effects. However, the Q-statistic of the difference between standard and additive network meta-analyses for vomiting suggests that the standard model explained the data better than the additive model (P = 0.03). This may be due to the fact that, for all drugs, the categories high and recommended for the same drug showed similar effect estimates, which generally were more effective than the corresponding low dose categories.

Sensitivity analysis of vomiting: comparability of doses between study arms

In 137 (60%) of 230 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of 15 treatments including placebo. Rolapitant and dimenhydrinate were not included in the sensitivity analysis due to lack of studies with comparable doses between intervention and control arms. Eight single drugs showed important benefit compared to placebo, including casopitant (RR 0.14, 95% CI 0.06 to 0.32); and promethazine, dexamethasone, ramosetron, tropisetron, granisetron, ondansetron, and droperidol (RR 0.60, 95% CI 0.52 to 0.70). Treatment effects were comparable to the primary network meta-analysis with all single drugs, except for promethazine, which showed important benefit in the sensitivity analysis; and for two drugs, aprepitant (RR 0.59, 95% CI 0.23 to 1.55) and dolasetron (RR 0.63, 95% CI 0.45 to 0.87), which showed uncertain benefit compared to placebo. The estimated value of between-study variance for this sensitivity network meta-analysis of vomiting was 0.060 (tau^2) (I^2 = 54.7%).

Additive effects of combinations of treatments (vomiting)

We tested the hypothesis of additivity of the components in combination prophylaxis by comparing the primary standard analysis (k = 282) with a second analysis, which assumes that the effects of combined treatments are additive sums of their components. This assumption is very strong and general, as the analysis assumes additive effects for all components included in the analysis. The Q-statistic of the difference between standard and additive network meta-analyses for vomiting suggests that the standard model explained the data better than the additive model (P = 0.006). On the level of individual comparisons, the additive model shrunk the effects compared to the standard model for aprepitant-palonosetron, aprepitant-ramosetron, dexamethasone-dolasetron, dexamethasone-metoclopramide-ondansetron, dexamethasone-ramosetron, haloperidol-ondansetron, metoclopramide-ondansetron, and penehyclidine-tropisetron. In these cases, effects in the standard model are larger (smaller RR) than expected under the additivity assumption, which may indicate positive interaction of the components. In contrast, the additive model enlarged effects compared to the standard model for aprepitant-dexamethasone-ondansetron, aprepitant-scopolamine, dexamethasone-metoclopramide, dexamethasone-promethazine, and metoclopramide-promethazine. In these cases, effects in the standard model are smaller (larger RR) than expected under the additivity assumption, which may indicate negative interaction of the components. For all other combinations of treatments, especially the combinations used most frequently (dexamethasone-ondansetron, droperidol-ondansetron, dexamethasone-granisetron), effects of standard and additive models were comparable, suggesting additive effects of the single components.

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Certainty of evidence: vomiting

The certainty of evidence of treatment estimates for vomiting evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 2).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for vomiting 0 to 24 hours ranged from low to high (Summary of findings 2). Ramosetron (RR 0.44, 95% CI 0.32 to 0.59) reduces vomiting compared to placebo with high-certainty evidence. The certainty of evidence for ondansetron (RR 0.55, 95% CI 0.51 to 0.60) and granisetron (RR 0.45, 95% CI 0.38 to 0.54), which also reduce vomiting compared to placebo, was also rated as high. However, high certainty of evidence applies to recommended and high doses of ondansetron and granisetron because low doses showed no clinically important benefit. Tropisetron (RR 0.52, 95% CI 0.43 to 0.63) and dolasetron (RR 0.56, 95% CI 0.43 to 0.74) may reduce vomiting compared to placebo, with low-certainty evidence for tropisetron (serious concerns for study limitation) and dolasetron (study limitation, heterogeneity-incoherence). Low certainty of evidence for tropisetron is restricted to recommended and high doses. Palonosetron (RR 0.62, 95% CI 0.48 to 0.80) may reduce vomiting, for which the certainty of evidence is low (study limitation, imprecision).

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for vomiting 0 to 24 hours ranged from very low to moderate (Summary of findings 2). Droperidol (RR 0.61, 95% CI 0.54 to 0.69) probably reduces vomiting, with moderate-certainty evidence (publication bias-heterogeneity). However, moderate certainty of evidence applies to recommended and high doses of droperidol. Amisulpride (RR 0.71, 95% CI 0.46 to 1.09), with direct evidence only, probably reduces vomiting, with moderate-certainty evidence (imprecision-heterogeneity). Haloperidol (RR 0.61, 95% CI 0.43 to 0.87) may reduce vomiting, with low-certainty evidence (imprecision, incoherence). We are uncertain whether metoclopramide (RR 0.73, 95% CI 0.63 to 0.86) reduces vomiting due to very low-certainty evidence (study limitation, imprecision, incoherence). No studies reporting vomiting were available for perphenazine.

For relevant NK_1 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for vomiting 0 to 24 hours ranged from very low to high (Summary of findings 2). Fosaprepitant (RR 0.06, 95% CI 0.02 to 0.21), casopitant (RR 0.16, 95% CI 0.07 to 0.35), and aprepitant (RR 0.26, 95% CI 0.18 to 0.38) were the most effective drugs for vomiting compared to placebo in the current network meta-analysis. Aprepitant reduces vomiting, with high-certainty evidence. Fosaprepitant, with indirect evidence only, probably reduces vomiting, with moderate-certainty evidence (incoherence). Casopitant, also with indirect evidence only, may reduce vomiting, with low-certainty evidence (study limitation, incoherence). We are uncertain whether rolapitant (RR 0.56, 95% CI 0.34 to 0.92) reduces vomiting, as the certainty of evidence was very low (serious concerns for study limitation, imprecision).

The only reported corticosteroid was dexamethasone (RR 0.51, 95% CI 0.44 to 0.57), which reduces vomiting, with high-certainty evidence (Summary of findings 2). However, high certainty of evidence applies to recommended and high doses of dexamethasone. No studies reporting vomiting were available for methylprednisolone.

For relevant antihistamines (compared to placebo), the certainty of evidence of network effect estimates for vomiting 0 to 24 hours was moderate and very low (Summary of findings 2). Promethazine (RR 0.53, 95% CI 0.33 to 0.86) probably reduces vomiting, with moderate-certainty evidence (imprecision). We are uncertain whether dimenhydrinate (RR 0.55, 95% CI 0.20 to 1.52) reduces vomiting, as certainty of evidence was very low (study limitation, incoherence, very serious concerns for imprecision). No studies reporting vomiting were available for meclizine.

The anticholinergic scopolamine (RR 0.61, 95% CI 0.44 to 0.84) may reduce vomiting, with low-certainty evidence (study limitation, imprecision) (Summary of findings 2).

SAEs within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of SAEs

Pairwise meta-analyses for SAEs comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for amisulpride (Analysis 1.2), dexamethasone (Analysis 3.2), dolasetron (Analysis 5.2), droperidol (Analysis 6.2), granisetron (Analysis 7.2), ondansetron (Analysis 11.2), palonosetron (Analysis 12.2), ramosetron (Analysis 15.2), scopolamine (Analysis 17.2), and tropisetron (Analysis 18.2). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of SAEs: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome SAEs are available in an online repository (Supplementary Files-2-SAE *; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

Twenty-nine studies with 10,886 participants were eligible for the network meta-analysis of SAEs. Twelve studies (41%) have reported zero events in all study arms. One study was not connected to the network and was excluded from the following analysis: Papadimitriou 2001; comparison: metoclopramide-tropisetron versus metoclopramide. The network of the remaining 28 studies with 52 pair-wise comparisons due to multi-arm studies included 22 treatments (nodes), of which placebo (k = 26) and ondansetron (k = 14) were the most frequent comparators (Figure 10). Of the 22 treatments, eight were two-fold drug combinations, 13 were single drugs, and one was placebo or no treatment. The most common comparisons with three studies each were between ondansetron versus placebo, dexamethasone versus placebo, dolasetron versus placebo, palonosetron versus placebo, and casopitant-ondansetron versus ondansetron. Of all single drugs of direct interest included in the network of SAEs, amisulpride, dolasetron, palonosetron, and scopolamine were connected only to placebo, and aprepitant was connected only to ondansetron.

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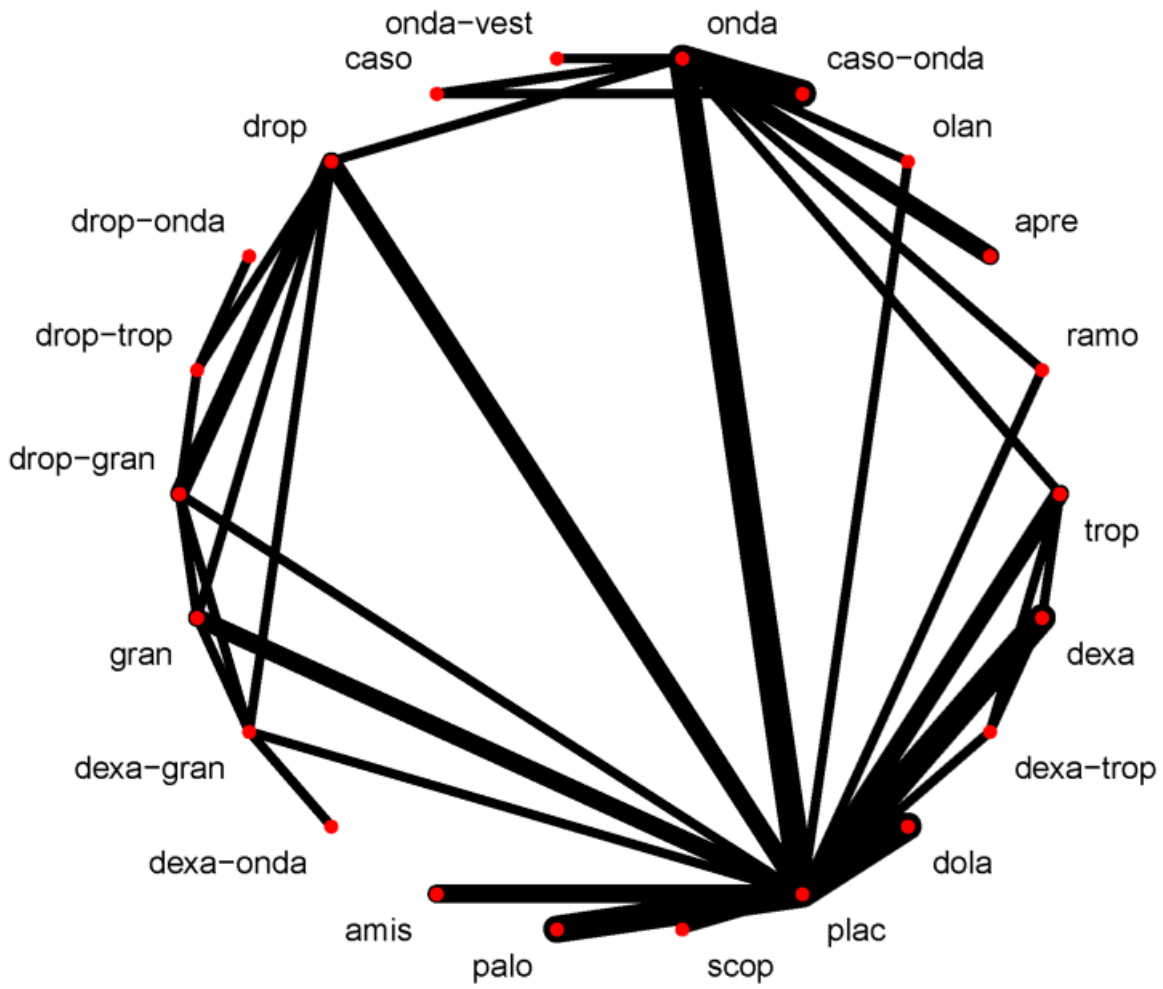
Figure 10. Network geometry of eligible comparisons for serious adverse events (SAE) within 7 days postoperatively. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 22 different treatments, 231 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 27 of 231 comparisons, direct and indirect evidence was available, whereas for nine comparisons, only direct evidence was available, and for 195 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (RR with 95% CIs) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 11. In terms of reducing the number of participants with SAEs, none of the 21 treatments showed important benefit (95% CI upper boundary < 0.9) or important harm (95% CI lower boundary > 1.11) compared to placebo. Of the 13 single drugs compared to placebo, seven showed benefit (dolasetron, tropisetron, palonosetron, olanzapine, amisulpride, droperidol, ramosetron), one showed no or minimal effect (scopolamine), five showed harm (dexamethasone, granisetron, aprepitant, ondansetron, casopitant), and all 13 treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs compared to placebo ranged between RR 0.31 (95% CI 0.10 to 1.00) for dolasetron and 3.64 (95%

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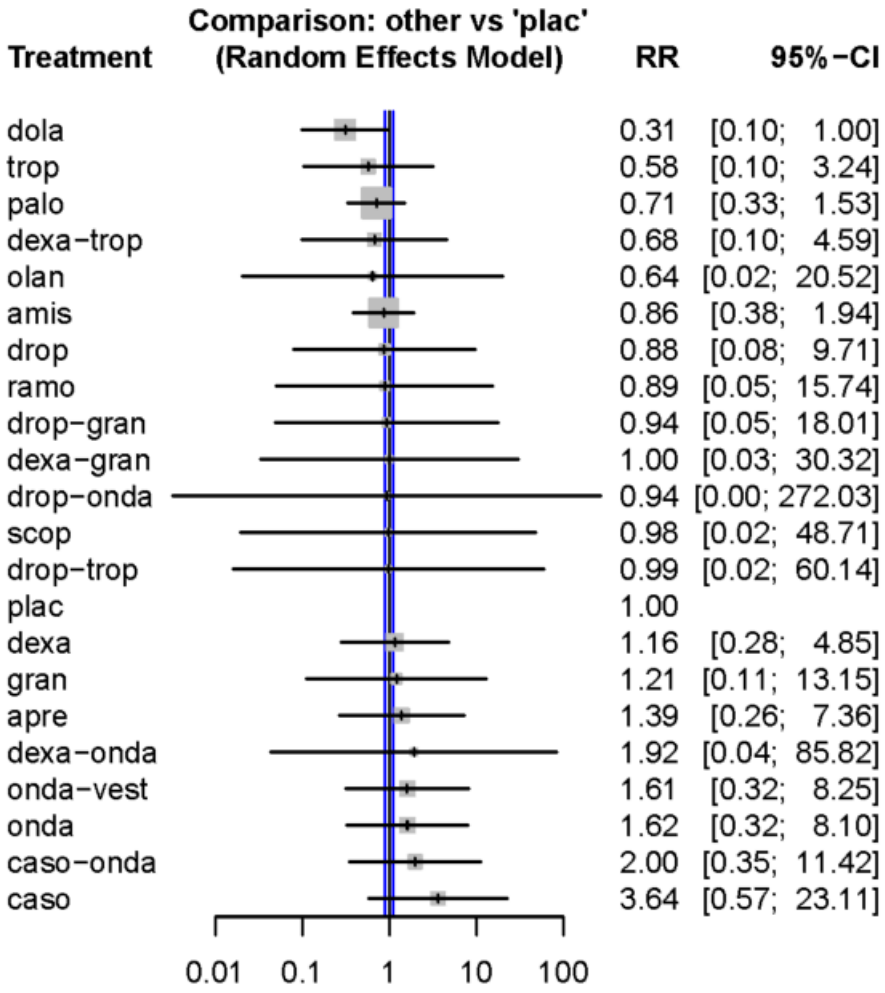
CI 0.57 to 23.11) for casopitant. Of the eight combination treatments, one showed benefit (dexamethasone-tropisetron), four showed no or minimal effect (droperidol-granisetron, dexamethasone-granisetron, droperidol-ondansetron, droperidol-tropisetron), three showed harm (dexamethasone-ondansetron, ondansetron-vestipitant, casopitant-ondansetron), and all eight treatment effects were associated with uncertainty. Treatment effects of drug combinations compared to placebo ranged between RR 0.68 (95% CI 0.10 to 4.59) for dexamethasone-tropisetron and RR 2.00 (95% CI 0.35 to 11.42) for casopitant-ondansetron.

Figure 11. Forest plot of network meta-analysis of all trials for serious adverse events (SAE) within 7 days postoperatively. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to 1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



The estimated value of between-study variance for the network meta-analysis of SAEs was 0 (tau^2) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 3.66, df = 8, P = 0.89) and no inconsistency between designs (Q = 4.49, df = 9, P = 0.88). No clinically relevant heterogeneity for relevant comparisons (single drugs of direct interest compared to placebo) was detectable because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and

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indirect evidence in the network meta-analysis and testing for local inconsistency revealed no relevant disagreement (direct versus indirect) for any of the 27 comparisons. There was no clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo.

Sensitivity analyses of SAEs

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of SAEs: risk of bias

Three (11%) of 28 studies were rated as having high risk of overall bias, 14 (50%) as unclear, and 11 (39%) as low. The sensitivity network meta-analysis including only studies at low risk of bias revealed a poorly connected network, with 11 treatments and 11 studies. Three treatments were two-fold combinations of antiemetic drugs, seven treatments were single drugs, and one was placebo or no treatment. Of the single drugs of direct interest, granisetron, tropisetron, ramosetron, dolasetron, and scopolamine were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Effect estimates of five single drugs (aprepitant, ondansetron, casopitant, dexamethasone, palonosetron) compared to placebo in this sensitivity analysis were not robust when compared to the primary network meta-analysis. Aprepitant, ondansetron, and casopitant with RR 0.23 (95% CI 0.00 to 11.55), RR 0.26 (95% CI 0.01 to 13.12), and RR 0.59 (95% CI 0.01 to 32.74), respectively, showed benefit associated with uncertainty. Dexamethasone and palonosetron showed no or minimal effects, with RR 1.00 (95% CI 0.02 to 49.75) and RR 1.00 (95% CI 0.02 to 49.43), respectively—both associated with uncertainty. The estimated value of between-study variance for the sensitivity network meta-analysis of SAEs was 0 (tau^2) (I^2 = 0%).

Sensitivity analysis of SAEs: risk of bias for monitoring and reporting of SAEs

In a sensitivity network meta-analysis for monitoring and reporting of SAEs, we included only studies that have defined SAEs in the study report according to an accepted international classification system. Only five (18%) of 28 studies were assessed as having low risk of bias for monitoring and reporting of SAEs. The five studies were not connected. Two studies compared either granisetron—Hanaoka 2004—or dexamethasone—Tarantino 2015—to placebo, and three studies from GlaxoSmithKline compared casopitant-ondansetron or casopitant to ondansetron (NKT102245; NKT102260; NKT102552). Compared to the primary analysis, the treatment effect for dexamethasone versus placebo was not robust and showed no or minimal effect associated with uncertainty (RR 1.00, 95% CI 0.02 to 49.75). Casopitant showed harm associated with uncertainty compared to ondansetron (RR 2.25, 95% CI 0.91 to 5.58).

Sensitivity analysis of SAEs: imbalance in baseline details and/or risk factors for PONV in study participants

We assessed studies with an imbalance in baseline details and/or risk factors for PONV between the study arms as having high risk of other bias. For SAEs, three (11%) of 28 studies were rated as high risk of other bias, 18 (64%) as unclear, and seven (25%) as low. The seven studies with low risk of other bias were not connected in one network. Four of these studies with 10 treatments including placebo as comparator were connected in one sub-network. Three other studies from GlaxoSmithKline with ondansetron as comparator were included in the other sub-network (NKT102245; NKT102260; NKT102552). Of the single drugs, dolasetron, aprepitant, scopolamine, and amisulpride were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Compared to the primary analysis, treatment effects for palonosetron, granisetron, droperidol, dexamethasone, all compared to placebo, were not robust and showed no or minimal effect associated with uncertainty.

Sensitivity analysis of SAEs: studies with PONV-related primary outcome(s)

Twenty-two (79%) of 28 studies have defined a PONV-related primary outcome in their published study report. The network of this sensitivity analysis consisted of 18 treatments including placebo (six combination and 11 single drug treatments). Of the single drugs, ramosetron and scopolamine were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. The relative treatment effects of all single drugs compared to placebo were comparable to the primary analysis, with RRs ranging between 0.31 (95% CI 0.10 to 1.00) for dolasetron and 4.07 (95% CI 0.60 to 27.64) for casopitant. The estimated value of between-study variance for this sensitivity network meta-analysis of SAE was 0 (tau^2) (I^2 = 0%).

Sensitivity analysis of SAEs: funding source

Seventeen (61%) of 28 studies were funded by industry, six (21%) were funded by non-industrial resources, and for another five studies (18%), information on funding source was not provided. Two sensitivity analyses—one for industry-funded and one for non-industry-funded studies—were performed. The network of the sensitivity analysis including only industry-funded studies consisted of 16 studies with 12 treatments, including nine single drugs and placebo. One study was not connected to the network and was excluded from the analyses (Gan 2005; comparison: dexamethasone-granisetron versus dexamethasone-ondansetron). Compared to the primary analysis, of the nine single drugs, treatment effects of casopitant and tropisetron compared to placebo were not robust. Casopitant (RR 38.81, 95% CI 1.95 to 770.47) showed important harm compared to placebo. However, only indirect evidence was available because casopitant was connected only to ondansetron. Tropisetron (RR 6.50, 95% CI 0.34 to 125.35) showed harm associated with uncertainty compared to placebo. The network of the sensitivity analysis including only studies funded by non-industrial resources consisted of six studies with three combinations, six single drugs, and placebo. Compared to the primary analysis, of the six single drugs, treatment effects of ondansetron, granisetron, dexamethasone, and palonosetron were not robust. Ondansetron (RR 0.38, 0.01 to 14.33) and granisetron (RR 0.70, 0.02 to 26.19) compared to placebo showed benefit, and both dexamethasone (RR 1.00, 95% CI 0.02 to 49.75) and palonosetron (RR 1.00, 95% CI 0.02 to 49.43) showed no or minimal effect compared to placebo; all effects were associated with uncertainty.

Six single drugs were funded only by industry (dolasetron, amisulpride, scopolamine, tropisetron, aprepitant, casopitant), and three solely by non-industrial resources (ramosetron, droperidol, dexamethasone). Three single drugs (ondansetron, granisetron, and palonosetron) were investigated in studies funded

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by either of the sources, and treatment effects were not robust in either analysis. Ondansetron and granisetron showed results that were more favourable in non-industry-funded studies than in industry-funded studies. Palonosetron showed results that were more favourable in industry-funded studies than in non-industry-funded studies. The comparison of results from both sensitivity analyses is associated with high uncertainty and should be viewed with caution due to the small number of included studies.

Reporting bias (SAE)

None of the direct pair-wise comparisons included 10 or more studies. Therefore, analyses investigating reporting or publication bias were not performed.

Subgroup analysis of SAEs: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis including single drugs only (and excluding combination treatments) with 22 studies and 14 treatments including placebo was conducted. Network geometry, effect estimates, and the ranking order of drugs with placebo as comparator were comparable to the primary analysis, including combination prophylaxis. The estimated value of between-study variance for the network meta-analysis of single drugs for SAEs was 0 (tau^2) (I^2 = 0%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The following drugs were split into dose categories: amisulpride, aprepitant, dolasetron, ondansetron, palonosetron, and ramosetron. For casopitant, dexamethasone, droperidol, granisetron, and tropisetron, only one dose category was available for subgroup analysis. Drugs without any dose recommendation according to Table 1 (scopolamine) and drugs not of direct interest (olanzapine) were included in the analysis and were lumped together, irrespective of the doses being analysed, in the category 'NA'. Three studies—Diemunsch 1998; Eberhart 2006; Warriner 1997—and one arm of Lee 2008a (0.1 mg oral ramosetron) were excluded from the subgroup analysis because they were not associated with one of the three dose categories. The network was poorly connected, with 19 studies and 14 treatments split into 21 nodes with dose categories. Ranking of drugs according to safety with placebo as comparator is presented in the online repository. All available dose categories for dolasetron and palonosetron compared to placebo showed benefit associated with uncertainty. For aprepitant, all dose categories compared to placebo showed harm associated with uncertainty. Amisulpride used as recommended or low doses showed benefit, high doses showed harm, and all treatment effects were associated with uncertainty. Low doses of ramosetron showed no or minimal effect and recommended doses showed harm, and both treatment effects were associated with uncertainty. Recommended doses of ondansetron showed harm, high doses showed benefit, and both treatment effects were associated with high uncertainty. Recommended doses of casopitant (RR 42.47, 95% CI 1.98 to 910.14) showed important harm. However, evidence for these results was restricted to only one study directly comparing recommended doses of casopitant and ondansetron. Casopitant was not otherwise connected in the network.

Additivity of dose categories (SAEs)

A network meta-analysis with the assumption of additivity of the dose categories revealed no difference between standard and additive models (P = 0.34), suggesting additive dose effects. The analysis was based on a few studies that currently make reliable statements on additive effects of drug doses impossible.

Sensitivity analysis of SAEs: comparability of doses

In 13 (46%) of 28 studies investigating single drugs, comparable doses of the antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that could be assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis was poorly connected, consisting of 11 treatments including placebo, which limited evidence. Aprepitant and scopolamine were not included in the sensitivity analysis due to lack of studies with comparable doses. Effect estimates of five single drugs (casopitant, droperidol, tropisetron, ramosetron, dexamethasone) compared to placebo in this sensitivity analysis were not robust when compared to the network meta-analysis including single drugs only. Casopitant (RR 42.47, 95% CI 1.98 to 910.14) showed important harm. Droperidol, tropisetron, and ramosetron, with RR 1.14 (95% CI 0.03 to 41.28), RR 6.50 (95% CI 0.34 to 125.35), and RR 17.25 (95% CI 0.14 to 2135.86), respectively, showed harm associated with high uncertainty. Dexamethasone showed no or minimal effect, with RR 1.01 (95% CI 0.06 to 15.98) associated with uncertainty. The estimated value of between-study variance for this sensitivity network meta-analysis of SAEs was 0 (tau^2) (I^2 = 0%).

Additive effects of combinations of treatments (SAEs)

We tested the hypothesis of additivity of the components in combination prophylaxis by comparing the primary standard analysis (k = 28) with a second analysis, which assumes that the effects of combined treatments are additive sums of their components. We detected no differences between standard and additive models (P = 0.89), suggesting additive dose effects. However, the analysis was based on only a few studies that currently make reliable statements on additive effects of drug combinations impossible.

Certainty of evidence: SAEs

Certainty of evidence of treatment estimates for the outcome SAEs evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 3).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for the outcome SAEs ranged from very low to low (Summary of findings 3). Dolasetron (RR 0.31, 95% CI 0.10 to 1.00), with direct evidence only, may reduce the number of participants with SAEs compared to placebo, with low-certainty evidence (study limitations, imprecision). The certainty of evidence for all other 5-HT_3 receptor antagonists was assessed as very low. We are uncertain whether ondansetron (RR 1.62, 95% CI 0.32 to 8.10) and granisetron (RR 1.21, 95% CI 0.11 to 13.15) compared to placebo increase the number of participants with SAEs, with very low-certainty evidence (study limitations, very serious concerns for imprecision). We are uncertain whether tropisetron (RR 0.58, 95% CI 0.10 to 3.24) and palonosetron (RR 0.71, 95% CI 0.33 to

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1.53) compared to placebo decrease the number of participants with SAEs, with very low-certainty evidence (study limitations, very serious concerns for imprecision). We are uncertain whether ramosetron (RR 0.89, 95% CI 0.05 to 15.74) compared to placebo decreases the number of participants with SAEs, with very low-certainty evidence (very serious concerns for study limitations and imprecision). For palonosetron, only direct evidence was available.

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for SAEs was assessed as low (Summary of findings 3). Droperidol (RR 0.88, 95% CI 0.08 to 9.71) and amisulpride (RR 0.86, 95% CI 0.38 to 1.94) may reduce the number of participants with SAEs compared to placebo, with low-certainty evidence (very serious concerns for imprecision). For amisulpride, only direct evidence was available. No studies reporting SAEs were available for metoclopramide, haloperidol, or perphenazine.

For relevant NK_1 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for SAEs was assessed as very low (Summary of findings 3). We are uncertain whether casopitant (RR 3.64, 95% CI 0.57 to 23.11) and aprepitant (RR 1.39, 95% CI 0.26 to 7.36), both with indirect evidence only, increase the number of participants with SAEs compared to placebo, with very low-certainty evidence (study limitation, incoherence, very serious concerns for imprecision). No studies reporting SAEs were available for fosaprepitant and rolapitant.

The only corticosteroid that was included in the network meta-analysis for SAEs was dexamethasone, with very low-certainty evidence. We are uncertain whether dexamethasone (RR 1.16, 95% CI 0.28 to 4.85) increases the number of participants with SAEs compared to placebo (study limitations, very serious concerns for imprecision) (Summary of findings 3). No studies reporting SAEs were available for methylprednisolone.

No studies reporting SAEs were available for relevant antihistamines (compared to placebo) (Summary of findings 3).

For the anticholinergic scopolamine, with only direct evidence, the certainty of evidence was considered as very low (very serious concerns for study limitations and imprecision) (Summary of findings 3). We are uncertain whether scopolamine (RR 0.98, 95% CI 0.02 to 48.71) compared to placebo has no or minimal effects on SAEs.

Any AE within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of any AE

Pairwise meta-analyses of any AE comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for amisulpride (Analysis 1.3), dexamethasone (Analysis 3.3), dolasetron (Analysis 5.3), droperidol (Analysis 6.3), granisetron (Analysis 7.3), metoclopramide (Analysis 10.2), ondansetron (Analysis 11.3), palonosetron (Analysis 12.3), ramosetron (Analysis 15.3), scopolamine (Analysis 17.3), and tropisetron (Analysis 18.3). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of any AE: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome any AE are available in an online repository (Supplementary Files-3-any AE *; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

Sixty-one studies with 93 pair-wise comparisons due to multi-arm studies and 19,423 participants were eligible for the network meta-analysis of any AE. Four studies (7%) have reported zero events in all study arms. The network included 27 treatments (nodes), of which placebo (k = 47) and ondansetron (k = 39) were the most frequent comparators (Figure 12). Of the 27 treatments, 11 were two-fold drug combinations, 15 were single drugs, and one was placebo or no treatment. The most common comparisons were ondansetron (k = 12 studies), dexamethasone (k = 6), granisetron (k = 6), metoclopramide (k = 3), scopolamine (k = 3), and tropisetron (k = 3), all compared to placebo, and casopitant-ondansetron (k = 5) and granisetron (k = 3) compared to ondansetron. Of the single drugs of direct interest, amisulpride, dolasetron, and scopolamine were connected only to placebo, and aprepitant and dimenhydrinate were connected only to ondansetron.

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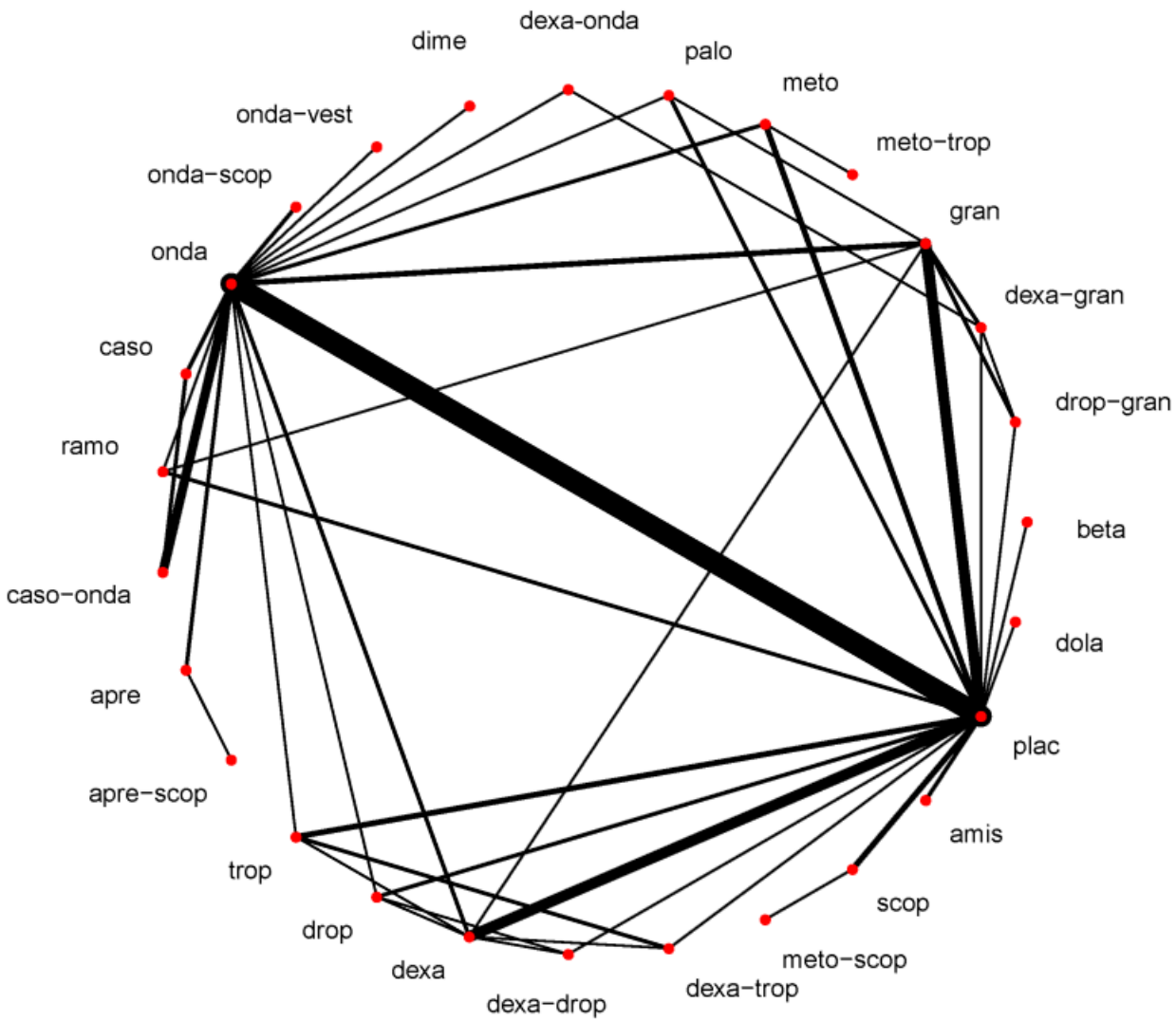
Figure 12. Network geometry of eligible comparisons for any adverse event (any AE) within 7 days postoperatively. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 27 treatments, 351 comparisons are possible, and the results of all network estimates are available in the online repository. For 35 of 351 comparisons, direct and indirect evidence was available, whereas for 12 comparisons, only direct evidence was available, and for 304 comparisons, only indirect evidence was available.

Relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 13. Of the 15 single drugs, scopolamine and dimenhydrinate showed important harm (95% CI lower boundary > 1.11) compared to placebo, with RRs of 2.12 (95% CI 1.71 to 2.64) and 5.70 (95% CI 1.36 to 23.93), respectively. Amisulpride (RR 0.97, 95% CI 0.90 to 1.06) showed no or minimal effect on any AE compared to placebo. Six single treatments showed benefit (betamethasone, dexamethasone, aprepitant, dolasetron, casopitant, droperidol), another six treatments showed no or minimal effect (granisetron, metoclopramide, ondansetron, palonosetron, ramosetron, tropisetron), and all 12 of these treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs compared to placebo ranged between RR 0.09 (95% CI 0.01

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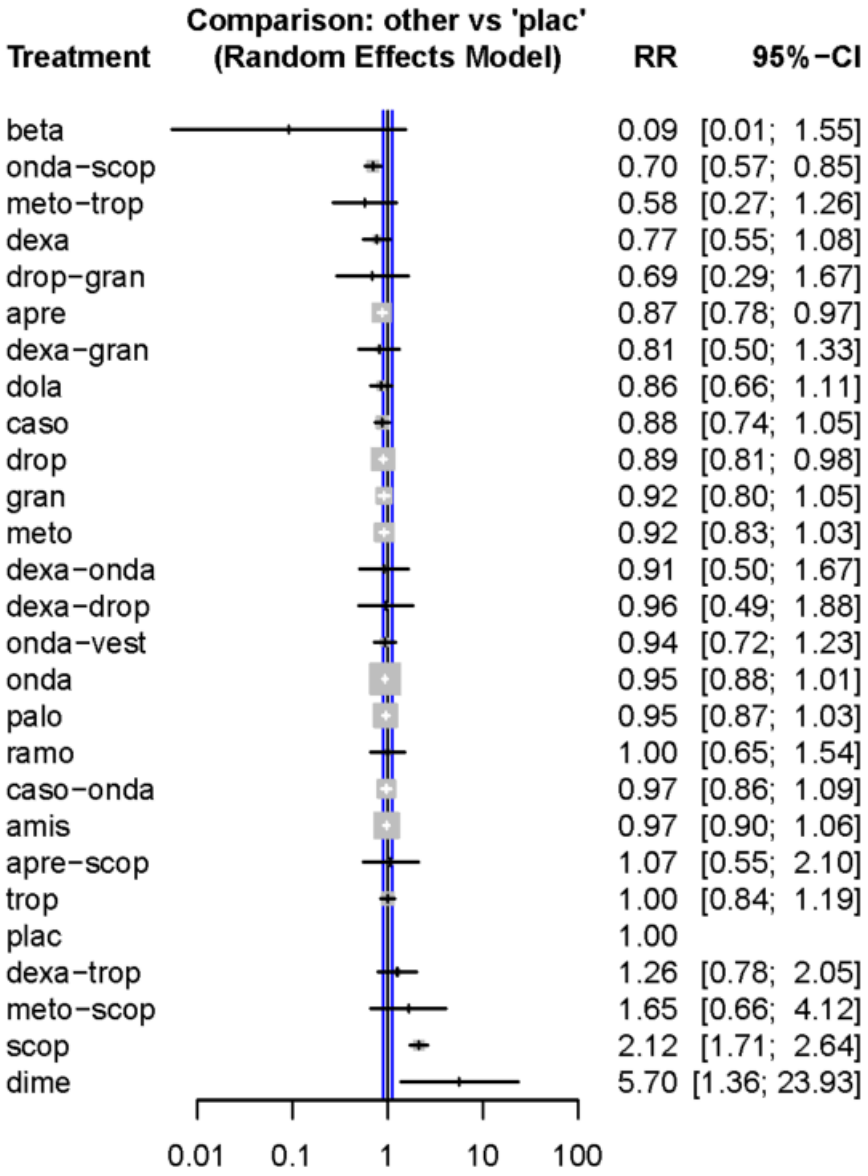
to 1.55) for betamethasone and RR 5.70 (95% CI 1.36 to 23.93) for dimenhydrinate. The only combination treatment showing important benefit compared to placebo (95% CI upper boundary < 0.9) was ondansetron-scopolamine with RR of 0.70 (95% CI 0.57 to 0.85). Of the other combination treatments compared to placebo, three combinations showed benefit (metoclopramide-tropisetron, droperidol-granisetron, dexamethasone-granisetron), five showed no or minimal effect (dexamethasone-ondansetron, dexamethasone-droperidol, ondansetron-vestipitant, casopitant-ondansetron, aprepitant-scopolamine), two showed harm (dexamethasone-tropisetron, metoclopramide-scopolamine), and all treatment effects were associated with uncertainty. Treatment effects of drug combinations compared to placebo ranged between RR 0.70 (95% CI 0.57 to 0.85) for ondansetron-scopolamine and RR 1.65 (95% CI 0.66 to 4.12) for metoclopramide-scopolamine.

Figure 13. Forest plot of network meta-analysis of all trials for any adverse events (any AE) within 7 days postoperatively. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to 1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



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The estimated value of between-study variance for the network meta-analysis of any AE was 0 (tau^2) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 25.27, df = 22, P = 0.28) and no inconsistency between designs (Q = 19.59, df = 28, P = 0.88). Clinically relevant heterogeneity for relevant comparisons (single drugs of direct interest compared to placebo) was detected only for dolasetron because the 95% PI included a different clinical implication compared to the 95% CI. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed no significant disagreement (direct versus indirect) for any of the 35 comparisons. There was no clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo.

Sensitivity analyses of any AE

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of any AE: risk of bias

Nine (15%) of 61 studies were rated as having high risk of overall bias, 31 (51%) as unclear, and 21 (34%) as low. The sensitivity network meta-analysis including only studies at low risk of bias revealed a poorly connected network, including 18 treatments. Six treatments were two-fold combinations of antiemetic drugs, 11 were single drugs, and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis of any AE, dolasetron, palonosetron, dimenhydrinate, and scopolamine were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Of the 11 single drugs, four drugs showed important benefit compared to placebo (aprepitant, casopitant, ondansetron, metoclopramide), with RRs ranging between 0.50 (95% CI 0.30 to 0.82) for aprepitant and 0.54 (95% CI 0.33 to 0.89) for metoclopramide. None of the four drugs showed important benefit compared to placebo in the primary network meta-analysis. Proof of data revealed one small outlier study comparing ondansetron versus placebo with extreme positive effects for ondansetron (Koyuncu 2017). Excluding Koyuncu 2017 and redoing the sensitivity analysis for risk of bias revealed that none of the treatments maintained important benefit compared to placebo. Thus, favourable effects for aprepitant, casopitant, ondansetron, and metoclopramide in the first sensitivity analysis for risk of bias may be due to strong effects reported by Koyuncu 2017.

Comparison of treatment effects of the sensitivity analysis for risk of bias without Koyuncu 2017, and the primary network meta-analysis for any AE revealed seven drugs compared to placebo with non-robust treatment effects (ramosetron, aprepitant, casopitant, droperidol, dexamethasone, ondansetron, metoclopramide). Ramosetron compared to placebo with RR 0.79 (95% CI 0.26 to 2.41) showed benefit with uncertainty. Aprepitant and casopitant compared to placebo, with RR 1.00 (95% CI 0.48 to 2.09) and RR 1.02 (95% CI 0.47 to 2.19), respectively, showed no or minimal effect associated with uncertainty. Droperidol compared to placebo, with RR 1.32 (95% CI 0.64 to 2.72), showed harm associated with uncertainty. For dexamethasone, ondansetron, and metoclopramide, the uncertainty of effect estimates was increased further in the sensitivity analysis compared to the primary network meta-analysis. The estimated value of between-study variance for the sensitivity network meta-analysis of any AE was 0 (tau^2) (I^2 = 0%).

Sensitivity analysis of any AE: risk of bias for monitoring and reporting of any AE

In a sensitivity network meta-analysis for monitoring and reporting of any AE, we included only studies that were assessed as low risk of bias with respect to monitoring and reporting for any AE. We assessed 11 (18%) of 61 studies as having low risk of bias for monitoring and reporting of any AE. The network including only studies at low risk of bias was poorly connected, with two sub-networks that were connected only via the route ondansetron to placebo. Of the single drugs of direct interest, dolasetron, droperidol, metoclopramide, palonosetron, amisulpride, tropisetron, and dimenhydrinate were not included in the sensitivity network meta-analysis due to lack of studies assessed as low risk. Treatment effects of three drugs compared to placebo were not robust in this sensitivity analysis (aprepitant, casopitant, ramosetron). Aprepitant (RR 0.97, 95% CI 0.82 to 1.16) and casopitant (RR 0.99, 95% CI 0.76 to 1.29) showed no or minimal effect on any AE associated with uncertainty. Ramosetron with RR 1.31 (95% CI 0.73 to 2.38) showed harm associated with uncertainty. The estimated value of between-study variance for the sensitivity network meta-analysis of any AE was 0 (tau^2) (I^2 = 0%).

Sensitivity analysis of any AE: imbalance in baseline details and/or risk factors for PONV in study participants

We assessed studies with an imbalance in baseline details and/or risk factors for PONV between the study arms as having high risk of other bias. For any AE, five (8%) of 61 studies were rated as having high risk of other bias, 48 (77%) as unclear, and eight (13%) as low. One study was not connected to the network (Chen 2006; comparison: dexamethasone versus placebo). The remaining seven studies with low risk of other bias with six treatments were poorly connected in one network in which placebo was not used as a comparator. We could not perform a network meta-analysis with placebo as reference compound.

Sensitivity analysis of any AE: studies with PONV-related primary outcome(s)

Thirty-four (56%) of 61 studies have defined a PONV-related primary outcome in their published study report. The network of this sensitivity analysis consisted of 21 treatments including placebo with 11 single drug treatments. Of the single drugs of direct interest, dolasetron, scopolamine, and dimenhydrinate were not included in this network due to lack of studies reporting a PONV-related primary outcome. Treatment effects of four drugs compared to placebo were not robust in this sensitivity analysis (ramosetron, droperidol, aprepitant, casopitant). Ramosetron with RR 0.74 (95% CI 0.32 to 1.73) showed benefit associated with uncertainty. Droperidol (RR 0.93, 95% CI 0.84 to 1.02), aprepitant (RR 0.94, 95% CI 0.83 to 1.07), and casopitant (RR 0.95, 95% CI 0.79 to 1.14) showed no or minimal effect on any AE associated with uncertainty. The estimated value of between-study variance for the sensitivity network meta-analysis of any AE was 0 (tau^2) (I^2 = 0%).

Sensitivity analysis of any AE: funding source

Twenty-seven (44%) of 61 studies were funded by industry, nine (15%) were funded by non-industrial resources, and for another 25 studies (41%), information on funding source was not provided. Two sensitivity analyses—one for industry-funded and one for non-industry-funded studies—were performed. The network of the sensitivity analysis including only industry-funded studies consisted of 26 studies with 16 treatments,

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including 10 single drugs. One study was not connected to the network and was excluded from the analyses (Gan 2005; comparison: dexamethasone-granisetron versus dexamethasone-ondansetron). Compared to the primary analysis, of the 10 single drugs, treatment effects of four drugs compared to placebo were not robust (droperidol, aprepitant, casopitant, metoclopramide). Droperidol (RR 0.91, 95% CI 0.83 to 1.00), aprepitant (RR 0.92, 95% CI 0.82 to 1.04), and casopitant (RR 0.93, 95% CI 0.78 to 1.11) showed no or minimal effect with uncertainty compared to placebo. Metoclopramide showed harm associated with uncertainty (RR 1.13, 95% CI 0.59 to 2.16). The network of the sensitivity analysis including only studies funded by non-industrial resources consisted of nine studies with nine treatments, including seven single drugs and placebo. Treatment effects for five of the nine drugs compared to placebo were not robust (ramosetron, palonosetron, metoclopramide, granisetron, ondansetron). Ramosetron (RR 0.16, 95% CI 0.01 to 3.13), palonosetron (RR 0.24, 95% CI 0.01 to 4.04), metoclopramide (RR 0.48, 95% CI 0.02 to 9.27), granisetron (RR 0.49, 95% CI 0.03 to 9.38), and ondansetron (RR 0.48, 95% CI 0.06 to 3.75) showed benefit associated with uncertainty compared to placebo.

Six single drugs were funded only by industry (droperidol, aprepitant, casopitant, amisulpride, tropisetron, scopolamine), and three solely by non-industrial resources (betamethasone, ramosetron, dexamethasone). Four single drugs (ondansetron, granisetron, metoclopramide, palonosetron) were investigated in studies funded by either of the sources and treatment effects were not robust, with treatment effects being more favourable in non-industry-funded studies. For two drugs (dimenhydrinate, dolasetron), the funding source was not specified.

Reporting bias (any AE)

The only pair-wise comparison including 10 or more studies was ondansetron versus placebo, for which small-study effects such as reporting or publication bias were investigated. Results of the funnel plot, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. According to the explorative analyses, we did not suspect publication bias for ondansetron versus placebo (P = 0.19).

Subgroup analysis of any AE: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis including single drugs only (and excluding combination treatments) with 48 studies and 16 treatments including placebo was conducted. Network geometry, effect estimates, and the ranking order of drugs with placebo as comparator were comparable to the primary analysis, including combination prophylaxis. The estimated value of between-study variance for the network meta-analysis of single drugs for any AE was 0 (tau^2) (I^2 = 0%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The following drugs were split into dose categories: amisulpride, aprepitant, dexamethasone, granisetron, ondansetron, palonosetron, ramosetron, and tropisetron. For casopitant, dimenhydrinate, dolasetron, droperidol, and metoclopramide, only one dose category was available for subgroup analysis. Drugs without any dose recommendation according to Table 1 (scopolamine) and drugs not of direct interest (betamethasone) were included in the analysis and were lumped together, irrespective of the doses being analysed, in the category 'NA'. Wagner 1996 and one arm of Bhatnagar 2007 (granisetron NA) were excluded from the subgroup analysis because they were not associated with one of the three dose categories. The network consisted of 47 studies with 16 treatments split into 29 nodes with dose categories and is presented in the online repository. In the ranking of treatments according to safety with placebo as comparator, high or recommended doses of dexamethasone, ondansetron, palonosetron, ramosetron, and granisetron ranked higher compared to recommended or low doses, respectively. All 95% CIs between different doses of the same drug were overlapping. Tropisetron used as recommended ranked over high and low doses, but 95% CIs included both benefit and harm. High and recommended doses of aprepitant compared to placebo had similar treatment effects.

Additivity of dose categories (any AE)

A network meta-analysis with the assumption of additivity of dose categories revealed no differences between standard and additive models (P = 0.96), suggesting additive dose effects.

Sensitivity analysis of any AE: comparability of doses

In 31 (51%) of 61 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis was poorly connected, consisting of 12 treatments including placebo, which limited available evidence. Of single drugs of direct interest included in the primary network meta-analysis, aprepitant, dimenhydrinate, and scopolamine were not included in the sensitivity analysis due to lack of studies with comparable doses. Treatment effects of ramosetron and metoclopramide compared to placebo were not robust in the sensitivity analysis. Ramosetron (RR 0.54, 95% CI 0.24 to 1.20) and metoclopramide (RR 0.61, 95% CI 0.31 to 1.20) showed benefit associated with uncertainty. The estimated value of between-study variance for this sensitivity network meta-analysis of any AE was 0.0069 (tau^2) (I^2 = 24.5%).

Additive effects of combinations of treatments (any AE)

We tested the hypothesis of additivity of the components in combination prophylaxis by comparing the primary standard network meta-analysis (k = 61) with a second analysis, which assumes that the effects of combined treatments are additive sums of their components. Standard and additive models were different (P < 0.0001), suggesting no additive effects of components.

Certainty of evidence: any AE

The certainty of evidence of treatment estimates for any AE evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 4).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for any

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AE ranged from very low to moderate (Summary of findings 4). Granisetron (RR 0.92, 95% CI 0.80 to 1.05) probably has little or no effect on any AE compared to placebo, with moderate-certainty evidence (imprecision). Ondansetron (RR 0.95, 95% CI 0.88 to 1.01) and palonosetron (RR 0.95, 95% CI 0.87 to 1.03) may have little or no effect on any AE compared to placebo, with low-certainty evidence (study limitations, imprecision). Tropisetron (RR 1.00, 95% CI 0.84 to 1.19) may also have little or no effect on any AE compared to placebo, as certainty of evidence has been assessed as low (very serious concerns for imprecision). We are uncertain whether ramosetron (RR 1.00, 95% CI 0.65 to 1.54) has little or no effect on any AE compared to placebo, with very low-certainty evidence (study limitations, very serious concerns for imprecision). We are uncertain whether dolasetron (RR 0.86, 95% CI 0.66 to 1.11), with direct evidence only, reduces any AE compared to placebo, with very low-certainty evidence (very serious concern for study limitations, imprecision-heterogeneity).

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for any AE was assessed as low to moderate (Summary of findings 4). Amisulpride (RR 0.97, 95% CI 0.90 to 1.06), with direct evidence only, probably has little or no effect on any AE compared to placebo, with moderate-certainty evidence (imprecision). Droperidol (RR 0.89, 95% CI 0.81 to 0.98) may reduce any AE compared to placebo, with low-certainty evidence (study limitations, imprecision). Metoclopramide (RR 0.92, 95% CI 0.83 to 1.03) may have little or no effect on any AE, with low-certainty evidence (study limitations, imprecision). No studies reporting any AE were available for haloperidol or perphenazine.

For relevant NK_1 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for any AE was assessed as very low (Summary of findings 4). We are uncertain whether casopitant (RR 0.88, 95% CI 0.74 to 1.05) and aprepitant (RR 0.87, 95% CI 0.78 to 0.97), with indirect evidence only, reduce any AE compared to placebo (study limitations, imprecision, incoherence). No studies reporting any AE were available for fosaprepitant and rolapitant.

The only corticosteroid that was included in the network meta-analysis for any AE was dexamethasone (RR 0.77, 95% CI 0.55 to 1.08), which may reduce any AE compared to placebo, with low-certainty evidence (study limitations, imprecision) (Summary of findings 4). No studies reporting any AE were available for methylprednisolone.

The only antihistamine that was included in the network meta-analysis for any AE was dimenhydrinate (RR 5.70, 95% CI 1.36 to 23.93), which may increase any AE compared to placebo, with direct evidence only and low certainty (study limitations, incoherence) (Summary of findings 4). No studies reporting any AE were available for promethazine or meclizine.

The anticholinergic scopolamine (RR 2.12, 95% CI 1.71 to 2.64) may increase any AE compared to placebo, with only direct evidence of low certainty (very serious concerns for study limitations) (Summary of findings 4).

Secondary outcomes (GRADE-relevant)

Headache within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of headache

Pairwise meta-analyses of headache comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for amisulpride (Analysis 1.4), aprepitant (Analysis 2.2), dexamethasone (Analysis 3.4), dimenhydrinate (Analysis 4.2), dolasetron (Analysis 5.4), droperidol (Analysis 6.4), granisetron (Analysis 7.4), haloperidol (Analysis 8.2), metoclopramide (Analysis 10.3), ondansetron (Analysis 11.4), palonosetron (Analysis 12.4), promethazine (Analysis 14.2), ramosetron (Analysis 15.4), scopolamine (Analysis 17.4), and tropisetron (Analysis 18.4). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of headache: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome headache are available in an online repository (Supplementary Files-4-headache *; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

In total, 208 studies with 426 pair-wise comparisons due to multi-arm studies and 42,445 participants were eligible for the network meta-analysis of headache. Twenty studies (10%) have reported zero events in all study arms. The network included 53 treatments (nodes) (Figure 14), with 29 drug combinations, 23 single drugs, and placebo or no treatment. The most common comparisons involved ondansetron (k = 57 studies), droperidol (k = 22), granisetron (k = 15), ramosetron (k = 14), and dexamethasone (k = 13), all compared to placebo. Of the single drugs of direct interest, amisulpride and scopolamine were poorly connected to the network, with placebo as the only comparator.

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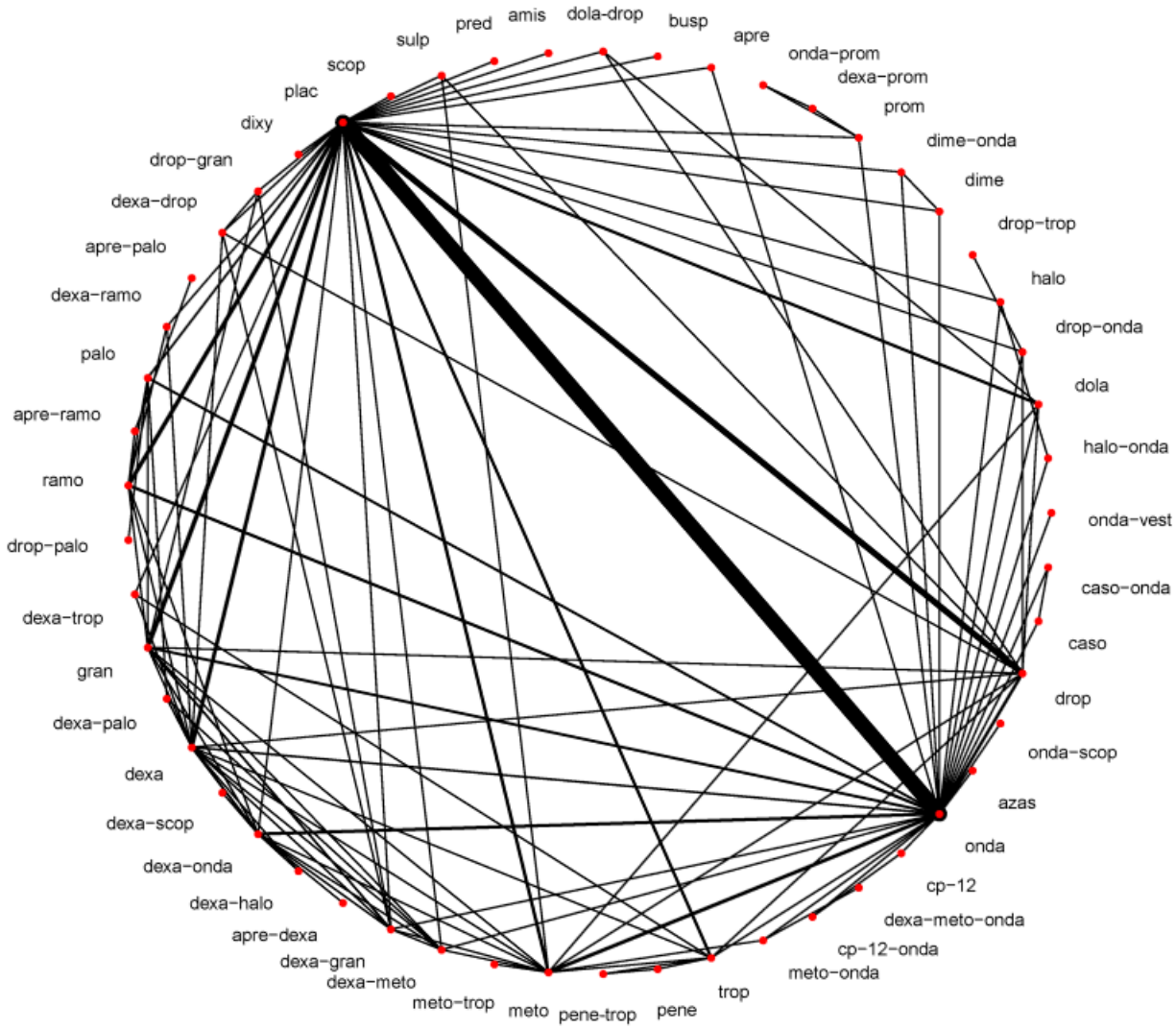
Figure 14. Network geometry of eligible comparisons for postoperative headache. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 53 different treatments, 1378 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 96 of 1378 comparisons, direct and indirect evidence was available, whereas for 26 comparisons, only direct evidence was available, and for 1256 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 15. Of the 23 single drugs, sulpiride and droperidol showed important benefit (95% CI upper boundary < 0.9) in terms of headache compared to placebo, with RRs of 0.10 (95% CI 0.01 to 0.71) and 0.76 (95% CI 0.67 to 0.86), respectively. Eight single treatments showed benefit (haloperidol, promethazine, prednisolone, penehyclidine, casopitant, dexamethasone, azasetron, aprepitant), three showed no or minimal effect (metoclopramide, scopolamine, tropisetron), 10 showed harm (dimenhydrinate, dolasetron, ramosetron, palonosetron, ondansetron, granisetron, dixyrazine, buspirone, amisulpride, CP-122,721), and all 21 of these treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs ranged between RR 0.10 (95% CI 0.01 to 0.71) for amisulpride and RR 5.82 (95% CI

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0.70 to 48.25) for CP-122,721. Of all combination treatments, the only combination treatment showing important benefit compared to placebo was droperidol-tropisetron, with RR of 0.20 (95% CI 0.05 to 0.84). Of the other combination treatments, 15 combinations showed benefit, seven showed no or minimal effect, six showed harm, and all treatment effects were associated with uncertainty. Treatment effects of drug combinations compared to placebo ranged between RR 0.20 (95% CI 0.05 to 0.84) for droperidol-tropisetron and RR 3.43 (95% CI 0.37 to 31.96) for CP-122,721-ondansetron.

Figure 15. Forest plot of network meta-analysis of all trials for postoperative headache. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to

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1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.

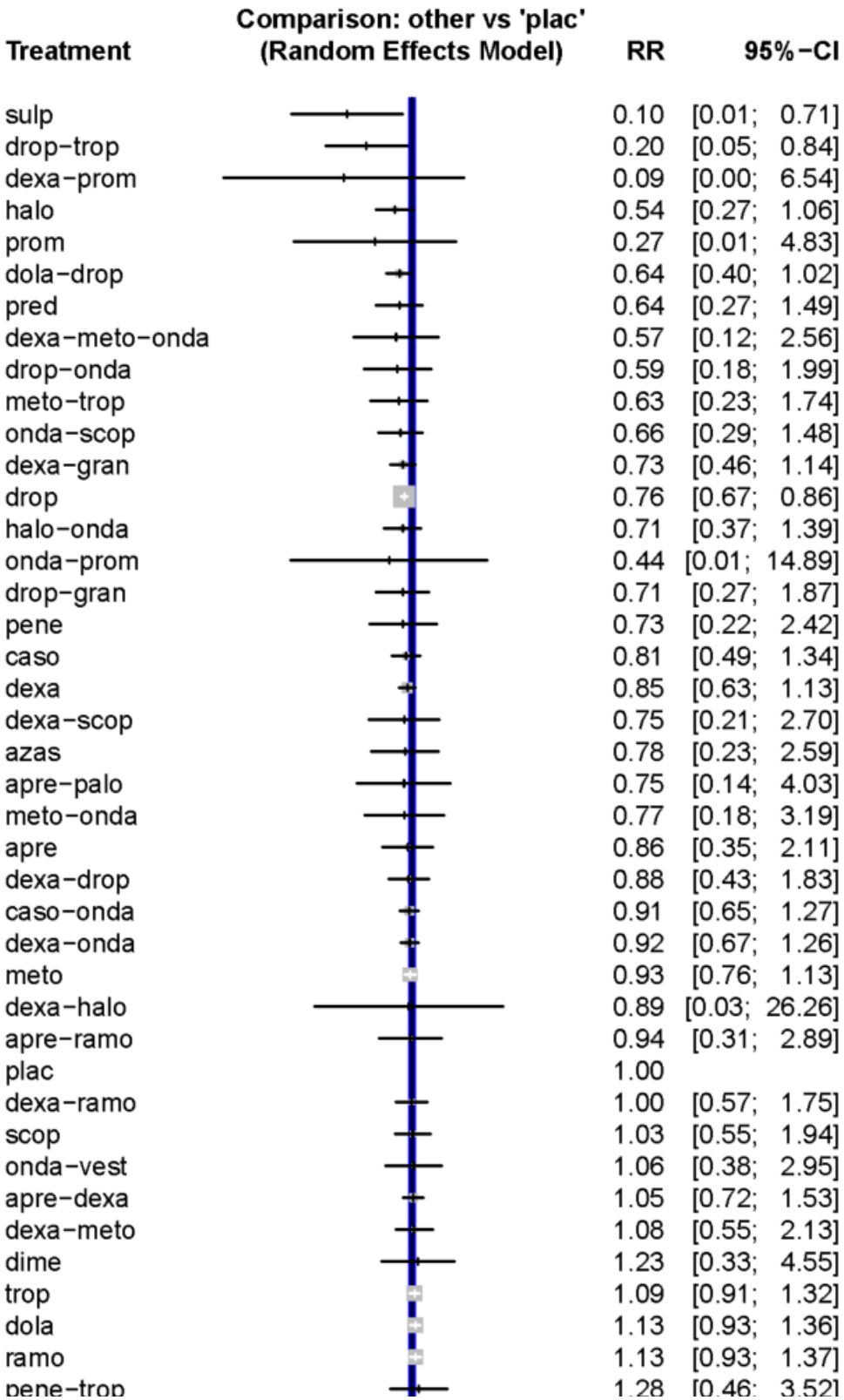

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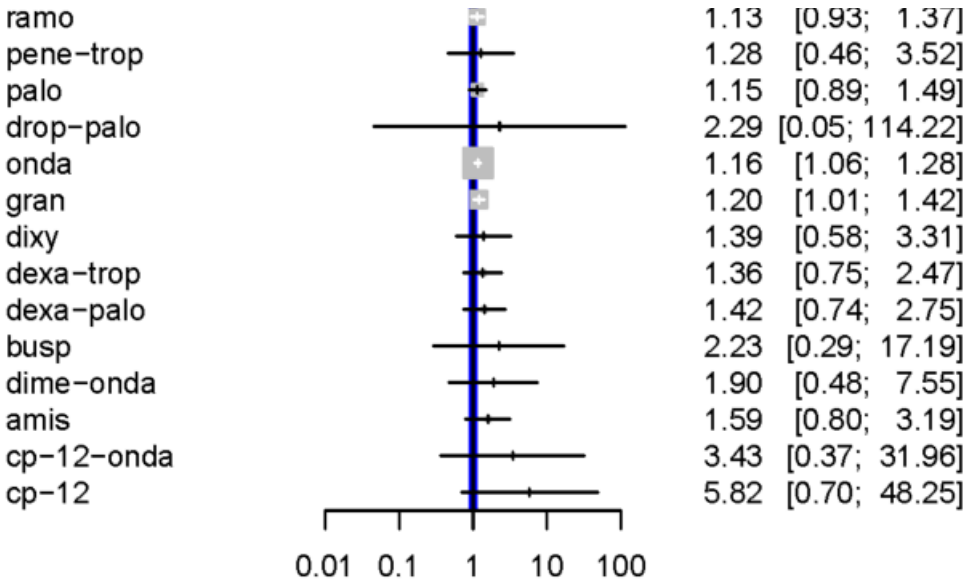
Figure 15. (Continued)



The estimated value of between-study variance for the network meta-analysis of headache was 0 (tau^2) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 82.42, df = 126, P = 1.00) and no inconsistency between designs (Q = 86.57, df = 126, P = 1.00). No clinically relevant heterogeneity for relevant comparisons (single drugs of direct interest compared to placebo) was detectable because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed disagreement (direct versus indirect) for five out of 96 comparisons, namely, dexamethasone-granisetron versus dexamethasone (P = 0.045), dolasetron-droperidol versus droperidol (P = 0.01), droperidol versus amisulpride (P = 0.04), ondansetron versus palonosetron (P = 0.005), and amisulpride versus placebo (P = 0.01). Clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo was found only for granisetron (95% CI direct estimate: 1.03 to 1.61; 95% CI indirect estimate: 0.83 to 1.41).

Sensitivity analyses of headache

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of headache: risk of bias

Twenty-five (12%) of 208 studies were rated as high risk of overall bias, 121 (58%) as unclear, and 62 (30%) as low. One study with low risk of bias was not connected to the network of low risk of bias studies and was excluded from the sensitivity analyses (DeOliveira 2011; comparison: dexamethasone-metoclopramide-ondansetron versus metoclopramide-ondansetron). The network geometry of the remaining 61 studies at low risk of bias included 32 treatments. Thirteen treatments were two-fold combinations of antiemetic drugs, 18 were single drugs, and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis of headache, promethazine, scopolamine, and dimenhydrinate were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Comparison of treatment effects of the sensitivity analysis for risk of bias and the primary network meta-analysis for headache with placebo as common comparator revealed eight single drugs of direct interest with non-robust treatment effects (droperidol, tropisetron, dolasetron, ramosetron, palonosetron, metoclopramide, granisetron, haloperidol). Droperidol and tropisetron, with RR 0.79 (95% CI 0.58 to 1.07) and RR 0.82 (95% CI 0.25 to 2.69), respectively, showed benefit with uncertainty compared to placebo. Dolasetron, ramosetron, and palonosetron, with RR 1.02 (95% CI 0.65 to 1.60), RR 1.08 (95% CI 0.82 to 1.41), and RR 1.09 (95% CI 0.75 to 1.60), respectively, showed no or minimal effect associated with uncertainty compared to placebo. Metoclopramide compared to placebo, with RR 1.23 (95% CI 0.51 to 2.96), showed harm associated with uncertainty. For granisetron with RR 1.12 (95% CI 0.63 to 1.97) and haloperidol with RR 0.40 (95% CI 0.04 to 4.13), the uncertainty of effect estimates was increased further in the sensitivity analysis compared to the primary network meta-analysis. The estimated value of between-study variance for the sensitivity network meta-analysis of headache was 0 (tau^2) (I^2 = 0%).

Reporting bias (headache)

Twelve direct pair-wise comparisons included 10 of more studies for which small-study effects such as reporting or publication bias were investigated: dexamethasone, dolasetron, droperidol, granisetron, metoclopramide, ondansetron, ramosetron, and tropisetron, all compared to placebo; and dexamethasone-ondansetron, droperidol, metoclopramide, and ramosetron, all compared to ondansetron. Results of the funnel plots, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. We did not suspect relevant publication bias for any of the comparisons mentioned above. The only P value < 0.1 was revealed for droperidol versus ondansetron (P = 0.047). However, we did not suspect relevant publication bias because trim and fill sensitivity analysis did not change the conclusion with respect to the range of equivalence.

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Subgroup analysis of headache: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis including single drugs only (and excluding combination treatments) with 176 studies and 24 treatments including placebo was conducted. Network geometry, effect estimates, and the ranking order of drugs were robust compared to the primary analysis, including combination prophylaxis, except for dexamethasone compared to placebo, with RR 0.91 (95% CI 0.67 to 1.23) showing no or minimal effect with uncertainty. The estimated value of between-study variance for the network meta-analysis of single drugs for headache was 0 (tau^2) (I^2 = 0%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The following drugs were split into dose categories: amisulpride, aprepitant, dexamethasone, dolasetron, droperidol, granisetron, haloperidol, ondansetron, palonosetron, ramosetron, and tropisetron. For casopitant, dimenhydrinate, metoclopramide, and promethazine, only one dose category was available for subgroup analysis. Drugs without any dose recommendation according to Table 1 (scopolamine) and drugs not of direct interest (azasetron, buspirone, CP-122,721, dixyrazine, penehyclidine, prednisolone, amisulpride) were included in the analysis and were lumped together, irrespective of the doses being analysed, in the category 'NA'. Five studies—Diemunsch 1998; Eberhart 2006; Jokela 2002; Prescott 1976; Warriner 1997—and one arm each of Bhatnagar 2007 (granisetron NA), Lee D 2009 (ramosetron NA), and Turhanoglu 1999 (dimenhydrinate NA) were excluded from the subgroup analysis because they were not associated with one of the three dose categories. The network consisted of 171 studies with 24 treatments split into 42 nodes with dose categories and is presented in the online repository. In the treatment ranking according to safety, with placebo as the reference compound, high and recommended doses of ramosetron, droperidol, granisetron, dexamethasone, tropisetron, and ondansetron ranked higher than low doses. However, all 95% CIs between different doses of the same drug overlapped, and the uncertainty of treatment effects was considerable. All doses of amisulpride and palonosetron compared to placebo showed harm with uncertainty. Both recommended and high doses of haloperidol compared to placebo showed benefit with uncertainty, and both recommended and high doses of dolasetron compared to placebo showed no or minimal effect associated with uncertainty. Recommended doses of aprepitant ranked higher than high doses compared to placebo. However, treatment effects were associated with uncertainty.

Sensitivity analysis of headache: comparability of doses

In 102 (51%) of 176 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of 15 treatments including placebo. Of single drugs of direct interest included in the primary network meta-analysis, dimenhydrinate and scopolamine were not included in the sensitivity analysis due to lack of studies with comparable doses. The favourable treatment effect of droperidol compared to placebo remained robust (RR 0.74, 95% CI 0.63 to 0.87). Treatment effects of three drugs (ramosetron, dexamethasone, tropisetron) compared to placebo were not robust in the sensitivity analysis. Ramosetron compared to placebo (RR 0.98, 95% CI 0.76 to 1.26) showed no or minimal effect associated with uncertainty. Dexamethasone (RR 1.25, 95% CI 0.72 to 2.16) and tropisetron (RR 1.48, 95% CI 0.82 to 2.67), compared to placebo, showed harm associated with uncertainty. The estimated value of between-study variance for this sensitivity network meta-analysis of headache was 0 (tau^2) (I^2 = 0%).

Certainty of evidence: headache

The certainty of evidence of treatment estimates for headache evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 5).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for headache ranged from very low to moderate (Summary of findings 5). Ondansetron (RR 1.16, 95% CI 1.06 to 1.28) probably increases headache compared to placebo, with moderate-certainty evidence (imprecision). Ramosetron (RR 1.13, 95% CI 0.93 to 1.37) and dolasetron (RR 1.13, 95% CI 0.93 to 1.36) may increase headache compared to placebo, with low-certainty evidence (study limitations, imprecision). Tropisetron (RR 1.09, 95% CI 0.91 to 1.32) may have little or no effect on headache compared to placebo, with low-certainty evidence (study limitations, imprecision). We are uncertain whether granisetron (RR 1.20, 95% CI 1.01 to 1.42) and palonosetron (RR 1.15, 95% CI 0.89 to 1.49) increase headache compared to placebo, with very low-certainty evidence (granisetron: study limitation, imprecision, incoherence; palonosetron: study limitation, very serious concerns for imprecision).

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for headache was assessed as very low to moderate (Summary of findings 5). Droperidol (RR 0.76, 95% CI 0.67 to 0.86) probably reduces headache compared to placebo, with moderate-certainty evidence (study limitations). Haloperidol (RR 0.54, 95% CI 0.27 to 1.06) may reduce headache compared to placebo, with low-certainty evidence (study limitation, imprecision). Amisulpride (RR 1.59, 95% CI 0.80 to 3.19), with direct evidence only, may increase headache compared to placebo, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether metoclopramide (RR 0.93, 95% CI 0.76 to 1.13) has little or no effect on headache compared to placebo, with very low-certainty evidence (study limitations, very serious concerns for imprecision). No studies reporting headache were available for perphenazine.

For relevant NK_1 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for headache was assessed as very low to low (Summary of findings 5). Aprepitant (RR 0.86, 95% CI 0.35 to 2.11) may reduce headache compared to placebo, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether casopitant (RR 0.81, 95% CI 0.49 to 1.34), with indirect evidence only, reduces headache, with very low-certainty evidence (incoherence, very serious concerns for imprecision). No studies reporting headache were available for fosaprepitant or rolapitant.

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The only corticosteroid that was included in the network meta-analysis for headache was dexamethasone (RR 0.85, 95% CI 0.63 to 1.13), which may reduce headache compared to placebo, with low-certainty evidence (very serious concerns for imprecision) (Summary of findings 5). No studies reporting headache were available for methylprednisolone.

For relevant antihistamines (compared to placebo), the certainty of evidence of network effect estimates for headache was assessed as very low (Summary of findings 5). We are uncertain whether dimenhydrinate (RR 1.23, 95% CI 0.33 to 4.55) increases or promethazine (RR 0.27, 95% CI 0.01 to 4.83) reduces headache compared to placebo (study limitations, very serious concerns for imprecision). No studies reporting headache were available for meclizine.

We are uncertain whether the anticholinergic scopolamine (RR 1.03, 95% CI 0.55 to 1.94) has little or no effect on headache compared to placebo, with only direct evidence of very low certainty (very serious concerns for study limitations and imprecision) (Summary of findings 5).

Sedation within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of sedation

Pairwise meta-analyses of sedation comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for amisulpride (Analysis 1.5), dexamethasone (Analysis 3.5), dimenhydrinate (Analysis 4.3), dolasetron (Analysis 5.5), droperidol (Analysis 6.5), granisetron (Analysis 7.5), methylprednisolone (Analysis 9.1), metoclopramide (Analysis 10.4), ondansetron (Analysis 11.5), palonosetron (Analysis 12.5), perphenazine (Analysis 13.1), promethazine (Analysis 14.3), ramosetron (Analysis 15.5), scopolamine (Analysis 17.5), and tropisetron (Analysis 18.5). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of sedation: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome sedation are available in an online repository (Supplementary Files-5-sedation *; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

In total, 117 studies with 280 pair-wise comparisons due to multi-arm studies and 21,440 participants were eligible for the network meta-analysis of sedation. Nineteen studies (16%) have reported zero events in all study arms. The network included 44 treatments (nodes) (Figure 16), with 19 drug combinations, 24 single drugs, and 1 placebo or no treatment. The most common comparisons were ondansetron (k = 36 studies), droperidol (k = 21), and metoclopramide (k = 15), all compared to placebo, and droperidol, compared to ondansetron (k = 10). Of the single drugs of direct interest, amisulpride and methylprednisolone were poorly connected to the network, with placebo as the only comparator.

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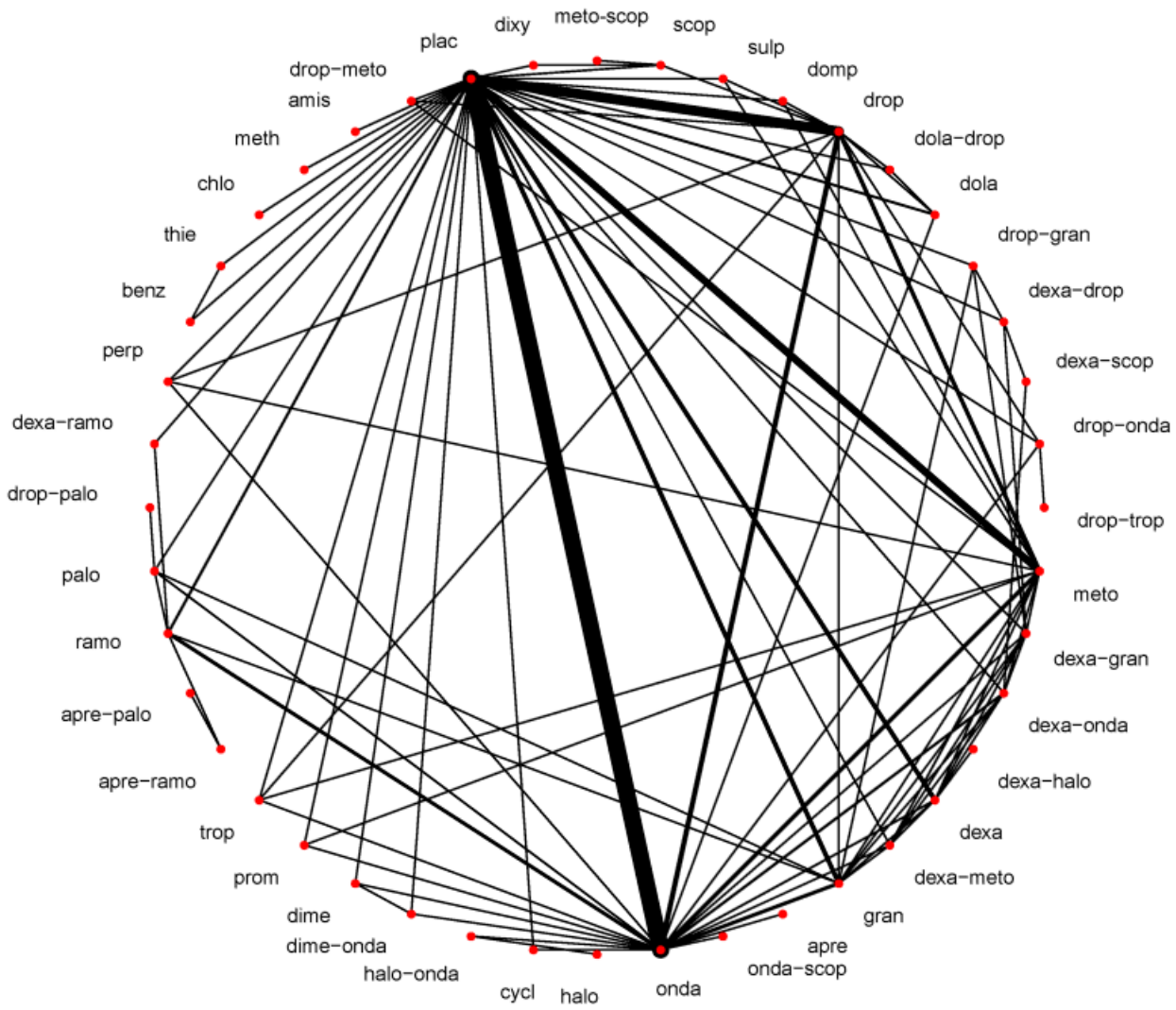
Figure 16. Network geometry of eligible comparisons for postoperative sedation. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 44 different treatments, 946 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 89 of 946 comparisons, direct and indirect evidence was available, whereas for 16 comparisons, only direct evidence was available, and for 841 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 17. In terms of sedation, only amisulpride out of the 24 single drugs showed important benefit (95% CI upper boundary < 0.9) compared to placebo, with RR of 0.03 (95% CI 0.00 to 0.50), and three drugs showed important harm (95% CI lower boundary > 1.11), namely,dimenhydrinate (RR 7.66, 95% CI 3.10 to 18.94), benzquinamide (RR 36.78, 95% CI 2.26 to 599.50), and thiethylperazine (RR 51.38, 95% CI 3.18 to 830.62). Seven single treatments showed benefit (dixyrazine, perphenazine, tropisetron, ondansetron, aprepitant, domperidone, ramosetron), nine showed no or minimal effect (haloperidol, metoclopramide, droperidol, chlorpromazine, amisulpride, dolasetron, granisetron, dexamethasone, promethazine), four showed harm (cyclizine, palonosetron, scopolamine, methylprednisolone), and all 20 of these treatment effects were associated with uncertainty (95% CI

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crossing the range of equivalence). Treatment effects of all single drugs ranged between RR 0.03 (95% CI 0.00 to 0.50) for amisulpride and RR 51.38 (95% CI 3.18 to 830.62) for thiethylperazine. Of the 19 drug combinations, the only combination showing important benefit compared to placebo was dexamethasone-metoclopramide (RR 0.41, 95% CI 0.24 to 0.71) and the only combination treatment with important harm compared to placebo was dimenhydrinate-ondansetron (RR 6.90, 95% CI 2.74 to 17.32). Of the other combination treatments, five combinations showed benefit, another five showed no or minimal effect, eight showed harm, and all treatment effects were associated with uncertainty. Treatment effects of drug combinations compared to placebo ranged between RR 0.41 (95% CI 0.24 to 0.71) for dexamethasone-metoclopramide and RR 6.90 (95% CI 2.74 to 17.32) for dimenhydrinate-ondansetron.

Figure 17. Forest plot of network meta-analysis of all trials for postoperative sedation. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to

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1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.

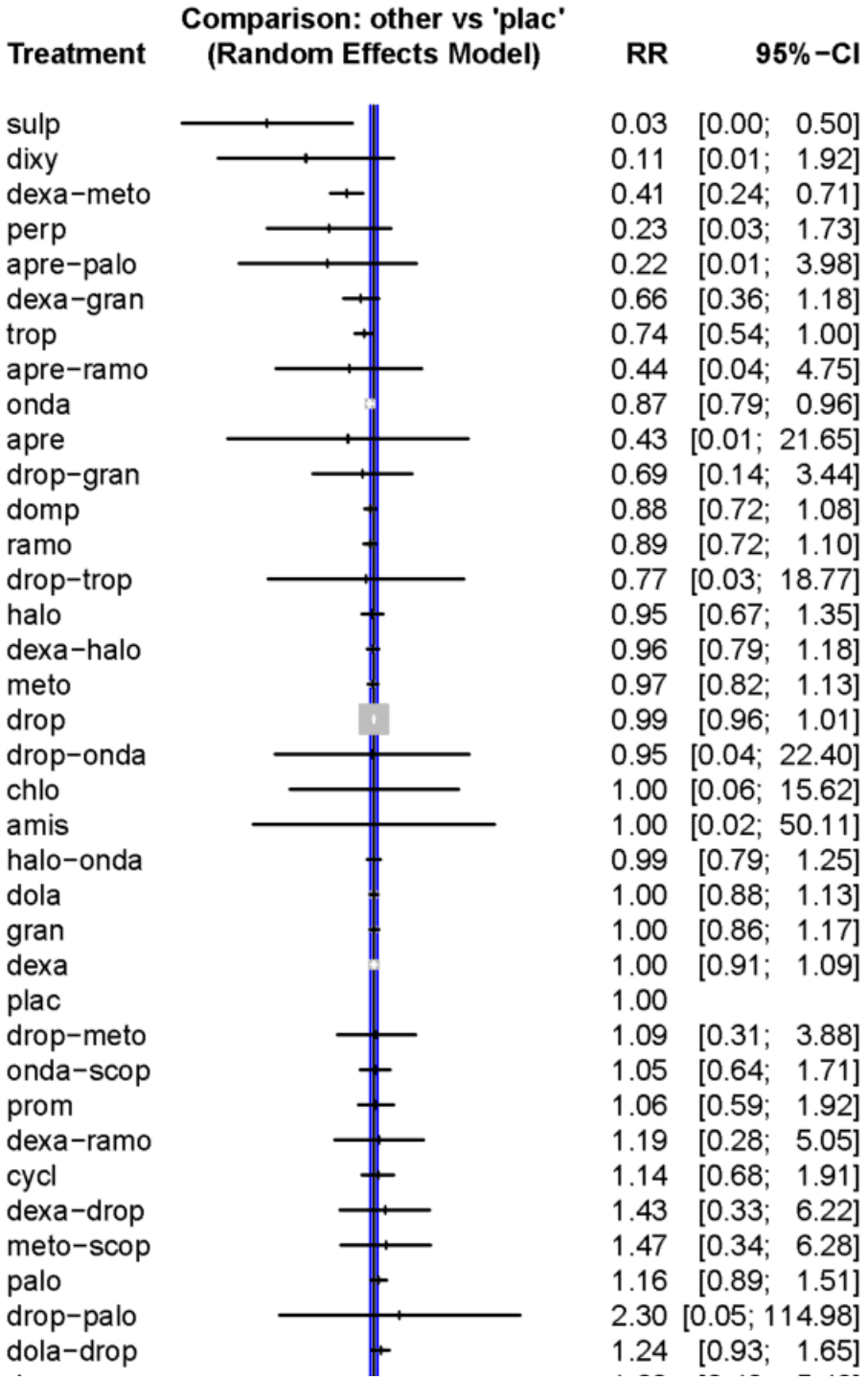

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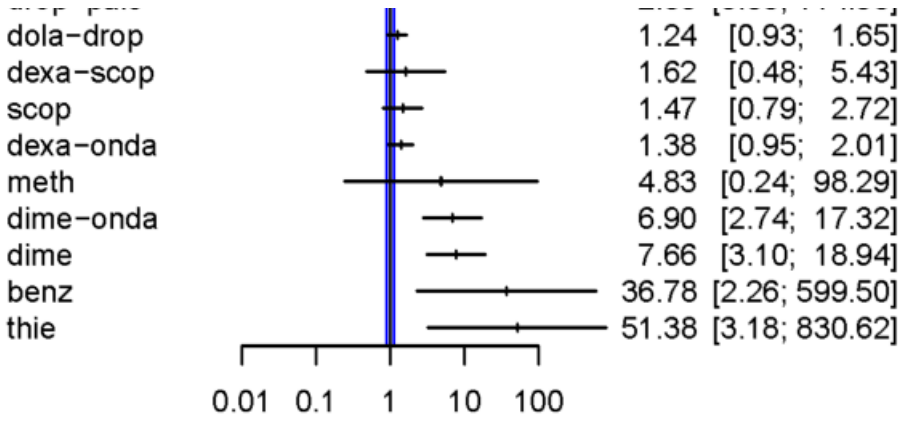
Figure 17. (Continued)



The estimated value of between-study variance for the network meta-analysis of sedation was 0 (tau²) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 30.85, df = 48, P = 0.98) and no inconsistency between designs (Q = 108.63, df = 93, P = 0.13). No clinically relevant heterogeneity for relevant comparisons (single drugs of direct interest compared to placebo) was detectable because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed disagreement (direct versus indirect) for 14 out of 89 comparisons. Three out of 14 comparisons with local inconsistency were of direct interest, namely, dexamethasone versus placebo (P = 0.02), droperidol versus placebo (P = 0.0002), and metoclopramide versus placebo (P = 0.04). For both dexamethasone and droperidol versus placebo, there was a contribution of direct evidence greater than 90%; thus there is no concern for incoherence. Clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo was found only for metoclopramide versus placebo (95% CI direct estimate: 0.90 to 1.35; 95% CI indirect estimate: 0.59 to 1.00).

Sensitivity analyses of sedation

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of sedation: risk of bias

Fourteen (12%) of 117 studies were rated as having high risk of overall bias, 75 (64%) as unclear, and 28 (24%) as low. The network geometry of the 28 studies at low risk of bias included 23 treatments. Eight treatments were two-fold combinations of antiemetic drugs, 14 were single drugs, and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis for sedation, haloperidol, perphenazine, scopolamine, and dimenhydrinate were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Comparison of treatment effects of the sensitivity analysis for risk of bias and the primary network meta-analysis of sedation with placebo as a common comparator revealed seven single drugs of direct interest with non-robust treatment effects (ramosetron, granisetron, palonosetron, droperidol, promethazine, tropisetron, metoclopramide). Granisetron and palonosetron, with RR 0.80 (95% CI 0.21 to 3.07) and RR 0.80 (95% CI 0.04 to 16.76), respectively, showed benefit with uncertainty compared to placebo. Promethazine, tropisetron, and metoclopramide, with RR 1.84 (95% CI 0.41 to 8.33), RR 2.52 (95% CI 0.21 to 30.54) and RR 2.36 (95% CI 0.42 to 13.14), respectively, showed harm associated with uncertainty compared to placebo. For ramosetron versus placebo, with RR 0.79 (95% CI 0.43 to 1.46), and for droperidol versus placebo, with RR 1.05 (95% CI 0.86 to 1.28), the uncertainty of the effect estimates was increased further in the sensitivity analysis compared to the primary network meta-analysis. The estimated value of between-study variance for the sensitivity network meta-analysis of sedation was 0 (tau²) (I^2 = 0%).

Reporting bias (sedation)

Four direct pair-wise comparisons included 10 or more studies for which small-study effects such as reporting or publication bias were investigated: droperidol, metoclopramide, and ondansetron, all compared to placebo; and droperidol compared to ondansetron. Results of the funnel plots, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. We did not suspect relevant publication bias for any of the comparisons mentioned above. For all comparisons, P values of the arcsine test were > 0.1, and trim and fill sensitivity analyses did not change the conclusions with respect to the range of equivalence.

Subgroup analysis of sedation: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low,

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recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis of sedation including single drugs only (and excluding combination treatments) with 99 studies and 24 treatments including placebo was conducted. Haloperidol was not included in the network meta-analysis of single drugs for sedation because no other single drug or placebo was a suitable comparator in the corresponding trials. Network geometry, effect estimates, and the ranking order of drugs were similar compared to the primary analysis, including combination prophylaxis. However, ondansetron (RR 0.91, 95% CI 0.81 to 1.01), domperidone (RR 0.92, 95% CI 0.74 to 1.14), and ramosetron (RR 0.92, 95% CI 0.74 to 1.15), each compared to placebo, showed slightly changed treatment effects, changing clinical interpretation of treatment effects from benefit to no or minimal effect with uncertainty. The estimated value of between-study variance for the network meta-analysis of single drugs for sedation was 0.0025 (tau^2) (I^2 = 4.9%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The following drugs were split into dose categories: aprepitant, dexamethasone, dolasetron, droperidol, granisetron, ondansetron, palonosetron, promethazine, and ramosetron. For amisulpride, dimenhydrinate, methylprednisolone, metoclopramide, perphenazine, and tropisetron, only one dose category was available for subgroup analysis. Drugs without any dose recommendation according to Table 1 (scopolamine) and drugs not of direct interest (benzquinamide, chlorpromazine, cyclizine, dixyrazine, domperidone, amisulpride, thiethylperazine) were included in the analysis and were lumped together, irrespective of the doses being analysed, in the category 'NA'. Rothenberg 1991 and Wagner 1996 and one arm each of Bhatnagar 2007 (granisetron NA) and Turhanoglu 1999 (dimenhydrinate NA) were excluded from the subgroup analysis because they were not associated with one of the three dose categories. The network consisted of 97 studies with 24 treatments split into 36 nodes with dose categories and is presented in the online repository. In the ranking of treatments according to safety, with placebo as the reference compound, high and recommended doses of ondansetron showed benefit with uncertainty, and low doses of ondansetron showed important harm with non-overlapping 95% CIs. In the case of palonosetron, promethazine, or ramosetron, high and recommended doses, respectively, ranked higher than low doses when compared to placebo. However, all 95% CIs between different doses of the same drug overlapped, and the uncertainty of treatment effects was considerable. In the case of dolasetron, droperidol, or granisetron, low and recommended doses, respectively, ranked higher than high doses when compared to placebo. However, all 95% CIs between different doses of the same drug overlapped, and the uncertainty of treatment effects was considerable. Recommended and high doses of aprepitant compared to placebo showed benefit associated with uncertainty. Both recommended and high doses of dexamethasone compared to placebo showed no or minimal effect. For recommended doses of dexamethasone, uncertainty was high.

Sensitivity analysis of sedation: comparability of doses

In 47 (48%) of 97 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of 12 treatments including placebo. Of the single drugs of direct interest included in the primary network meta-analysis, aprepitant, dimenhydrinate, perphenazine, scopolamine, and tropisetron were not included in the sensitivity analysis due to lack of studies with comparable doses. Treatment effects of three drugs (dolasetron, droperidol, promethazine) were not robust in the sensitivity analysis with placebo as common comparator. Dolasetron (RR 0.68, 95% CI 0.44 to 1.05) compared to placebo showed benefit associated with uncertainty. Droperidol (RR 0.98, 95% CI 0.95 to 1.00) showed no effect, and promethazine (RR 3.76, 95% CI 1.32 to 10.73) showed important harm, both compared to placebo. The estimated value of between-study variance for this sensitivity network meta-analysis of sedation was 0 (tau^2) (I^2 = 0%).

Certainty of evidence: sedation

The certainty of evidence of treatment estimates for sedation evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 6).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for sedation ranged from very low to moderate (Summary of findings 6). Ondansetron (RR 0.87, 95% CI 0.79 to 0.96) probably reduces sedation compared to placebo, with moderate-certainty evidence (imprecision). However, moderate certainty of evidence for ondansetron is restricted to recommended and high doses. Ramosetron (RR 0.89, 95% CI 0.72 to 1.10) and tropisetron (RR 0.74, 95% CI 0.54 to 1.00) may reduce sedation compared to placebo, with low-certainty evidence (study limitations, imprecision). Dolasetron (RR 1.00, 95% CI 0.88 to 1.13) may have little or no effect on sedation compared to placebo, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether granisetron (RR 1.00, 95% CI 0.86 to 1.17) has little or no effect compared to placebo, with very low-certainty evidence (study limitation, very serious concerns for imprecision). We are uncertain whether palonosetron (RR 1.16, 95% CI 0.89 to 1.51) increases sedation compared to placebo, with very low-certainty evidence (study limitation, very serious concerns for imprecision).

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for sedation was assessed as very low to low (Summary of findings 6). Droperidol (RR 0.99, 95% CI 0.96 to 1.01) may have little or no effect on sedation compared to placebo, with low-certainty evidence (very serious concerns for study limitations). Amisulpride (RR 1.00, 95% CI 0.02 to 50.11), with direct evidence only, may have little or no effect on sedation compared to placebo, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether haloperidol (RR 0.95, 95% CI 0.67 to 1.35), with indirect evidence only, and metoclopramide (RR 0.97, 95% CI 0.82 to 1.13), both compared to placebo, have little or no effect on sedation, with very low-certainty evidence (haloperidol: study limitations, incoherence, very serious concerns for imprecision; metoclopramide: study limitations, very serious concerns for imprecision, incoherence). We are uncertain whether perphenazine (RR 0.23, 95% CI 0.03 to 1.73) compared to placebo reduces sedation, with very low-certainty evidence (study limitations, very serious concerns for imprecision).

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For relevant NK_1 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for sedation was assessed as very low (Summary of findings 6). We are uncertain whether aprepitant (RR 0.43, 95% CI 0.01 to 21.65), with indirect evidence only, reduces sedation compared to placebo, with very low-certainty evidence (incoherence, very serious concerns for imprecision). No studies reporting sedation were available for casopitant, fosaprepitant, and rolapitant.

For relevant corticosteroids (compared to placebo), the certainty of evidence of network effect estimates for sedation was assessed as high to low (Summary of findings 6). Dexamethasone (RR 1.00, 95% CI 0.91 to 1.09) has no effect on sedation compared to placebo, with high-certainty evidence. Methylprednisolone (RR 4.83, 95% CI 0.24 to 98.29), with direct evidence only, may increase sedation compared to placebo, with low-certainty evidence (very serious concerns for imprecision).

For relevant antihistamines (compared to placebo), the certainty of evidence of network effect estimates for sedation was assessed as moderate to very low (Summary of findings 6). Dimenhydrinate (RR 7.66, 95% CI 3.10 to 18.94) probably increases sedation compared to placebo, with moderate-certainty evidence (study limitations). We are uncertain whether promethazine (RR 1.06, 95% CI 0.59 to 1.92) has no or minimal effect on sedation compared to placebo, with very low-certainty evidence (study limitations, very serious concerns for imprecision). No studies reporting sedation were available for meclizine.

We are uncertain whether the anticholinergic scopolamine (RR 1.47, 95% CI 0.79 to 2.72) increases sedation compared to placebo, with very low-certainty evidence (study limitations, very serious concerns for imprecision) (Summary of findings 6).

Extrapyramidal symptoms within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of extrapyramidal symptoms

Pairwise meta-analyses for extrapyramidal symptoms comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for amisulpride (Analysis 1.6), dexamethasone (Analysis 3.6), dolasetron (Analysis 5.6), droperidol (Analysis 6.6), granisetron (Analysis 7.6), haloperidol (Analysis 8.3), metoclopramide (Analysis 10.5), ondansetron (Analysis 11.6), palonosetron (Analysis 12.6), perphenazine (Analysis 13.2), and tropisetron (Analysis 18.6). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of extrapyramidal symptoms: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome extrapyramidal symptoms are available in an online repository (Supplementary Files-6-extrapyramidal symptoms; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).

In total, 64 studies with 172 pair-wise comparisons due to multi-arm studies and 10,724 participants were eligible for the network meta-analysis of extrapyramidal symptoms. Forty-eight studies (75%) have reported zero events in all study arms. The network included 30 treatments (nodes), with 13 drug combinations, 16 single drugs, and 1 placebo or no treatment (Figure 18). The most common comparisons were droperidol (k = 22 studies) and metoclopramide (k = 12) compared to placebo. Of the single drugs of direct interest, amisulpride and palonosetron were poorly connected to the network, with placebo as the only comparator.

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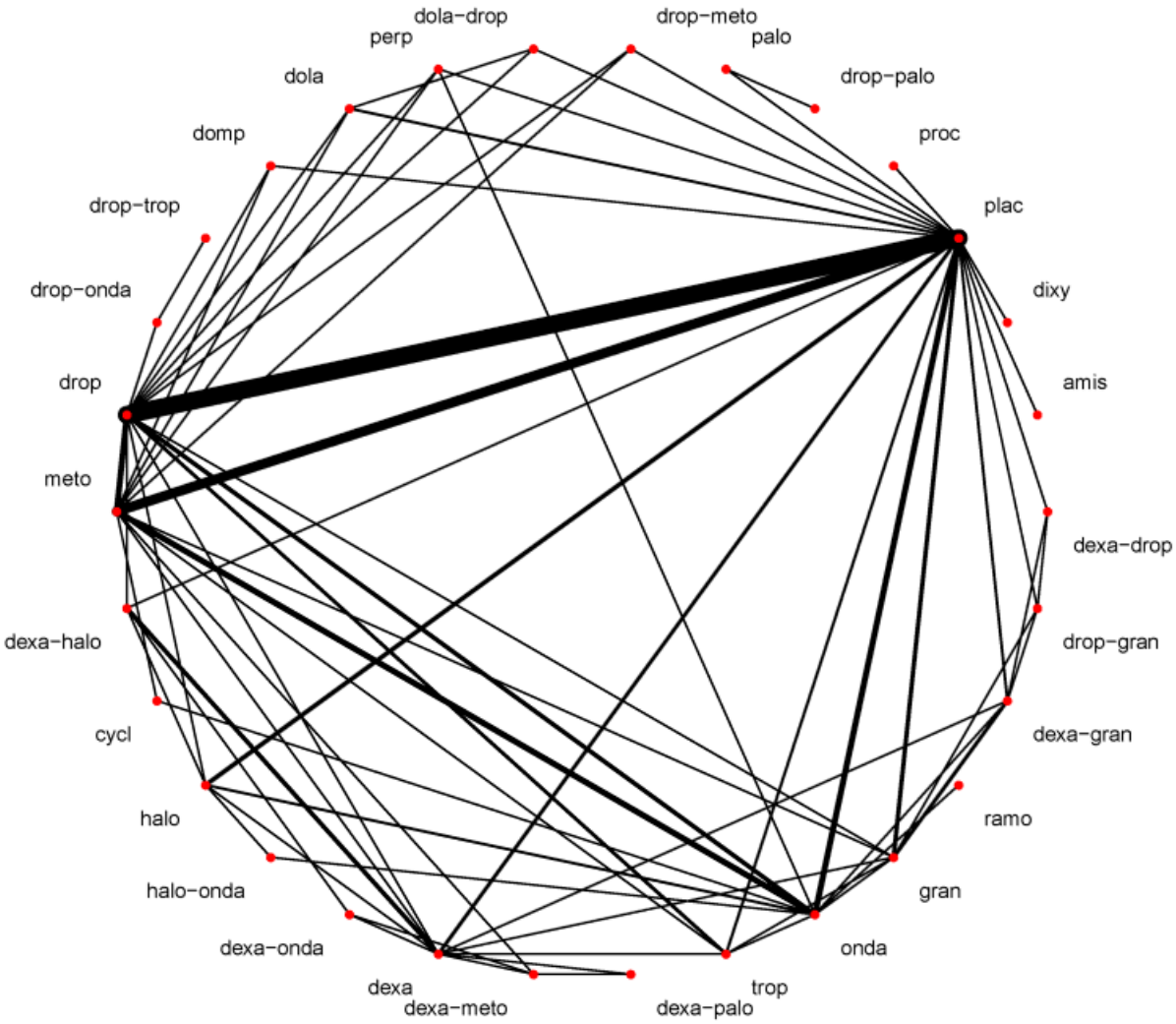
Figure 18. Network geometry of eligible comparisons for postoperative extrapyramidal symptoms. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 30 different treatments, 435 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 65 of 435 comparisons, direct and indirect evidence was available, whereas for eight comparisons, only direct evidence was available, and for 362 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 19. In terms of extrapyramidal symptoms, none of the 16 single drugs showed important benefit (95% CI upper boundary < 0.9) or important harm (95% CI lower boundary > 1.11) compared to placebo. Six single treatments showed benefit (ondansetron, dexamethasone, dolasetron, tropisetron, ramosetron, granisetron), another six treatments showed no or minimal effect (cyclizine, palonosetron, amisulpride, prochlorperazine, dixyrazine, perphenazine), four treatments showed harm (metoclopramide, haloperidol, droperidol, domperidone), and all treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs ranged between RR 0.73 (95% CI 0.39 to 1.38) for ondansetron and RR 2.05 (95% CI 0.79 to 5.31) for domperidone. None of the combination treatments showed

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important benefit or important harm compared to placebo. Six combination treatments showed benefit, five showed no or minimal effect, two showed harm, and all treatment effects were associated with uncertainty. Treatment effects of combination treatments ranged between RR 0.42 (95% CI 0.07 to 2.68) for dexamethasone-haloperidol and RR 1.99 (95% CI 0.01 to 490.88) for droperidol-palonosetron.

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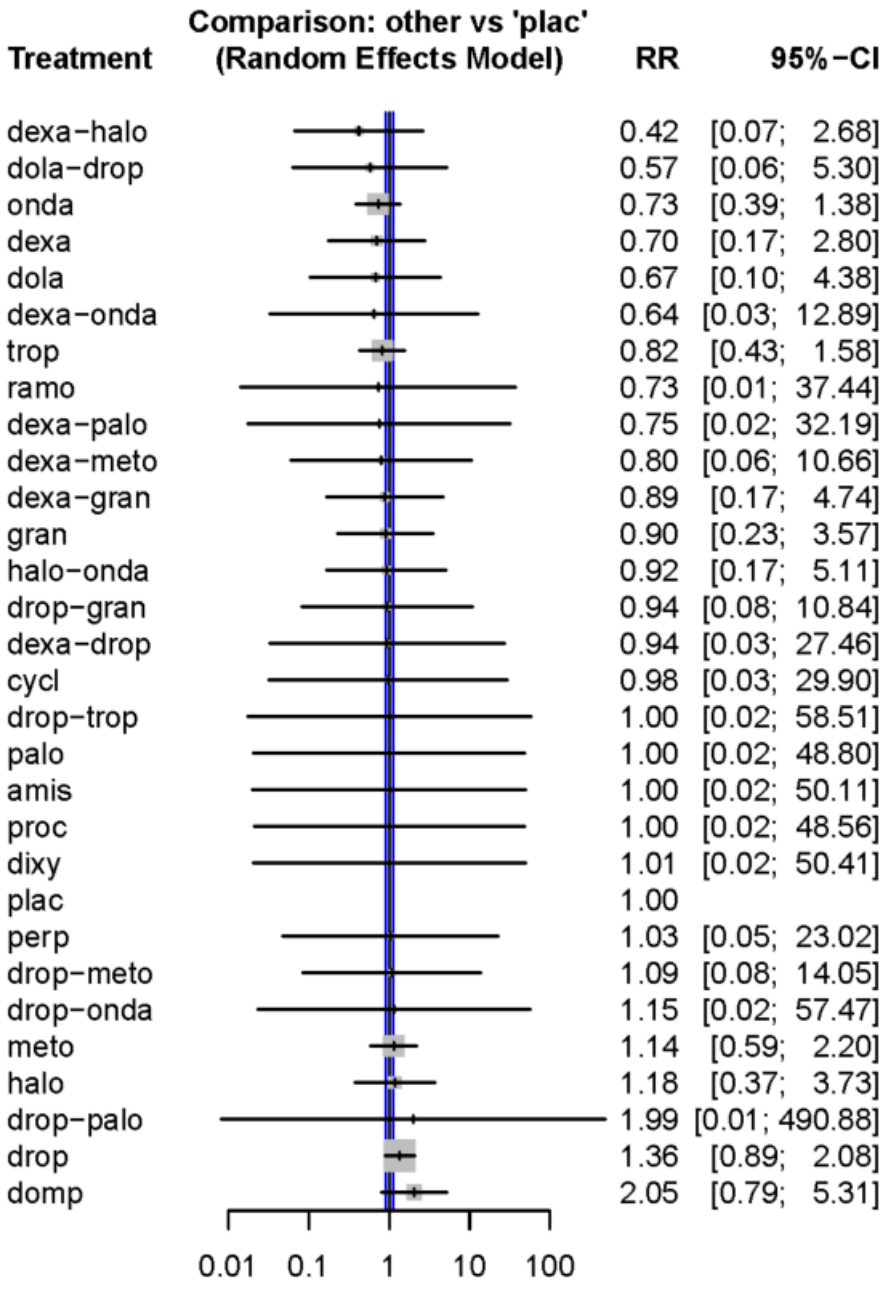
Figure 19. Forest plot of network meta-analysis of all trials for postoperative extrapyramidal symptoms. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to 1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



The estimated value of between-study variance for the network meta-analysis of extrapyramidal symptoms was 0 (tau^2) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 6.86, df = 20, P = 1.00) and no inconsistency between designs (Q = 9.34, df = 58, P = 1.00). No clinically relevant heterogeneity for relevant comparisons (single drugs of

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direct interest compared to placebo) was detectable because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed no disagreement (direct versus indirect) for all 65 comparisons. There was no clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo.

Sensitivity analyses of extrapyramidal symptoms

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of extrapyramidal symptoms: risk of bias

Fifteen (23%) of 64 studies were rated as having high risk of overall bias, 33 (52%) as unclear, and 16 (25%) as low. One study with low risk of bias was not connected to the network of low risk of bias studies and was excluded from the sensitivity analysis (Hu 2017; comparison: droperidol-palonosetron versus palonosetron). The network geometry of the remaining 15 studies at low risk of bias included 15 treatments. Five treatments were two-fold combinations of antiemetic drugs, nine were single drugs, and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis for extrapyramidal symptoms, palonosetron, perphenazine, ramosetron, and tropisetron were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Comparison of treatment effects of the sensitivity analysis for risk of bias and the primary network meta-analysis for extrapyramidal symptoms with placebo as common comparator revealed robust treatment effects for all single drugs of direct interest except for ondansetron and granisetron. Ondansetron compared to placebo, with RR 1.10 (95% CI 0.32 to 3.79), and granisetron compared to placebo, with RR 1.00 (95% CI 0.02 to 48.80), showed no or minimal effect associated with uncertainty. The estimated value of between-study variance for the sensitivity network meta-analysis of extrapyramidal symptoms was 0 (tau^2) (I^2 = 0%).

Reporting bias (extrapyramidal symptoms)

Two direct pair-wise comparisons included 10 or more studies for which small-study effects such as reporting or publication bias were investigated (droperidol and metoclopramide compared to placebo). Results of the funnel plots, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. We did not suspect relevant publication bias for any of the comparisons mentioned above. For all comparisons, P values of the arcsine test were > 0.1, and trim and fill sensitivity analyses did not change the conclusions with respect to the range of equivalence.

Subgroup analysis of extrapyramidal symptoms: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis for extrapyramidal symptoms including single drugs only (and excluding combination treatments) with 50 studies and 17 treatments including placebo was conducted. Network geometry, effect estimates, and the ranking order of drugs, with placebo as the reference compound, were robust compared to the primary analysis including combination prophylaxis. The estimated value of between-study variance for the network meta-analysis of single drugs for extrapyramidal symptoms was 0 (tau^2) (I^2 = 0%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The following drugs were split into dose categories: dexamethasone, droperidol, haloperidol, and ondansetron. For amisulpride, dolasetron, granisetron, metoclopramide, palonosetron, perphenazine, ramosetron, and tropisetron, only one dose category was available for subgroup analysis. Drugs not of direct interest were included in the analysis and were lumped together, irrespective of the doses being analysed, in the category 'NA' (cyclizine, dixyrazine, domperidone, prochlorperazine). Mathia 1988 was excluded from the subgroup analysis because the intervention was not associated with one of the three dose categories (metoclopramide 'NA'). The network consisted of 49 studies with 17 treatments including placebo split into 23 nodes with dose categories and is presented in the online repository. In the ranking of treatments according to safety with placebo as the reference compound, all 95% CIs between different doses of the same drug overlapped, and the uncertainty of treatment effects was considerable. High and recommended doses of ondansetron compared to placebo ranked higher than low doses. Low and recommended doses of droperidol compared to placebo showed harm associated with uncertainty, and high doses showed benefit associated with uncertainty. For both dexamethasone and haloperidol, recommended doses ranked higher than high doses. All treatment effects were associated with uncertainty.

Sensitivity analysis of extrapyramidal symptoms: comparability of doses

In 24 (48%) of 50 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of 11 treatments including placebo. Of the single drugs of direct interest included in the primary network meta-analysis, perphenazine and tropisetron were not included in the sensitivity analysis due to lack of studies with comparable doses. Treatment effects of six single drugs of direct interest (dolasetron, granisetron, metoclopramide, ondansetron, ramosetron, droperidol) were not robust in the sensitivity analysis with placebo as the reference compound. Dolasetron (RR 0.94, 95% CI 0.09 to 9.52), granisetron (RR 1.01, 95% CI 0.13 to 7.97), metoclopramide (RR 1.00, 95% CI 0.02 to 47.28), ondansetron (RR 1.04, 95% CI 0.07 to 16.44), and ramosetron (RR 1.04, 95% CI 0.01 to 122.62), all compared to placebo, showed no or minimal effects associated with uncertainty. Droperidol compared to placebo showed important harm, with RR 2.78 (95% CI 1.15 to 6.73). The estimated value of between-study variance for this sensitivity network meta-analysis of extrapyramidal symptoms was 0 (tau^2) (I^2 = 0%).

Certainty of evidence: extrapyramidal symptoms

The certainty of evidence of treatment estimates for extrapyramidal symptoms evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 7).

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For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for extrapyramidal symptoms ranged from very low to low (Summary of findings 7). Dolasetron (RR 0.67; 95% CI 0.10 to 4.38) may reduce extrapyramidal symptoms compared to placebo, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether ondansetron (RR 0.73, 95% CI 0.39 to 1.38) and granisetron (RR 0.90, 95% CI 0.23 to 3.57) reduce extrapyramidal symptoms compared to placebo, with very low-certainty evidence (study limitation, very serious concerns for imprecision). We are uncertain whether ramosetron (RR 0.73, 95% CI 0.01 to 37.44), with indirect evidence only, reduces extrapyramidal symptoms compared to placebo, with very low-certainty evidence (study limitation, incoherence, very serious concerns for imprecision). We are also uncertain whether tropisetron (RR 0.82, 95% CI 0.43 to 1.58) reduces extrapyramidal symptoms compared to placebo, with very low-certainty evidence (very serious concerns for study limitations and imprecision). We are uncertain whether palonosetron (RR 1.00, 95% CI 0.02 to 48.80), with direct evidence only, has little or no effect on extrapyramidal symptoms compared to placebo, with very low-certainty evidence (study limitation, very serious concerns for imprecision).

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for extrapyramidal symptoms was assessed as very low and low (Summary of findings 7). Droperidol (RR 1.36, 95% CI 0.89 to 2.08), haloperidol (RR 1.18, 95% CI 0.37 to 3.73), and metoclopramide (RR 1.14, 95% CI 0.59 to 2.20) may increase extrapyramidal symptoms compared to placebo, with low-certainty evidence (very serious concerns for imprecision). Amisulpride (RR 1.00, 95% CI 0.02 to 50.11), with direct evidence only, may have little or no effect on extrapyramidal symptoms compared to placebo, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether perphenazine (RR 1.03, 95% CI 0.05 to 23.02) compared to placebo has little or no effect on extrapyramidal symptoms, with very low-certainty evidence (study limitations, very serious concerns for imprecision).

No studies reporting extrapyramidal symptoms were available for relevant NK_1 receptor antagonists (compared to placebo) (Summary of findings 7).

For relevant corticosteroids (compared to placebo), the certainty of evidence of network effect estimates for extrapyramidal symptoms was assessed as low for dexamethasone (Summary of findings 7). Dexamethasone (RR 0.70, 95% CI 0.17 to 2.80) may reduce extrapyramidal symptoms compared to placebo, with low-certainty evidence (very serious concerns for imprecision).

No studies reporting extrapyramidal symptoms were available for methylprednisolone.

No studies reporting extrapyramidal symptoms were available for relevant antihistamines (compared to placebo) (Summary of findings 7).

No studies reporting extrapyramidal symptoms were available for the anticholinergic scopolamine (Summary of findings 7).

Constipation within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of constipation

Pairwise meta-analyses of constipation comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for amisulpride (Analysis 1.7), dexamethasone (Analysis 3.7), granisetron (Analysis 7.7), metoclopramide (Analysis 10.6), ondansetron (Analysis 11.7), palonosetron (Analysis 12.7), ramosetron (Analysis 15.6), and tropisetron (Analysis 18.7). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of constipation: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome constipation are available in an online repository (Supplementary Files-7-constipation*; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

In total, 44 RCTs including 11,540 participants were eligible for the network meta-analysis of constipation. Six studies (14%) have reported zero events in all study arms. One study was not connected to the network and was excluded from the following analysis: Awad 2002; comparison: droperidol-ondansetron versus droperidol. The network geometry of the remaining 43 studies with 74 pair-wise comparisons due to multi-arm studies included 23 different treatments (nodes) (Figure 20). The 23 treatments included 10 drug combinations, 12 single drugs, and placebo or no treatment. The most common comparisons were ondansetron (k = 8 studies), dexamethasone (k = 3), dexamethasone-granisetron (k = 3), granisetron (k = 3), and palonosetron (k = 3), all compared to placebo; casopitant-ondansetron (k = 4) and aprepitant (k = 3) compared to ondansetron; and ondansetron compared to palonosetron (k = 3). Of the single drugs of direct interest, amisulpride was poorly connected to the network, with placebo as the only comparator.

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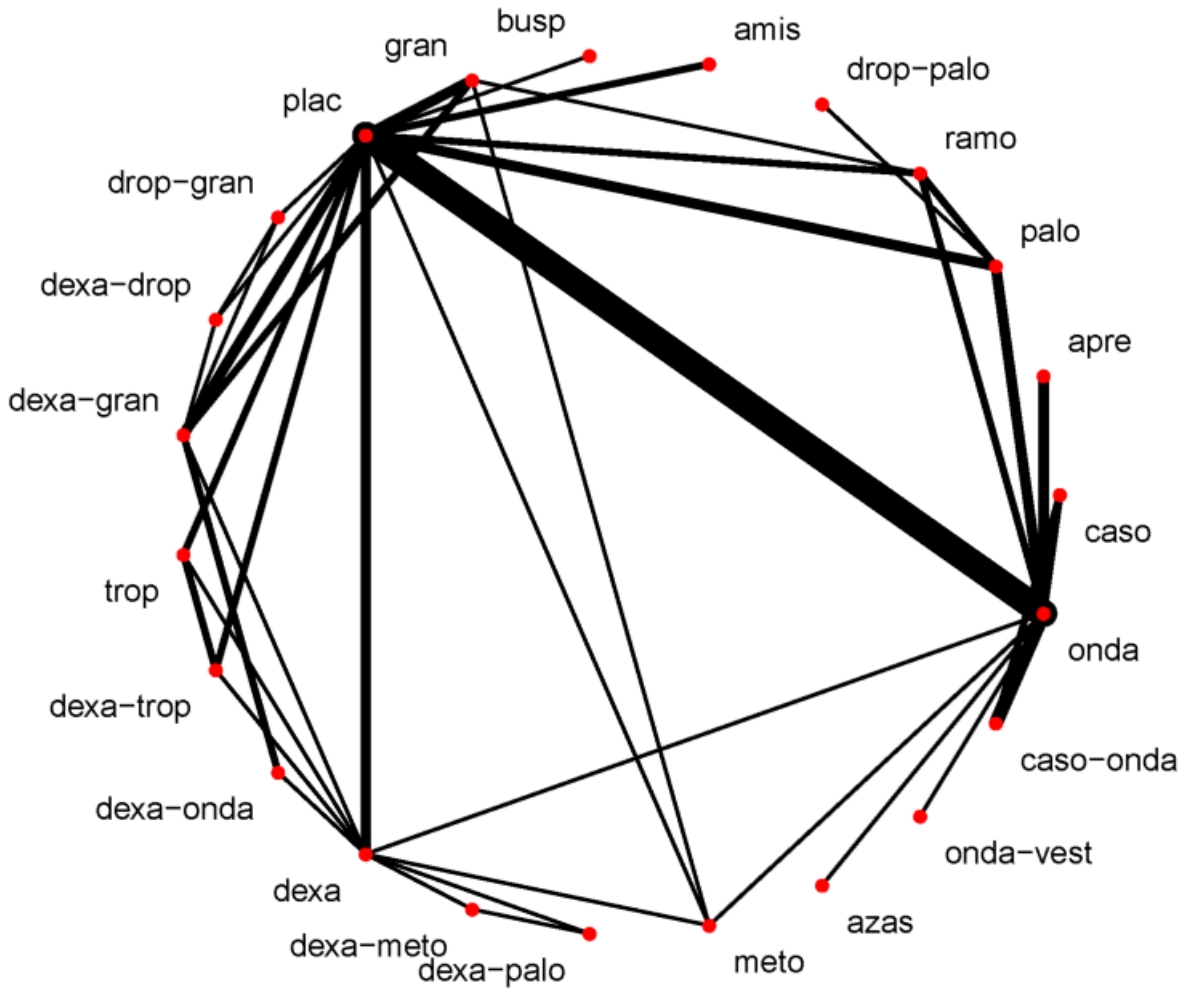
Figure 20. Network geometry of eligible comparisons for postoperative constipation. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 253 different treatments, 253 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 30 of 253 comparisons, direct and indirect evidence was available, whereas for 11 comparisons, only direct evidence was available, and for 212 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 21. In terms of constipation, none of the 12 single drugs showed important benefit (95% CI upper boundary < 0.9) or important harm (95% CI lower boundary > 1.11) compared to placebo. Five single treatments showed benefit (granisetron, azasetron, ramosetron, casopitant, dexamethasone), three treatments showed no or minimal effect (ondansetron, aprepitant, palonosetron), four treatments showed harm (buspirone, tropisetron, amisulpride, metoclopramide), and all treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs ranged between RR 0.59 (95% CI 0.21 to 1.63) for granisetron and RR 1.90 (95% CI 0.34 to 10.68) for metoclopramide. None of the combination treatments showed important benefit or important harm compared to placebo. Six combination treatments

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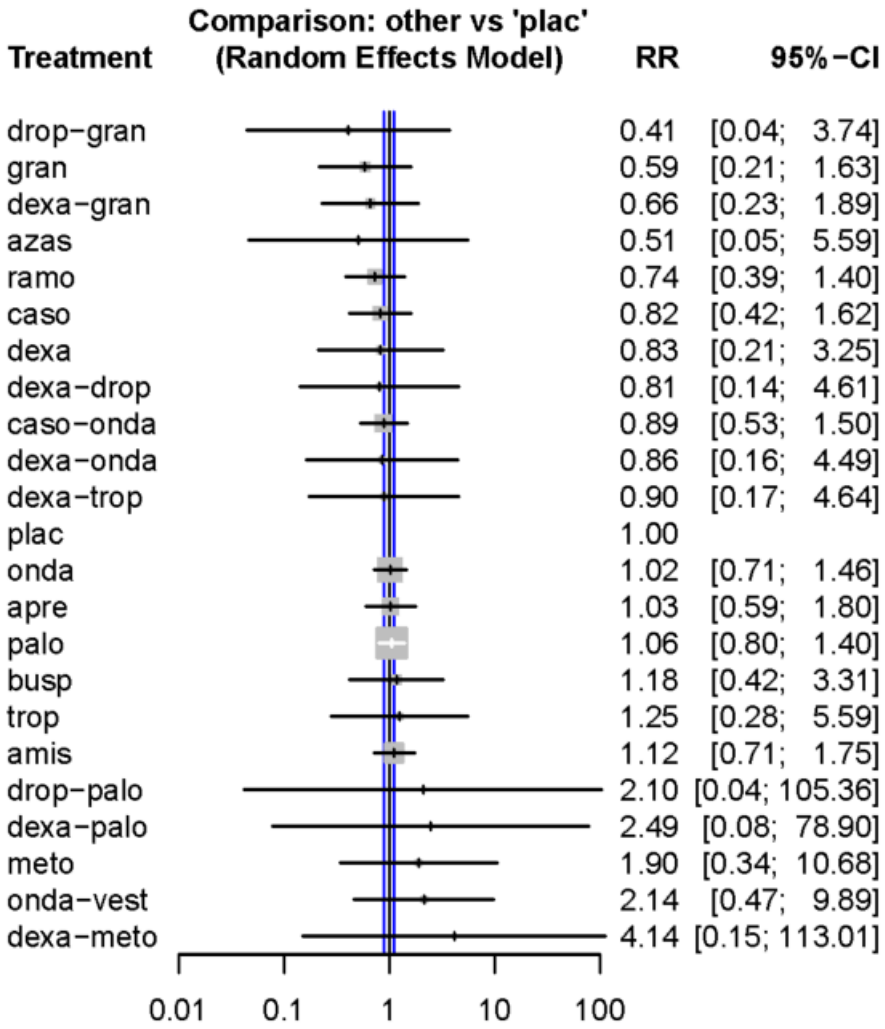
showed benefit, four showed harm, and all treatment effects were associated with uncertainty. Treatment effects of combination treatments ranged between RR 0.41 (95% CI 0.04 to 3.74) for droperidol-granisetron and RR 4.14 (95% CI 0.15 to 113.01) for dexamethasone-metoclopramide.

Figure 21. Forest plot of network meta-analysis of all trials for postoperative constipation. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to 1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



The estimated value of between-study variance for the network meta-analysis of constipation was 0 (tau^2) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 7.68, df = 20, P = 0.99) and no inconsistency between designs (Q = 14.43, df = 15, P = 0.49). No clinically relevant heterogeneity for relevant comparisons (single drugs of direct interest compared to placebo) was detectable because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed disagreement (direct versus indirect) for two out of 30 comparisons, namely, casopitant versus ondansetron (P = 0.0006) and casopitant-ondansetron versus casopitant (P = 0.0006). There was no clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo.

Sensitivity analyses of constipation

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of constipation: risk of bias

Five (12%) of 43 studies were rated as having high risk of overall bias, 23 (53%) as unclear, and 15 (35%) as low. Two studies with low

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risk of bias were not connected to the network of low risk of bias studies and were excluded from the sensitivity analysis (Hu 2017, comparison: droperidol-palonosetron versus palonosetron; Park 2013, comparison: ramosetron versus palonosetron). The network geometry of the remaining 13 studies at low risk of bias included 13 treatments. Three treatments were two-fold combinations of antiemetic drugs, nine were single drugs, and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis for constipation, palonosetron, ramosetron, and tropisetron were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Comparison of treatment effects of the sensitivity analysis for risk of bias and the primary network meta-analysis for constipation with placebo as the reference compound revealed non-robust treatment effects for five single drugs of direct interest (granisetron, casopitant, amisulpride, aprepitant, ondansetron). Granisetron, casopitant, and amisulpride, with RR 1.00 (95% CI 0.02 to 49.06), RR 1.09 (95% CI 0.18 to 6.52), and RR 1.11 (95% CI 0.60 to 2.02), respectively, showed no or minimal effect associated with uncertainty. Aprepitant and ondansetron, with RR 1.34 (95% CI 0.26 to 6.79) and RR 1.37 (95% CI 0.30 to 6.19), respectively, showed harm associated with uncertainty. The estimated value of between-study variance for the sensitivity network meta-analysis of constipation was 0.0743 (tau^2) (I^2 = 22.2%).

Reporting bias (constipation)

None of the direct pair-wise comparisons included 10 or more studies. Therefore, analyses investigating reporting or publication bias were not performed.

Subgroup analysis of constipation: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis for constipation including single drugs only (and excluding combination treatments) with 35 studies and 13 treatments including placebo was conducted. Network geometry, effect estimates, and the ranking order of drugs with placebo as reference compound were robust compared to the primary analysis including combination prophylaxis. The estimated value of between-study variance for the network meta-analysis of single drugs for constipation was 0 (tau^2) (I^2 = 0%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The following drugs were split into dose categories: amisulpride, aprepitant, dexamethasone, ondansetron, palonosetron, and ramosetron. For casopitant, granisetron, metoclopramide, and tropisetron, only one dose category was available for subgroup analysis. Drugs not of direct interest were included in the analysis and were lumped together, irrespective of the doses being analysed, in the category 'NA' (azasetron, buspirone). Eberhart 2006 was excluded from the subgroup analysis because the interventions were not associated with one of the three dose categories (dexamethasone 'NA', droperidol 'NA'). The network consisted of 34 studies with 13 treatments including placebo split into 23 nodes with dose categories and is presented in the online repository. In the ranking of treatments according to safety with placebo as reference compound, all 95% CIs between different doses of the same drug overlapped, and the uncertainty of treatment effects was considerable. High doses of aprepitant, dexamethasone, and palonosetron compared to placebo ranked higher than recommended and low doses of the same drug. High and recommended doses of ondansetron compared to placebo ranked higher than low doses. High and low doses of amisulpride compared to placebo ranked higher than recommended doses. Recommended doses of ramosetron compared to placebo ranked higher than high and low doses. All of the above mentioned treatment effects were associated with uncertainty.

Sensitivity analysis of constipation: comparability of doses

In 24 (69%) of 35 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of nine treatments including placebo. Of the single drugs of direct interest included in the primary network meta-analysis, aprepitant and metoclopramide were not included in the sensitivity analysis due to lack of studies with comparable doses. Treatment effects of two single drugs of direct interest (dexamethasone, tropisetron) were not robust in the sensitivity analysis with placebo as reference compound. Dexamethasone (RR 1.00, 95% CI 0.02 to 49.39) and tropisetron (RR 1.00, 95% CI 0.02 to 49.02) compared to placebo showed no or minimal effect associated with uncertainty. The estimated value of between-study variance for this sensitivity network meta-analysis of constipation was 0 (tau^2) (I^2 = 0%).

Certainty of evidence: constipation

The certainty of evidence of treatment estimates for constipation evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 8).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for constipation was assessed as very low (Summary of findings 8). The certainty of evidence of network effect estimates was downgraded due to study limitations and very serious concerns for imprecision. We are uncertain whether granisetron (RR 0.59, 95% CI 0.21 to 1.63) and ramosetron (RR 0.74, 95% CI 0.39 to 1.40) compared to placebo reduce constipation. We are uncertain whether ondansetron (RR 1.02, 95% CI 0.71 to 1.46) and palonosetron (RR 1.06, 95% CI 0.80 to 1.40) compared to placebo have little or no effect on constipation. We are also uncertain whether tropisetron (RR 1.25, 95% CI 0.28 to 5.59) compared to placebo increases constipation. No studies reporting constipation were available for dolasetron.

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for constipation was assessed as very low and low (Summary of findings 8). Metoclopramide (RR 1.90, 95% CI 0.34 to 10.68) compared to placebo may increase constipation, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether amisulpride (RR 1.12, 95% CI 0.71 to 1.75) compared to placebo, with direct evidence only, increases constipation, with very low-certainty evidence (study limitations, very serious concerns for imprecision). No studies reporting constipation were available for droperidol, haloperidol, and perphenazine.

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For relevant NK_1 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for constipation was assessed as very low (Summary of findings 8). We are uncertain whether casopitant (RR 0.82, 95% CI 0.42 to 1.62) compared to placebo reduces constipation, with very low-certainty evidence (study limitations, incoherence, very serious concerns for imprecision). We are uncertain whether aprepitant (RR 1.03, 95% CI 0.59 to 1.80) compared to placebo has little or no effect on constipation, with very low-certainty evidence (study limitations, incoherence, very serious concerns for imprecision). For both aprepitant and casopitant, only indirect evidence was available. No studies reporting constipation were available for fosaprepitant and rolapitant.

For relevant corticosteroids (compared to placebo), the certainty of evidence of network effect estimates for constipation was assessed as low for dexamethasone (Summary of findings 8). Dexamethasone (RR 0.83, 95% CI 0.21 to 3.25) compared to placebo may reduce constipation, with low-certainty evidence (very serious concerns for imprecision). No studies reporting constipation were available for methylprednisolone.

No studies reporting constipation were available for relevant antihistamines (compared to placebo) (Summary of findings 8).

No studies reporting constipation were available for the anticholinergic scopolamine (Summary of findings 8).

Wound infection within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of wound infection

Pairwise meta-analyses for wound infection comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for dexamethasone (Analysis 3.8), methylprednisolone (Analysis 9.2), metoclopramide (Analysis 10.7), and tropisetron (Analysis 18.8). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of wound infection: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome wound infection are available in an online repository (Supplementary Files-8-wound infection ; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).

In total, 35 RCTs including 4531 participants were eligible for the network meta-analysis of wound infection. Twenty-eight studies (80%) have reported zero events in all study arms. Three studies were not connected to the network and were excluded from the following analyses: Baxendale 1993, comparison: dexamethasone-scopolamine versus scopolamine; Corcoran 2017, comparison: dexamethasone-granisetron versus granisetron; Eberhart 2011, comparison: dexamethasone-dolasetron versus dolasetron. The network geometry of the remaining 32 studies with 44 pair-wise comparisons due to multi-arm studies included 10 different treatments (nodes) (Figure 22). The 10 treatments included three drug combinations, six single drugs, and placebo or no treatment. The most common comparison was dexamethasone versus placebo (k = 24). Of the single drugs of direct interest, methylprednisolone was poorly connected to the network, with placebo as the only comparator.

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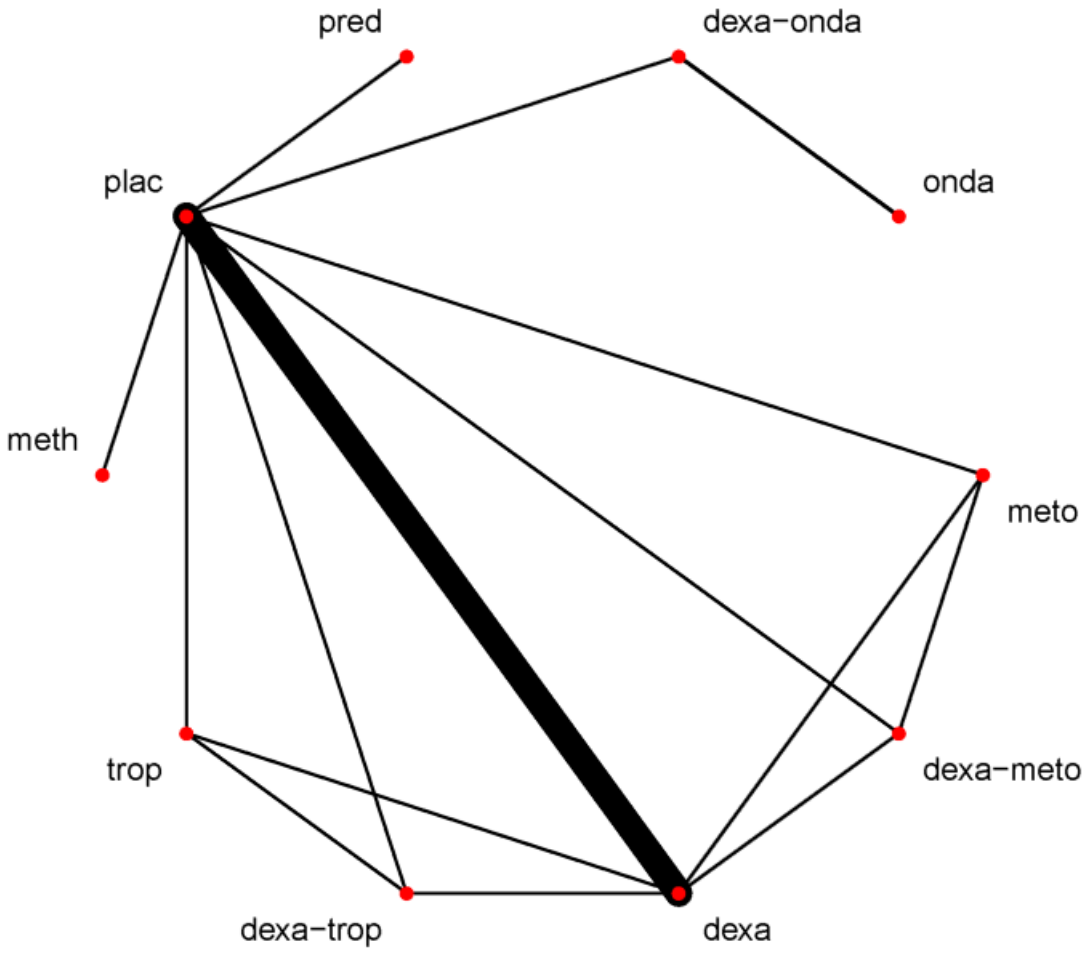
Figure 22. Network geometry of eligible comparisons for wound infection within 7 days postoperatively. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 10 different treatments, 45 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For nine of 45 comparisons, direct and indirect evidence was available, whereas for six comparisons, only direct evidence was available, and for 30 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 23. In terms of wound infection, none of the six single drugs showed important benefit (95% CI upper boundary < 0.9) or important harm (95% CI lower boundary > 1.11) compared to placebo. Two single treatments showed benefit (prednisolone, tropisetron), three treatments showed no or minimal effect (methylprednisolone, metoclopramide, dexamethasone), one treatment showed harm (ondansetron), and all treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs ranged between RR 0.14 (95% CI 0.01 to 2.61) for prednisolone and RR 1.28 (95% CI 0.01 to 115.24) for ondansetron. None of the combination treatments showed important benefit or important harm compared to placebo. One combination treatment showed benefit, two showed no or minimal effect, and all treatment

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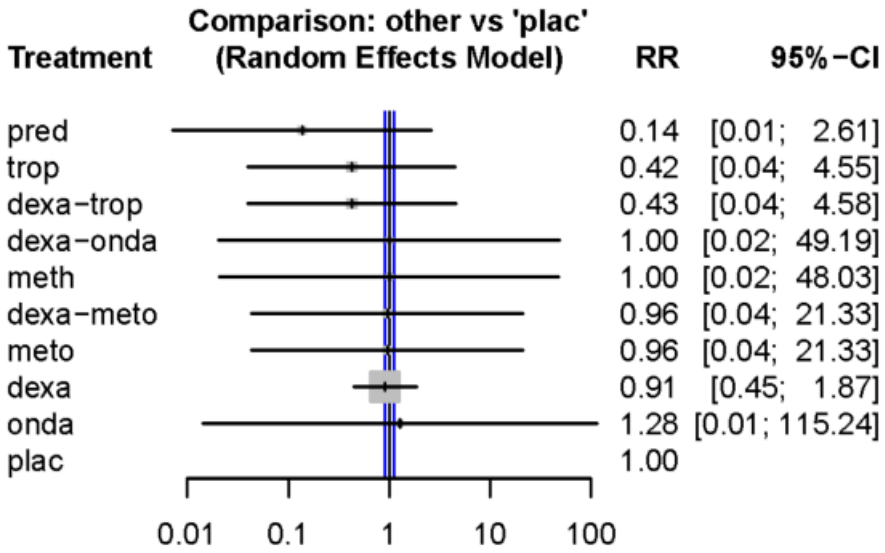
effects were associated with uncertainty. Treatment effects of combination treatments ranged between RR 0.43 (95% CI 0.04 to 4.58) for dexamethasone-tropisetron and RR 0.96 (95% CI 0.04 to 21.33) for dexamethasone-metoclopramide.

Figure 23. Forest plot of network meta-analysis of all trials for wound infection within 7 days postoperatively. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to 1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



The estimated value of between-study variance for the network meta-analysis of wound infection was 0 (tau^2) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 3.5, df = 23, P = 1.00) and no inconsistency between designs (Q = 0.29, df = 5, P = 1.00). No clinically relevant heterogeneity for relevant comparisons (single drugs of direct interest compared to placebo) was detectable because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed no disagreement (direct versus indirect) for any of the nine comparisons. There was no clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo.

Sensitivity analyses of wound infection

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of wound infection: risk of bias

Two (6%) of 32 studies were rated as having high risk of overall bias, 12 (38%) as unclear, and 18 (56%) as low. One study with low risk of bias was not connected to the network of low risk of bias studies and was excluded from the sensitivity analysis (Ko Iam 2015, comparison: dexamethasone-metoclopramide versus metoclopramide). The network geometry of the remaining 17 studies at low risk of bias included seven treatments. Two treatments were two-fold combinations of antiemetic drugs, four were single drugs, and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis for wound infection, methylprednisolone and metoclopramide were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Comparison of treatment effects of the sensitivity analysis for risk of bias and the primary network meta-analysis for wound infection with placebo as the reference compound revealed a non-robust treatment effect for dexamethasone. Dexamethasone compared to placebo, with RR 0.69 (95% CI 0.26 to 1.84), showed benefit associated with uncertainty. The estimated value of between-study variance for the sensitivity network meta-analysis of wound infection was 0 (tau^2) (I^2 = 0%).

Reporting bias (wound infection)

One direct pair-wise comparison included 10 or more studies for which small-study effects such as reporting or publication bias were investigated (dexamethasone versus placebo). Results of the funnel plot, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. We did not suspect relevant publication bias for this comparison (P = 0.22).

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Subgroup analysis of wound infection: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis for wound infection including single drugs only (and excluding combination treatments), with 27 studies and 6 treatments including placebo, was conducted. Ondansetron was not included in the network meta-analysis of single drugs for wound infection because no other single drug or placebo was a suitable comparator in the corresponding trials. Network geometry, effect estimates, and the ranking order of the remaining drugs were similar compared to the primary analysis including combination prophylaxis. The estimated value of between-study variance for the network meta-analysis of single drugs for wound infection was 0 (tau^2) (I^2 = 0%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The only drug that was split into dose categories was dexamethasone. For metoclopramide and tropisetron, only one dose category was available for subgroup analysis. Drugs not of direct interest were included in the analysis and were lumped together, irrespective of the doses being analysed, in the category 'NA' (prednisolone). Methylprednisolone, reported in only one study (Kizilkaya 2004), was attributed to dose category 'NA' due to an unusual route of application (intraarticular). Two studies were excluded from the subgroup analysis because the interventions were not associated with one of the three dose categories (dexamethasone 'NA', tropisetron 'NA') (Eberhart 2006; Hefni 2014). The network consisted of 25 studies with six treatments including placebo split into eight nodes with dose categories and is presented in the online repository. Low doses of dexamethasone compared to placebo ranked higher than recommended and high doses. However, all 95% CIs between different doses of dexamethasone overlapped, and the uncertainty of treatment effects was considerable.

Sensitivity analysis of wound infection: comparability of doses

In 22 (88%) of 25 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of dexamethasone, tropisetron, and placebo. Of the single drugs of direct interest included in the primary network meta-analysis, metoclopramide and methylprednisolone were not included in the sensitivity analysis due to lack of studies with comparable doses. The treatment estimate for dexamethasone was robust in the sensitivity analysis with placebo as reference compound, and the estimate for tropisetron was not robust. Tropisetron (RR 0.96, 95% CI 0.02 to 51.15) compared to placebo showed no or minimal effect associated with uncertainty. The estimated value of between-study variance for this sensitivity network meta-analysis of wound infection was 0 (tau^2) (I^2 = 0%).

Certainty of evidence: wound infection

The certainty of evidence of treatment estimates for wound infection evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 9).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for wound infection was assessed as very low to low (Summary of findings 9). Tropisetron (RR 0.42, 95% CI 0.04 to 4.55) compared to placebo may reduce wound infection, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether ondansetron (RR 1.28, 95% CI 0.01 to 115.24) increases wound infection compared to placebo, with indirect evidence only and very low-certainty evidence (incoherence, very serious concerns for imprecision). No studies reporting wound infection were available for dolasetron, granisetron, palonosetron, and ramosetron.

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for wound infection was assessed as very low (Summary of findings 9). We are uncertain whether metoclopramide (RR 0.96, 95% CI 0.04 to 21.33) compared to placebo has little or no effect on wound infection, with very low-certainty evidence (study limitations, very serious concerns for imprecision). No studies reporting wound infection were available for amisulpride, droperidol, haloperidol, and perphenazine.

No studies reporting wound infection were available for relevant NK_1 receptor antagonists (Summary of findings 9).

For relevant corticosteroids (compared to placebo), the certainty of evidence of network effect estimates for wound infection was assessed as very low (Summary of findings 9). We are uncertain whether dexamethasone (RR 0.91, 95% CI 0.45 to 1.87) compared to placebo has little or no effect on wound infection, with very low-certainty evidence (study limitations, very serious concerns for imprecision). We are uncertain whether methylprednisolone (RR 1.00, 95% CI 0.02 to 48.03) compared to placebo, with direct evidence only, has little or no effect on wound infection, with very low-certainty evidence (very serious concerns for study limitations and imprecision).

No studies reporting wound infection were available for relevant antihistamines (Summary of findings 9).

No studies reporting wound infection were available for the anticholinergic scopolamine (Summary of findings 9).

Arrhythmia within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of arrhythmia

Pairwise meta-analyses for arrhythmia comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for dexamethasone Analysis 3.9), dolasetron (Analysis 5.7), droperidol (Analysis 6.7), granisetron (Analysis 7.8), haloperidol (Analysis 8.4), methylprednisolone (Analysis 9.3), metoclopramide (Analysis 10.8), ondansetron (Analysis 11.8), ramosetron (Analysis 15.7), and tropisetron (Analysis 18.9). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

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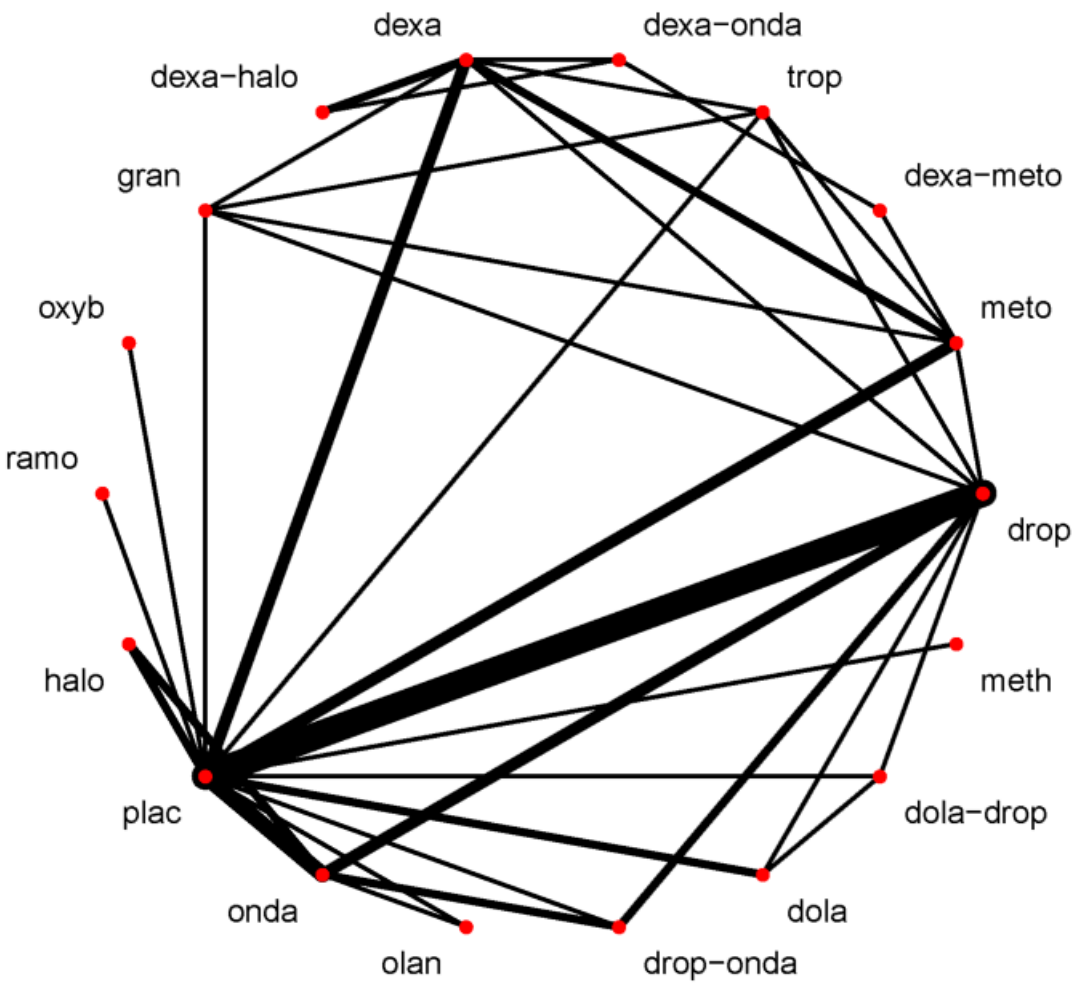
Primary analysis of arrhythmia: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome arrhythmia are available in an online repository (Supplementary Files-9-arrhythmia *; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

In total, 25 RCTs including 5067 participants were eligible for the network meta-analysis of arrhythmia. Eighteen studies (72%) have reported zero events in all study arms. The network included 18 different treatments (nodes) and consisted of 59 pair-wise comparisons due to multi-arm studies (Figure 24). The 18 treatments included five two-fold drug combinations, 12 single drugs, and placebo or no treatment. The most common comparisons were droperidol (k = 7), ondansetron (k = 4), dexamethasone (k = 3), metoclopramide (k = 3), all compared to placebo, and droperidol compared to ondansetron (k = 3). Of the single drugs of direct interest, methylprednisolone and ramosetron were poorly connected to the network, with placebo as the only comparator.

Figure 24. Network geometry of eligible comparisons for postoperative arrhythmia. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



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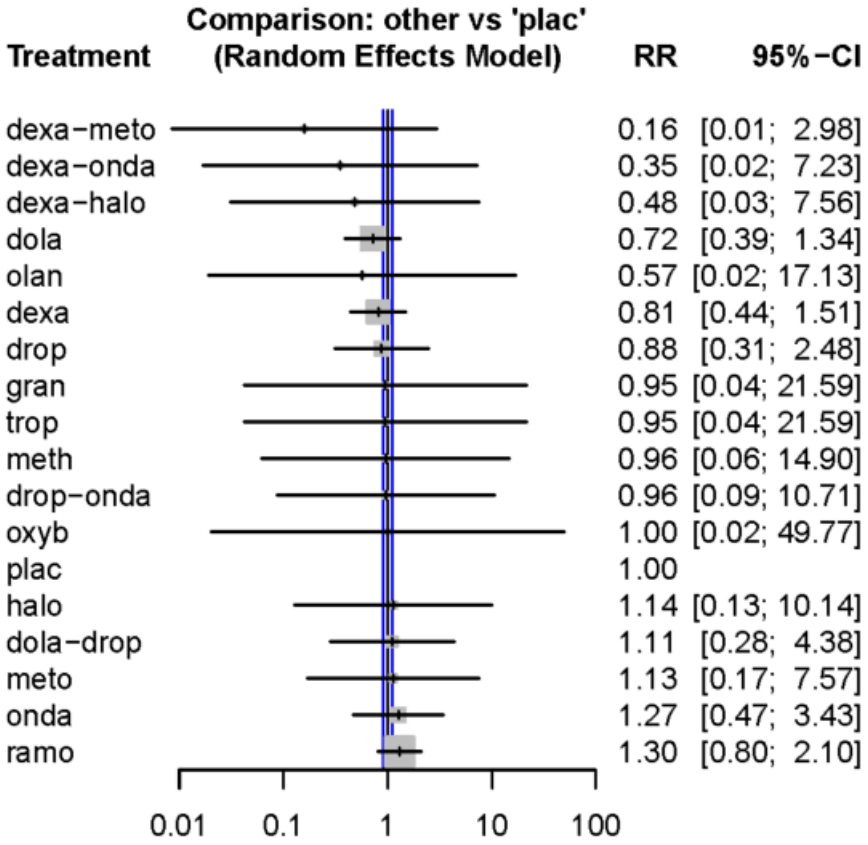
For 18 different treatments, 153 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 33 of 153 comparisons, direct and indirect evidence was available, whereas for four comparisons, only direct evidence was available, and for 116 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 25. In terms of arrhythmia, none of the 12 single drugs showed important benefit (95% CI upper boundary < 0.9) or important harm (95% CI lower boundary > 1.11) compared to placebo. Four single treatments showed benefit (dolasetron, olanzapine dexamethasone, droperidol), four showed no or minimal effect (granisetron, tropisetron, methylprednisolone, oxybutynin), four showed harm (haloperidol, metoclopramide, ondansetron, ramosetron), and all treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs ranged between RR 0.72 (95% CI 0.39 to 1.34) for dolasetron and RR 1.30 (95% CI 0.80 to 2.10) for ramosetron. None of the five combination treatments showed important benefit or important harm compared to placebo. Three combination treatments showed benefit, one showed little or no effect, and one showed harm, and all treatment effects were associated with uncertainty. Treatment effects of combination treatments ranged between RR 0.16 (95% CI 0.01 to 2.98) for dexamethasone-metoclopramide and RR 1.11 (95% CI 0.28 to 4.38) for dolasetron-droperidol.

Figure 25. Forest plot of network meta-analysis of all trials for postoperative arrhythmia. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to 1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



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The estimated value of between-study variance for the network meta-analysis of arrhythmia was 0 (tau^2) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 0.10, df = 3, P = 0.99) and no inconsistency between designs (Q = 0.78, df = 18, P = 1.00). No clinically relevant heterogeneity for relevant comparisons (single drugs of direct interest compared to placebo) was detectable because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed no disagreement (direct versus indirect) for any of the 33 comparisons There was no clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo.

Sensitivity analyses of arrhythmia

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of arrhythmia: risk of bias

Three (12%) of 25 studies were rated as having high risk of overall bias, eight (25%) as unclear, and 14 (56%) as low. One study with low risk of bias was not connected to the network of low risk of bias studies and was excluded from the sensitivity analysis (Ko Iam 2015, comparison: dexamethasone-metoclopramide versus metoclopramide). The network geometry of the remaining 13 studies at low risk of bias included 11 treatments. Three treatments were two-fold combinations of antiemetic drugs, seven were single drugs, and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis for arrhythmia, granisetron, methylprednisolone, metoclopramide, and tropisetron were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Comparison of treatment effects of the sensitivity analysis for risk of bias and the primary network meta-analysis for arrhythmia with placebo as reference compound revealed non-robust treatment effects for two drugs of direct interest (ondansetron, haloperidol). Haloperidol and ondansetron compared to placebo with RR 0.95 (95% CI 0.05 to 18.64) and RR 0.90 (95% CI 0.10 to 7.88), respectively, showed no or minimal effect associated with uncertainty. The estimated value of between-study variance for the sensitivity network meta-analysis of arrhythmia was 0 (tau^2) (I^2 = 0%).

Reporting bias (arrhythmia)

None of the direct pair-wise comparisons included 10 or more studies. Therefore, analyses investigating reporting or publication bias were not performed.

Subgroup analysis of arrhythmia: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis for arrhythmia including single drugs only (and excluding combination treatments) with 21 studies and 13 treatments including placebo was conducted. Network geometry, effect estimates, and the ranking order of drugs were similar compared to the primary analysis including combination prophylaxis. However, the comparison metoclopramide versus placebo (RR 0.93, 95% CI 0.13 to 6.80) showed a slightly changed treatment effect, changing clinical interpretation from harm to no or minimal effect, both associated with uncertainty. The estimated value of between-study variance for the network meta-analysis of single drugs for arrhythmia was 0 (tau^2) (I^2 = 0%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The following drugs were split into dose categories: dexamethasone, dolasetron, droperidol, haloperidol, and ondansetron. For granisetron, methylprednisolone, metoclopramide, ramosetron, and tropisetron only one dose category was available for subgroup analysis. Drugs not of direct interest were lumped together, irrespective of the doses being analysed, in the category 'NA' (olanzapine, oxybutynin). The network consisted of 21 studies with 13 treatments including placebo split into 19 nodes with dose categories. In the ranking of treatments according to safety with placebo as the reference compound, recommended doses of ondansetron showed harm associated with uncertainty, with RR 2.88 (95% CI 1.09 to 7.61). Low (RR 0.11, 95% CI 0.01 to 1.99) and high doses (RR 0.23, 95% CI 0.02 to 2.37) of ondansetron showed benefit associated with uncertainty. High doses of dexamethasone ranked higher than recommended doses. All doses of dolasetron showed benefit, all doses of haloperidol showed harm, and all estimates were associated with uncertainty. Overall, the 95% CIs between different doses of all single drugs overlapped, and the uncertainty of treatment effects was considerable, limiting reliable conclusions.

Sensitivity analysis of arrhythmia: comparability of doses

In 15 (71%) of 21 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of eight treatments including placebo. Of the single drugs of direct interest included in the primary network meta-analysis, granisetron, metoclopramide, and tropisetron were not included in the sensitivity analysis due to lack of studies with comparable doses. Estimated treatment effects for other single drugs of direct interest were robust in the sensitivity analysis with placebo as reference compound, except for haloperidol, with no or little effect associated with uncertainty (RR 1.09, 95% CI 0.08 to 14.13). The estimated value of between-study variance for this sensitivity network meta-analysis of arrhythmia was 0 (tau^2) (I^2 = 0%).

Certainty of evidence: arrhythmia

The certainty of evidence of treatment estimates for arrhythmia evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 10).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for arrhythmia ranged from very low to low (Summary of findings 10). Ramosetron (RR 1.30, 95% CI 0.80 to 2.10), with direct evidence only, may increase and dolasetron (RR 0.72, 95% CI 0.39 to 1.34) may reduce arrhythmia compared to placebo, both with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether ondansetron (RR 1.27, 95% CI 0.47 to 3.43) compared to placebo increases arrhythmia, with very low-certainty evidence (study limitations, very serious concerns for imprecision). We are uncertain whether granisetron (RR 0.95, 95% CI 0.04 to 21.59) and

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tropisetron (RR 0.95, 95% CI 0.04 to 21.59) compared to placebo have little or no effect on arrhythmia, with very low-certainty evidence (study limitations, very serious concerns for imprecision). No studies reporting arrhythmia were available for palonosetron.

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for arrhythmia was assessed as very low (Summary of findings 10) (study limitations and very serious concerns for imprecision). We are uncertain whether droperidol (RR 0.88, 95% CI 0.31 to 2.48) compared to placebo reduces arrhythmia. We are uncertain whether metoclopramide (RR 1.13, 95% CI 0.17 to 7.57) and haloperidol (RR 1.14, 95% CI 0.13 to 10.14) compared to placebo increase arrhythmia. No studies reporting arrhythmia were available for amisulpride and perphenazine.

No studies reporting arrhythmia were available for relevant NK_1 receptor antagonists (Summary of findings 10).

For relevant corticosteroids (compared to placebo), the certainty of evidence of network effect estimates for arrhythmia was assessed as low and very low (Summary of findings 10). Dexamethasone (RR 0.81, 95% CI 0.44 to 1.51) may reduce arrhythmia compared to placebo, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether methylprednisolone (RR 0.96, 95% CI 0.06 to 14.90) compared to placebo, with direct evidence only, has little or no effect on arrhythmia, with very low-certainty evidence (very serious concerns for study limitations and imprecision).

No studies reporting arrhythmia were available for relevant antihistamines (Summary of findings 10).

No studies reporting arrhythmia were available for the anticholinergic scopolamine (Summary of findings 10).

Visual disturbances within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of visual disturbances

Pairwise meta-analyses of visual disturbances comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for dexamethasone (Analysis 3.10), droperidol (Analysis 6.8), methylprednisolone (Analysis 9.4), metoclopramide (Analysis 10.9), ondansetron (Analysis 11.9), scopolamine (Analysis 17.6), and tropisetron (Analysis 18.10). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of visual disturbances: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome visual disturbances are available in an online repository (Supplementary Files-10-visual disturbances *; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

In total, 23 RCTs including 3815 participants were eligible for the network meta-analysis of visual disturbances. All studies have reported events in at least one study arm. Two studies were not connected to the network and were excluded from two analyses (Green 2012, comparison: aprepitant-scopolamine versus aprepitant; White 2007-1, comparison: dexamethasone-droperidol versus dexamethasone-scopolamine). The network of the remaining 21 studies included 12 different treatments (nodes) with 36 pair-wise comparisons due to multi-arm studies (Figure 26). The 12 treatments included one two-fold drug combination, 10 single drugs, and placebo or no treatment. The most common comparisons were scopolamine (k = 8), droperidol (k = 5), and ondansetron (k = 3), all compared to placebo. Of the single drugs of direct interest, dexamethasone and methylprednisolone were poorly connected to the network, with placebo as the only comparator.

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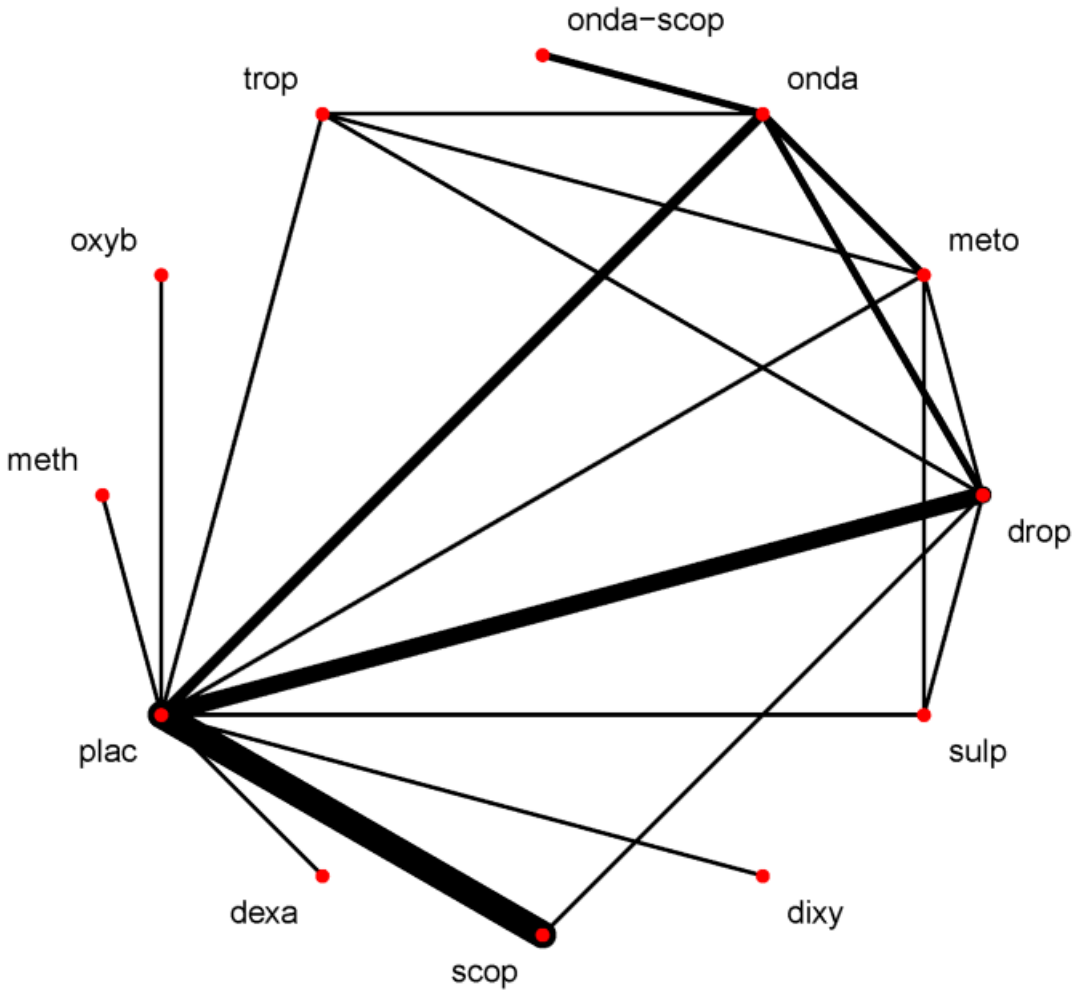
Figure 26. Network geometry of eligible comparisons for postoperative visual disturbances. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 12 different treatments, 66 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 15 of 66 comparisons, direct and indirect evidence was available, whereas for five comparisons, only direct evidence was available, and for 46 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 27. Of the 10 single drugs, scopolamine with RR 2.01 (95% CI 1.28 to 3.17) showed important harm (95% CI lower boundary > 1.11) compared to placebo for visual disturbances. Two single treatments showed harm (ondansetron, metoclopramide), one showed no or minimal effect (dixyrazine), six showed benefit (oxybutynin, methylprednisolone, droperidol, amisulpride, dexamethasone, tropisetron), and all treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects for all single drugs ranged between RR 0.20 (95% CI 0.01 to 4.25) for oxybutynin and RR 1.29 (95% CI 0.73 to 2.27) for ondansetron. Ondansetron-scopolamine, the only combination treatment, showed important harm compared to placebo, with RR 8.13 (95% CI 2.24 to 29.47).

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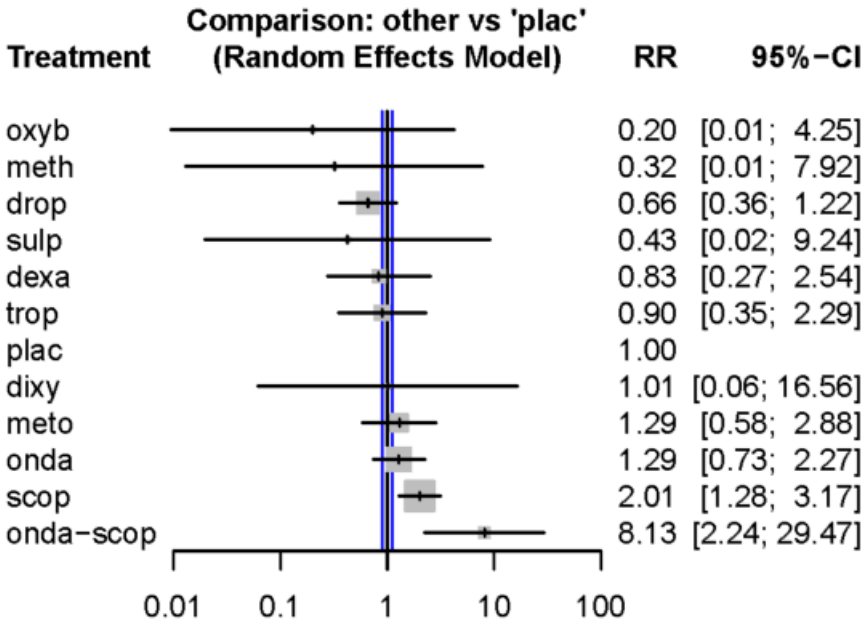
Figure 27. Forest plot of network meta-analysis of all trials for postoperative visual disturbances. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to 1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



The estimated value of between-study variance for the network meta-analysis of visual disturbances was 0.0567 (tau^2) (I^2 = 11.9%). For the random-effects model, there was no heterogeneity within designs (Q = 11.23, df = 9, P = 0.26) and no inconsistency between designs (Q = 8.06, df = 8, P = 0.43). Clinically relevant heterogeneity for comparisons of direct interest (single drugs of direct interest compared to placebo) was detected only for scopolamine because the 95% PI included a different clinical implication compared to the 95% CI. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed no disagreement (direct versus indirect) for any of the 15 comparisons. There was no clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo.

Sensitivity analyses of visual disturbances

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of visual disturbances: risk of bias

Seven (33%) of 21 studies were rated as having high risk of overall bias, nine (43%) as unclear, and five (24%) as low. The network geometry of the five studies with low risk of bias included seven treatments. Six treatments were single drugs, and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis for visual disturbances, methylprednisolone, scopolamine, and tropisetron were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Comparison of treatment effects of

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the sensitivity analysis for risk of bias and the primary network meta-analysis for visual disturbances with placebo as reference compound revealed a non-robust treatment effect for droperidol. Droperidol compared to placebo with RR 1.06 (95% CI 0.12 to 9.25) showed no or minimal effect associated with uncertainty. No between-study variance for this sensitivity network meta-analysis of visual disturbances was estimable because each comparison was represented by only one study.

Reporting bias (visual disturbances)

None of the direct pair-wise comparisons included 10 or more studies. Therefore, analyses investigating reporting or publication bias were not performed.

Subgroup analysis of visual disturbances: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis for visual disturbances including single drugs only (and excluding combination treatments) with 19 studies and 11 treatments including placebo was conducted. Network geometry, effect estimates, and the ranking order of drugs were robust compared to the primary analysis, including combination prophylaxis. The estimated value of between-study variance for the network meta-analysis of single drugs for visual disturbances was 0.0787 (tau^2) (I^2 = 16.3%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. Droperidol and ondansetron were split into high and recommended dose categories. For dexamethasone, methylprednisolone, metoclopramide, and tropisetron, only one dose category was available for subgroup analysis. Drugs without any dose recommendation according to Table 1 (scopolamine) and drugs not of direct interest (dixyrazine, oxybutynin, sulpiride) were lumped together, irrespective of the doses being analysed, in the category 'NA'. Jokela 2002 was excluded from the subgroup analysis because the interventions were not associated with one of the three dose categories (metoclopramide 'NA', tropisetron 'NA'). The network consisted of 18 studies, with 11 treatments including placebo split into 13 nodes with dose categories. In the ranking of treatments according to safety with placebo as the reference compound, recommended doses of ondansetron ranked higher than high doses. High doses of droperidol ranked higher than recommended doses. Overall, the 95% CIs between different doses of all single drugs overlapped, and the uncertainty of treatment effects was considerable, limiting reliable conclusions. The estimated value of between-study variance for this subgroup network meta-analysis of single drugs for visual disturbances was 0.1842 (tau^2) (I^2 = 28.6%).

Sensitivity analysis of visual disturbances: comparability of doses

In four (21%) of 19 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of five treatments including placebo. Of the single drugs of direct interest included in the primary network meta-analysis for visual disturbances, metoclopramide, scopolamine, and tropisetron were not included in the sensitivity analysis due to lack of studies with comparable doses. Estimated treatment effects for all other single drugs of direct interest were robust in the sensitivity analysis with placebo as the reference compound. The estimated value of between-study variance for this sensitivity network meta-analysis of visual disturbances was 0 (tau^2) (I^2 = 0%).

Certainty of evidence: visual disturbances

The certainty of evidence of treatment estimates for visual disturbances evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 11).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for visual disturbances ranged from very low to low (Summary of findings 11). Ondansetron (RR 1.29, 95% CI 0.73 to 2.27) compared to placebo may increase visual disturbances, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether tropisetron (RR 0.90, 95% CI 0.35 to 2.29) compared to placebo reduces visual disturbances, with very low-certainty evidence (very serious concerns for study limitations and imprecision). No studies reporting visual disturbances were available for dolasetron, granisetron, palonosetron, and ramosetron.

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for visual disturbances ranged from very low to low (Summary of findings 11). Metoclopramide (RR 1.29, 95% CI 0.58 to 2.88) compared to placebo may increase visual disturbances, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether droperidol (RR 0.66, 95% CI 0.36 to 1.22) compared to placebo reduces visual disturbances, with very low-certainty evidence (study limitations, very serious concerns for imprecision). No studies reporting visual disturbances were available for amisulpride, haloperidol, and perphenazine.

No studies reporting visual disturbances were available for relevant NK_1 receptor antagonists (Summary of findings 11).

For relevant corticosteroids (compared to placebo), the certainty of evidence of network effect estimates for visual disturbances was assessed as low and very low (Summary of findings 11). Dexamethasone (RR 0.83, 95% CI 0.27 to 2.54) may reduce visual disturbances compared to placebo, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether methylprednisolone (RR 0.32, 95% CI 0.01 to 7.92) compared to placebo reduces visual disturbances, with very low-certainty evidence (very serious concerns for study limitations and imprecision). For both comparisons, only direct evidence was available.

No studies reporting visual disturbances were available for relevant antihistamines (Summary of findings 11).

The anticholinergic scopolamine (RR 2.01, 95% CI 1.28 to 3.17) may increase visual disturbances compared to placebo, with low-certainty evidence (Summary of findings 11). The certainty of evidence was limited due to study limitations and heterogeneity.

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QT prolongation within seven days postoperatively

Pairwise meta-analyses (single drugs of direct interest versus placebo) of QT prolongation

Pairwise meta-analyses for QT prolongation comparing single drugs of direct interest versus placebo are presented in the Data and analyses section and were available for dexamethasone (Analysis 3.11), droperidol (Analysis 6.9), haloperidol (Analysis 8.5), ondansetron (Analysis 11.10), palonosetron (Analysis 12.8), and tropisetron (Analysis 18.11). Studies or study arms were separated according to dose categories of single drugs (low, recommended, high, NA).

Primary analysis of QT prolongation: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome QT prolongation are available in an online repository (Supplementary Files-11-QT prolongation *; including direct and indirect effect estimates to the primary NMA, network graphs, and forest plots to all sensitivity and subgroup analyses, explorative analyses of reporting bias, and funnel plots).*

In total, 18 RCTs with 37 pair-wise comparisons due to multi-arm studies including 4440 participants were eligible for the network meta-analysis of QT prolongation. Eight studies (44%) have reported zero events in all study arms. The network consisted of 13 different treatments (nodes), including four two-fold drug combinations, eight single drugs, and placebo or no treatment (Figure 28). The most common comparisons were haloperidol (k = 4) and droperidol (k = 3) compared to placebo, aprepitant (k = 3), and haloperidol (k = 3) compared to ondansetron, and dexamethasone-haloperidol compared to dexamethasone (k = 3). Of the single drugs of direct interest, aprepitant and tropisetron were poorly connected to the network, with ondansetron and placebo, respectively, as the only comparators.

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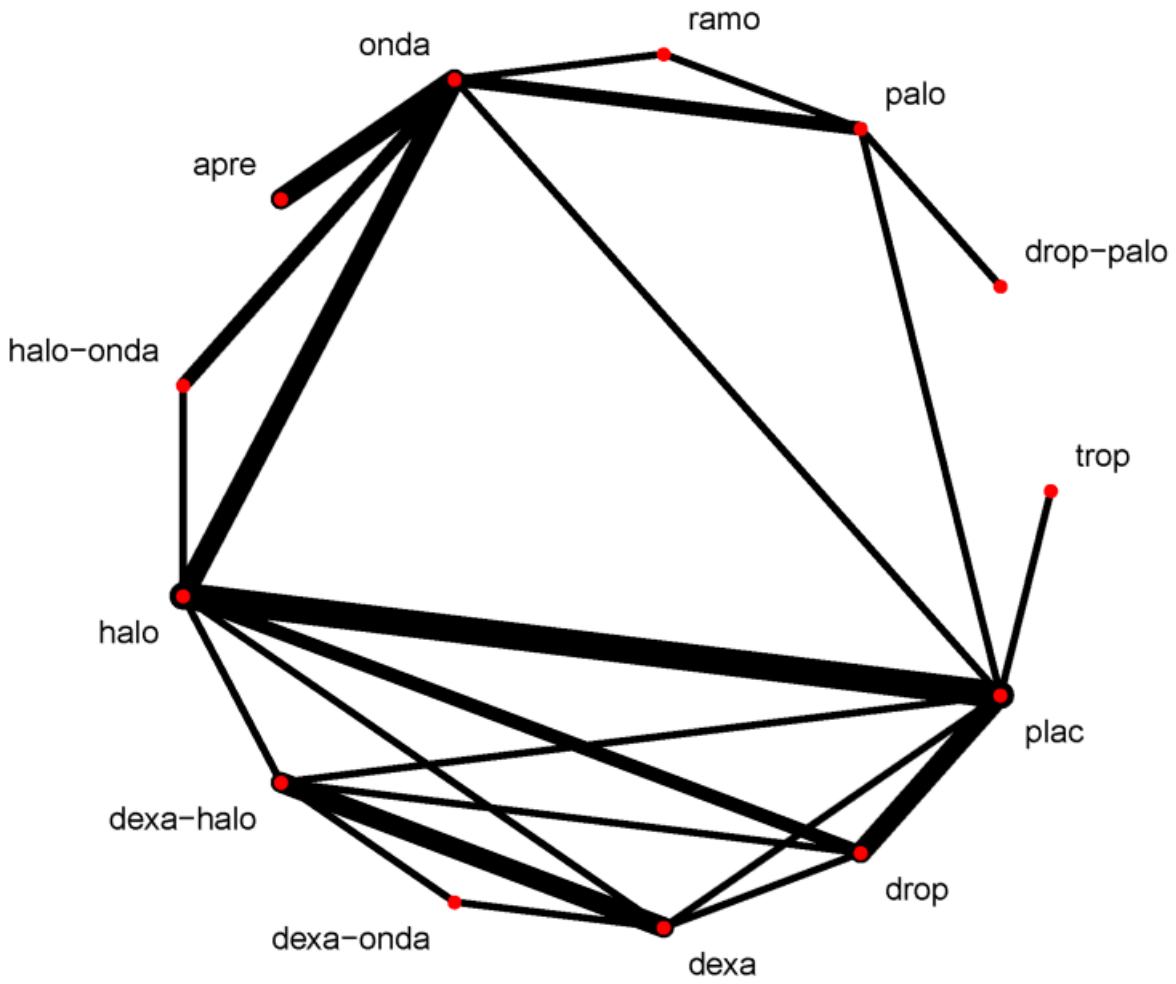
Figure 28. Network geometry of eligible comparisons for postoperative QT prolongation. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 13 different treatments, 78 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 19 of 78 comparisons, direct and indirect evidence was available, whereas for four comparisons, only direct evidence was available, and for 55 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (risk ratio, RR) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 29. In terms of QT prolongation, none of the eight single drugs showed important benefit (95% CI upper boundary < 0.9) or important harm (95% CI lower boundary > 1.11) compared to placebo. Three single treatments showed benefit (palonosetron, ramosetron, dexamethasone), four showed no or minimal effect (ondansetron, tropisetron, aprepitant, haloperidol), one showed harm (droperidol), and all treatment effects were associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs ranged between RR 0.16 (95% CI 0.02 to 1.39) for palonosetron and RR 1.29 (95% CI 0.71 to 2.34) for droperidol. None of the combination treatments showed important benefit or important harm compared to placebo. One combination treatment showed benefit, two showed no or minimal effect, one showed harm, and all treatment effects were associated with

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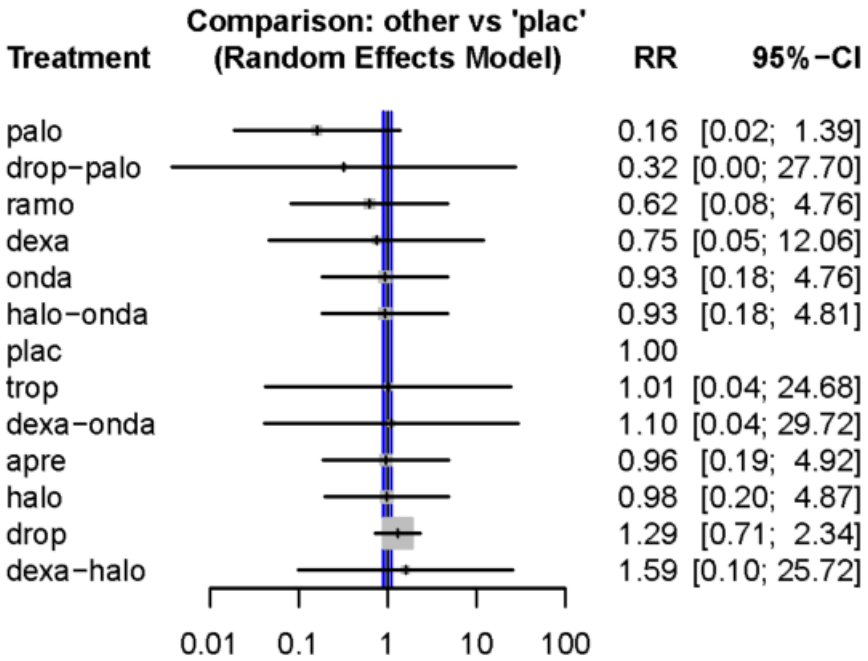
uncertainty. Treatment effects of combination treatments ranged between RR 0.32 (95% CI 0.00 to 27.70) for droperidol-palonosetron and RR 1.59 (95% CI 0.10 to 25.72) for dexamethasone-haloperidol.

Figure 29. Forest plot of network meta-analysis of all trials for postoperative QT prolongation. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.9 to 1.11). Treatments are ranked according to safety based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



The estimated value of between-study variance for the network meta-analysis of QT prolongation was 0 (tau^2) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 3.32, df = 2, P = 0.19) and no inconsistency between designs (Q = 1.78, df = 12, P = 1.00). No clinically relevant heterogeneity for comparisons of direct interest (single drugs of direct interest compared to placebo) was noted because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed no disagreement (direct versus indirect) for any of the 19 comparisons. There was no clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo.

Sensitivity analyses of QT prolongation

Sensitivity analyses included all single drugs and drug combinations, but results are described only for single drugs of direct interest compared to placebo.

Sensitivity analysis of QT prolongation: risk of bias

For QT prolongation, five (28%) of 18 studies were rated as having high risk of overall bias, six (33%) as unclear, and seven (39%) as low. One study with low risk of bias was not connected to the network for low risk of bias studies and was excluded from the sensitivity analysis (Hu 2017, comparison: droperidol-palonosetron versus palonosetron). The network geometry of the six remaining studies with low risk of bias included five treatments, of which

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four were single drugs and one was placebo. Of the single drugs of direct interest included in the primary network meta-analysis for QT prolongation, dexamethasone, palonosetron, ramosetron, and tropisetron were not included in the sensitivity network meta-analysis due to lack of studies with low risk of bias. Comparison of treatment effects of the sensitivity analysis for risk of bias and the primary network meta-analysis for QT prolongation with placebo as the reference compound revealed robust treatment effects for all included single drugs of direct interest. The estimated value of between-study variance for the sensitivity network meta-analysis of QT prolongation was 0 (tau^2) (I^2 = 0%).

Reporting bias (QT prolongation)

None of the direct pair-wise comparisons included 10 or more studies. Therefore, analyses investigating reporting or publication bias were not performed.

Subgroup analysis of QT prolongation: dose effects

The treatment effect modifier dose was investigated in a subgroup network meta-analysis splitting drugs into the categories low, recommended, and high doses according to Table 1. Splitting of doses was restricted to single drugs.

First, a network meta-analysis for QT prolongation including single drugs only (and excluding combination treatments) with 14 studies and nine treatments including placebo was conducted. Network geometry, effect estimates, and the ranking order of drugs were similar compared to the primary analysis, including combination prophylaxis. However, the comparison dexamethasone versus placebo (RR 1.09, 95% CI 0.04 to 27.88) showed a slightly changed treatment effect, changing clinical interpretation from benefit to no or minimal effect, both associated with uncertainty. The estimated value of between-study variance for the network meta-analysis of single drugs for QT prolongation was 0 (tau^2) (I^2 = 0%).

Second, the subgroup analysis of dose was conducted for the network of single drugs only. The following drugs were split into dose categories: aprepitant, haloperidol, palonosetron, and tropisetron. For dexamethasone, droperidol, ondansetron, and ramosetron, only one dose category was available for subgroup analysis. The network consisted of 14 studies with eight treatments including placebo split into 14 nodes with dose categories. In the ranking of treatments according to safety with placebo as the reference compound, high and recommended doses of tropisetron ranked higher than low doses. Low and recommended doses of palonosetron showed benefit associated with uncertainty, and recommended and high doses of haloperidol showed harm associated with uncertainty. Recommended and high doses of aprepitant showed harm, which is in contrast to the primary network meta-analysis of QT prolongation. Overall, the 95% CIs between different doses of all single drugs overlapped, and the uncertainty of treatment effects was considerable, limiting reliable conclusions. The estimated value of between-study variance for this subgroup network meta-analysis of single drugs for QT prolongation was 0 (tau^2) (I^2 = 0%).

Sensitivity analysis of QT prolongation: comparability of doses

In eight (57%) of 14 studies investigating single drugs, comparable doses of antiemetic drugs were analysed (comparable dose categories). The analysis included only studies investigating drugs of direct interest for which dose recommendations were described and that were assigned to one of the dose categories according to Table 1. The network of this sensitivity analysis consisted of seven treatments including placebo. Of the single drugs of direct interest included in the primary network meta-analysis for QT prolongation, aprepitant and dexamethasone were not included in the sensitivity analysis due to lack of studies with comparable doses. Estimated treatment effects for the other single drugs of direct interest were robust in the sensitivity analysis with placebo as the reference compound, except for ondansetron. Ondansetron (RR 0.75, 95% CI 0.05 to 10.48) showed benefit associated with uncertainty compared to placebo. The estimated value of between-study variance for this sensitivity network meta-analysis of QT prolongation was 0 (tau^2) (I^2 = 0%).

Certainty of evidence: QT prolongation

The certainty of evidence of treatment estimates for QT prolongation evaluated with CINeMA is summarized in the 'Summary of findings' table for drugs of direct interest compared to placebo (Summary of findings 12).

For relevant 5-HT_3 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for QT prolongation ranged from very low to low (Summary of findings 12). Ondansetron (RR 0.93, 95% CI 0.18 to 4.76) compared to placebo may have little or no effect on QT prolongation, with low-certainty evidence (very serious concerns for imprecision). We are uncertain whether palonosetron (RR 0.16, 95% CI 0.02 to 1.39) reduces QT prolongation compared to placebo, with very low-certainty evidence (study limitations, very serious concerns for imprecision). We are uncertain whether tropisetron (RR 1.01, 95% CI 0.04 to 24.68) compared to placebo has little or no effect on QT prolongation, with very low-certainty evidence (very serious concerns for study limitations and imprecision) and direct evidence only. We are uncertain whether ramosetron (RR 0.62, 95% CI 0.08 to 4.76) reduces QT prolongation, with only indirect evidence and very low-certainty evidence (study limitations, incoherence, very serious concerns for imprecision). No studies reporting QT prolongation were available for dolasetron and granisetron.

For relevant D_2 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for QT prolongation was assessed as low (Summary of findings 12). Droperidol (RR 1.29, 95% CI 0.71 to 2.34) may increase QT prolongation, and haloperidol (RR 0.98, 95% CI 0.20 to 4.87) may have little or no effect on QT prolongation, compared to placebo, both with low-certainty evidence (very serious concerns for imprecision). No studies reporting QT prolongation were available for amisulpride, metoclopramide, and perphenazine.

For the relevant NK_1 receptor antagonists (compared to placebo), the certainty of evidence of network effect estimates for QT prolongation was assessed as very low (Summary of findings 12). We are uncertain whether aprepitant (RR 0.96, 95% CI 0.19 to 4.92) may have little or no effect on QT prolongation, with very low-certainty evidence (incoherence, very serious concerns for imprecision) and indirect evidence only. No studies reporting QT prolongation were available for casopitant, fosaprepitant, and rolapitant.

For relevant corticosteroids (compared to placebo), the certainty of evidence of network effect estimates for QT prolongation was assessed as very low (Summary of findings 12). We are uncertain whether dexamethasone (RR 0.75, 95% CI 0.05 to 12.06)

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reduces QT prolongation compared to placebo, with very low-certainty evidence (study limitations, very serious concerns for imprecision). No studies reporting QT prolongation were available for methylprednisolone.

No studies reporting QT prolongation were available for relevant antihistamines (Summary of findings 12).

No studies reporting QT prolongation were available for the anticholinergic scopolamine (Summary of findings 12).

Secondary outcomes (not GRADE-relevant)

Assessment of the certainty of evidence was not performed for the following secondary outcomes.

Mortality within seven days postoperatively

Primary analysis of mortality: network meta-analyses with all single drugs and drug combinations

In total, 17 RCTs including 6840 participants have reported mortality in the published study report. Only one participant with ondansetron died due to pulmonary embolism during the observation period in the study of Morris 1998 comparing metoclopramide, ondansetron, and placebo. Study authors reported that the participant's death was not drug-related. All other studies have reported zero events in all study arms. Due to the low event rate, we did not perform a network meta-analysis. In total, data on mortality were reported for five drug combinations (casopitant-ondansetron, dexamethasone-granisetron, dexamethasone-ondansetron, dexamethasone-palonosetron, ondansetron-vestipitant) and seven single drugs (amisulpride, casopitant, dexamethasone, dolasetron, metoclopramide, ondansetron, palonosetron).

Early vomiting within 0 to 2 to 6 hours postoperatively or in PACU

Primary analysis of early vomiting: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome early vomiting are available in an online repository (Supplementary Files-12-early vomiting *; including direct and indirect effect estimates to the primary NMA, explorative analyses of reporting bias, and funnel plots).*

In total, 264 RCTs including 37,928 participants were eligible for the network meta-analysis of early vomiting. Twenty-one studies (8%) have reported zero events in all study arms. One study was not connected to the network and was excluded from the following analysis: Rennemo 1982, comparison: droperidol-scopolamine versus levomepromazine-scopolamine. The network of the remaining 263 studies included 69 different treatments (nodes), with 564 pair-wise comparisons due to multi-arm studies (Figure 30). The 69 treatments included 34 drug combinations (28 times: two-fold, five times: three-fold, once: four-fold), 34 single drugs, and placebo or no treatment. The most common comparisons were ondansetron (k = 60 studies), dexamethasone (k = 39), droperidol (k = 28), metoclopramide (k = 21), and granisetron (k = 13), all compared to placebo, and dexamethasone-ondansetron (k = 19), as well as dexamethasone (k = 16), compared to ondansetron. Of the single drugs of direct interest, aprepitant and fosaprepitant were poorly connected to the network, with placebo and ondansetron as the only comparators, respectively.

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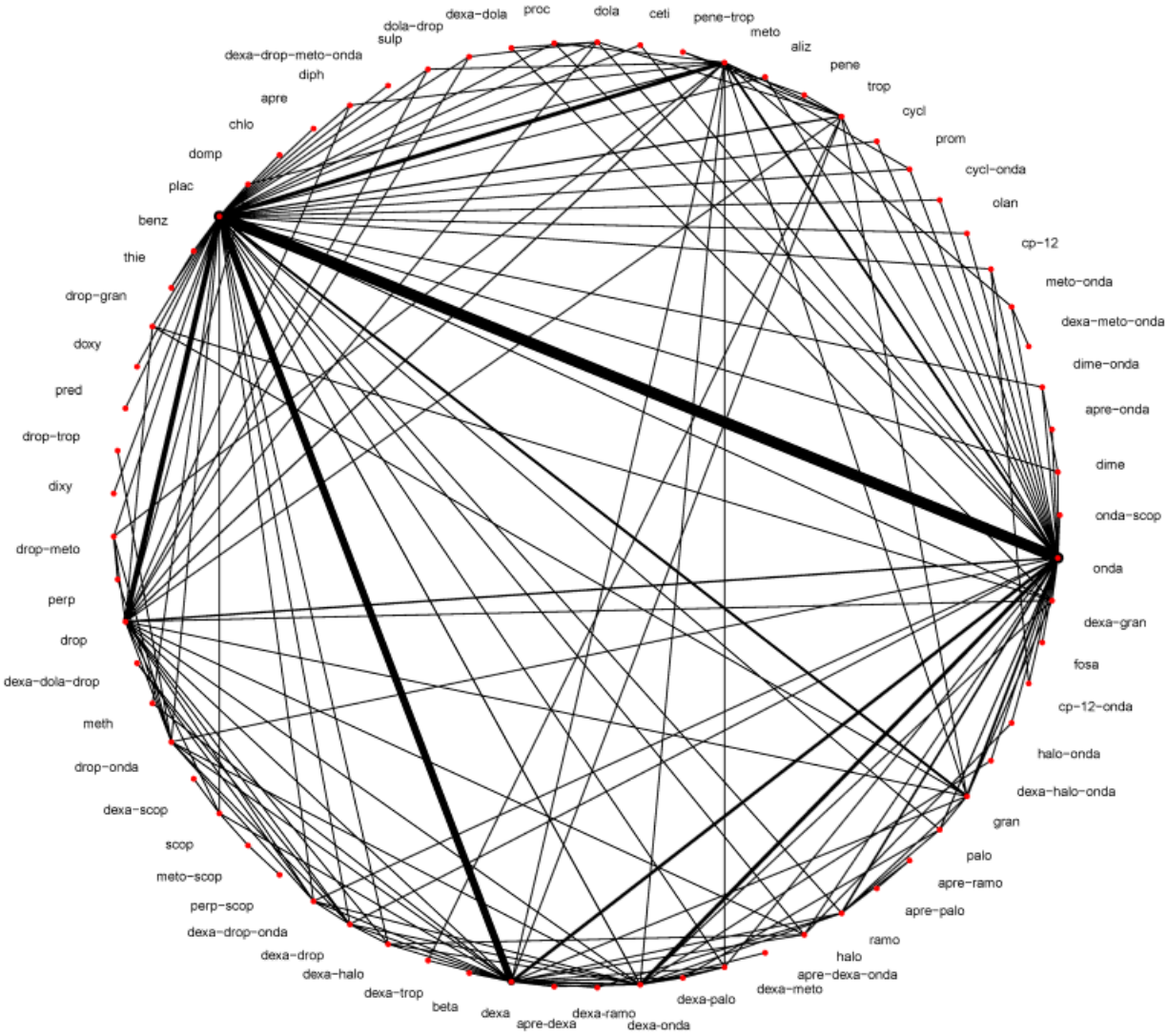
Figure 30. Network geometry of eligible comparisons for early postoperative vomiting. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 69 different treatments, 2346 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 149 of 1378 comparisons, direct and indirect evidence was available, whereas for 24 comparisons, only direct evidence was available, and for 2173 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (RR with 95% CI) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 31. In terms of preventing early vomiting, 14 of all 34 single drugs showed important benefit (95% CI upper boundary < 0.8) compared to placebo, with RRs ranging between 0.10 (95% CI 0.03 to 0.34) for fosaprepitant and 0.50 (95% CI 0.43 to 0.59) for dexamethasone. Amongst the most effective single drugs of direct interest with important benefit for early vomiting prophylaxis compared to placebo in decreasing order according to P scores were fosaprepitant, promethazine, haloperidol, granisetron, dolasetron, ramosetron, droperidol, ondansetron, tropisetron, palonosetron, and dexamethasone. Fosaprepitant, the most effective drug in the network meta-analysis, was poorly connected to the network, with only three studies comparing fosaprepitant to ondansetron. Fifteen single drugs—four of direct interest (perphenazine, aprepitant, methylprednisolone,

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dimenhydrinate)—showed benefit associated with uncertainty (95% CI crossing the range of equivalence). Five single drugs—two of direct interest (metoclopramide, scopolamine)—showed little or no effect associated with uncertainty. Treatment effects of all single drugs compared to placebo ranged between RR 0.10 (95% CI 0.03 to 0.34) for fosaprepitant and RR 0.89 (95% CI 0.55 to 1.44) for alizapride. Of all drug combinations, 23 out of 34 combinations showed important benefit compared to placebo, with RRs ranging between 0.01 (95% CI 0.00 to 0.31) for aprepitant-palonosetron and 0.38 (95% CI 0.23 to 0.64) for dexamethasone-metoclopramide. Ten drug combinations showed benefit associated with uncertainty (95% CI crossing the range of equivalence) compared to placebo, and one combination (perphenazine-scopolamine) showed harm associated with uncertainty. Treatment effects of drug combinations compared to placebo ranged between RR 0.01 (95% CI 0.00 to 0.31) for aprepitant-palonosetron and RR 1.50 (95% CI 0.41 to 5.46) for perphenazine-scopolamine.

Figure 31. Forest plot of network meta-analysis of all trials for early postoperative vomiting. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.8 to

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1.25). Treatments are ranked according to efficacy based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.

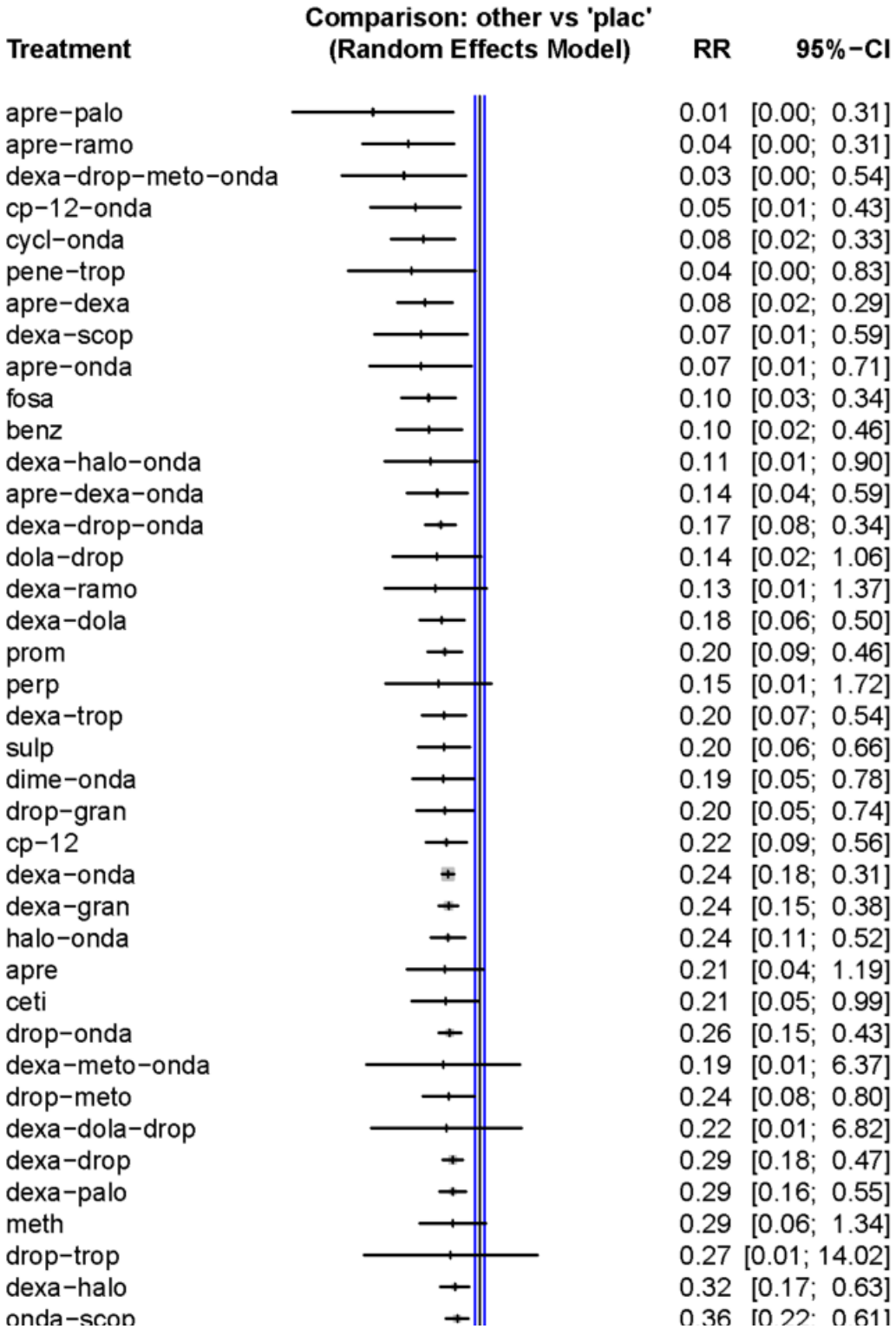

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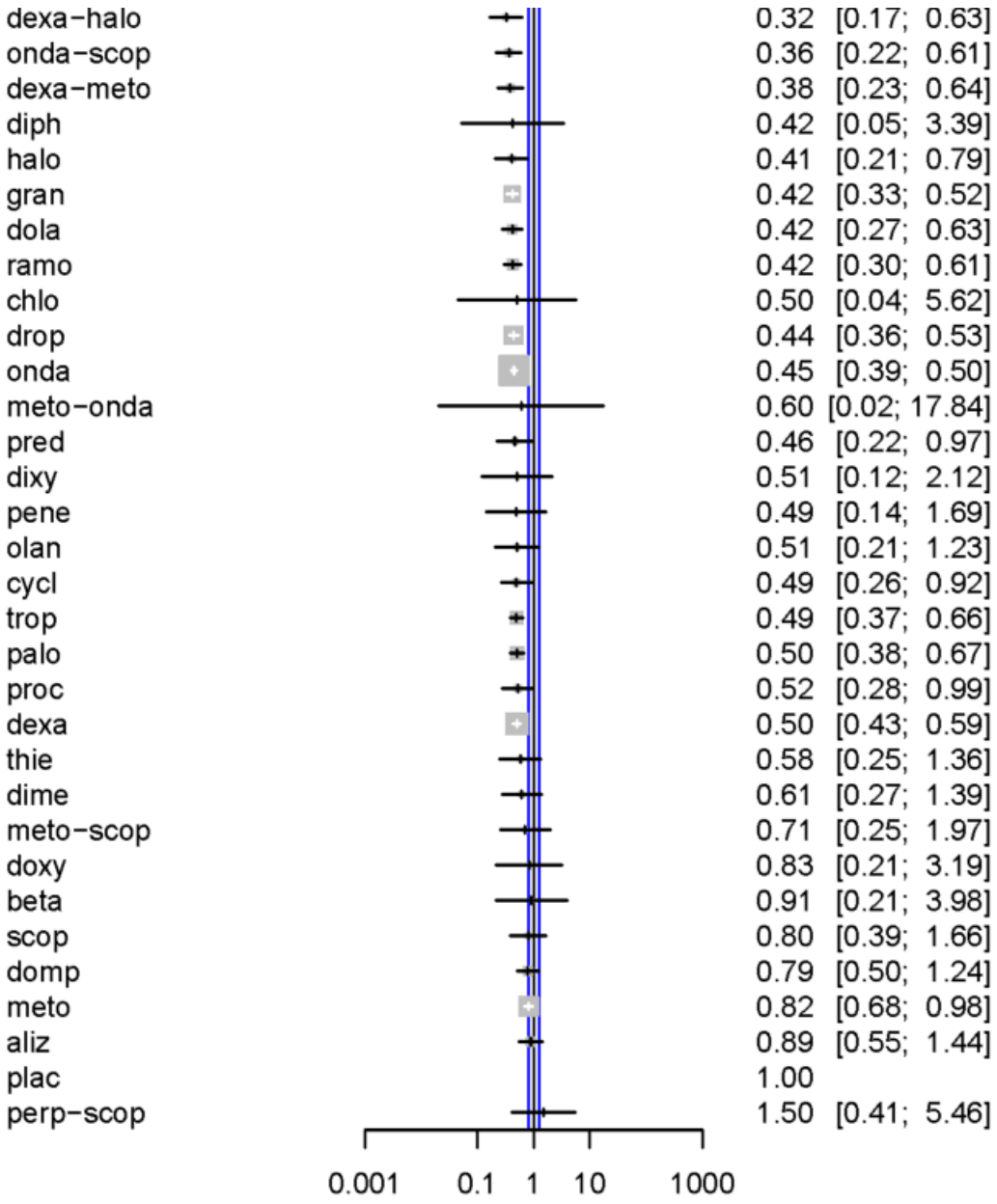
Figure 31. (Continued)



The estimated value of between-study variance for the network meta-analysis of early vomiting was 0.0574 (tau^2) (I^2 = 17.4%). For the random-effects model, there was no heterogeneity within designs (Q = 150.33, df = 153, P = 0.55) but inconsistency between designs (Q = 232.32, df = 163, P = 0.0003). When the full random-effects design-by-treatment interaction model was used, there was evidence of residual statistical inconsistency (Q = 232.32, df = 163, P = 0.0003). Clinically relevant heterogeneity for comparisons of direct interest (single drugs of direct interest compared to placebo) was detected for dexamethasone, haloperidol, metoclopramide, palonosetron, and tropisetron. In these cases, 95% PIs of treatment estimates included different clinical implications compared to the 95% CIs. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed disagreement (direct versus indirect) for nine out of 149 comparisons (dexamethasone versus ondansetron (P = 0.004), dexamethasone versus placebo (P = 0.02), dexamethasone-droperidol versus placebo (P = 0.04), dexamethasone-ondansetron versus dexamethasone-palonosetron (P = 0.02), dexamethasone-ondansetron versus ramosetron (P = 0.01), domperidone versus metoclopramide (P = 0.03), granisetron versus palonosetron (P = 0.01), palonosetron versus placebo (P = 0.005), palonosetron versus ramosetron (P = 0.045)). Clinically relevant incoherence of direct and indirect treatment estimates for single drugs of

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direct interest compared to placebo was found for dolasetron, haloperidol, metoclopramide, palonosetron, and tropisetron.

Reporting bias (early vomiting)

Eleven direct pair-wise comparisons included 10 or more studies for which small-study effects such as reporting or publication bias were investigated: dexamethasone, droperidol, granisetron, metoclopramide, and ondansetron, all compared to placebo; dexamethasone, dexamethasone-ondansetron, granisetron, metoclopramide, and ramosetron, all compared to ondansetron; and dexamethasone-ondansetron compared to dexamethasone. Results of the funnel plots, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. According to the explorative analyses, we did not suspect publication bias for any of the above mentioned comparisons. Small P values when the arcsine test was used to detect funnel plot asymmetry were found for ondansetron versus placebo (P = 0.09), dexamethasone versus placebo (P =0.003), dexamethasone versus ondansetron (P = 0.04), and droperidol versus placebo (P = 0.06). The contour-enhanced funnel plots suggested asymmetry for granisetron versus placebo and ondansetron versus placebo. However, we did not suspect relevant publication bias for these comparisons because trim and fill sensitivity analysis did not change the conclusion with respect to the range of equivalence.

Late vomiting (or dry retching) within 2 to 24 hours postoperatively

Primary analysis of late vomiting: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome late vomiting are available in an online repository (Supplementary Files-13-late vomiting *; including direct and indirect effect estimates to the primary NMA, explorative analyses of reporting bias, and funnel plots).*

In total, 206 RCTs including 28,547 participants were eligible for the network meta-analysis of late vomiting. Ten studies (5%) have reported zero events in all study arms. The network of the 206 studies included 51 different treatments (nodes), with 438 pair-wise comparisons due to multi-arm studies (Figure 32). The 51 treatments included 26 drug combinations (21 times: two-fold, four times: three-fold, once: four-fold), 24 single drugs, and placebo or no treatment. The most common comparisons were ondansetron (k = 46 studies), dexamethasone (k = 30), and droperidol (k = 21), all compared to placebo, and dexamethasone-ondansetron (k = 15), as well as dexamethasone (k = 14), compared to ondansetron. Of the single drugs of direct interest, aprepitant was poorly connected to the network, with placebo as the only comparator.

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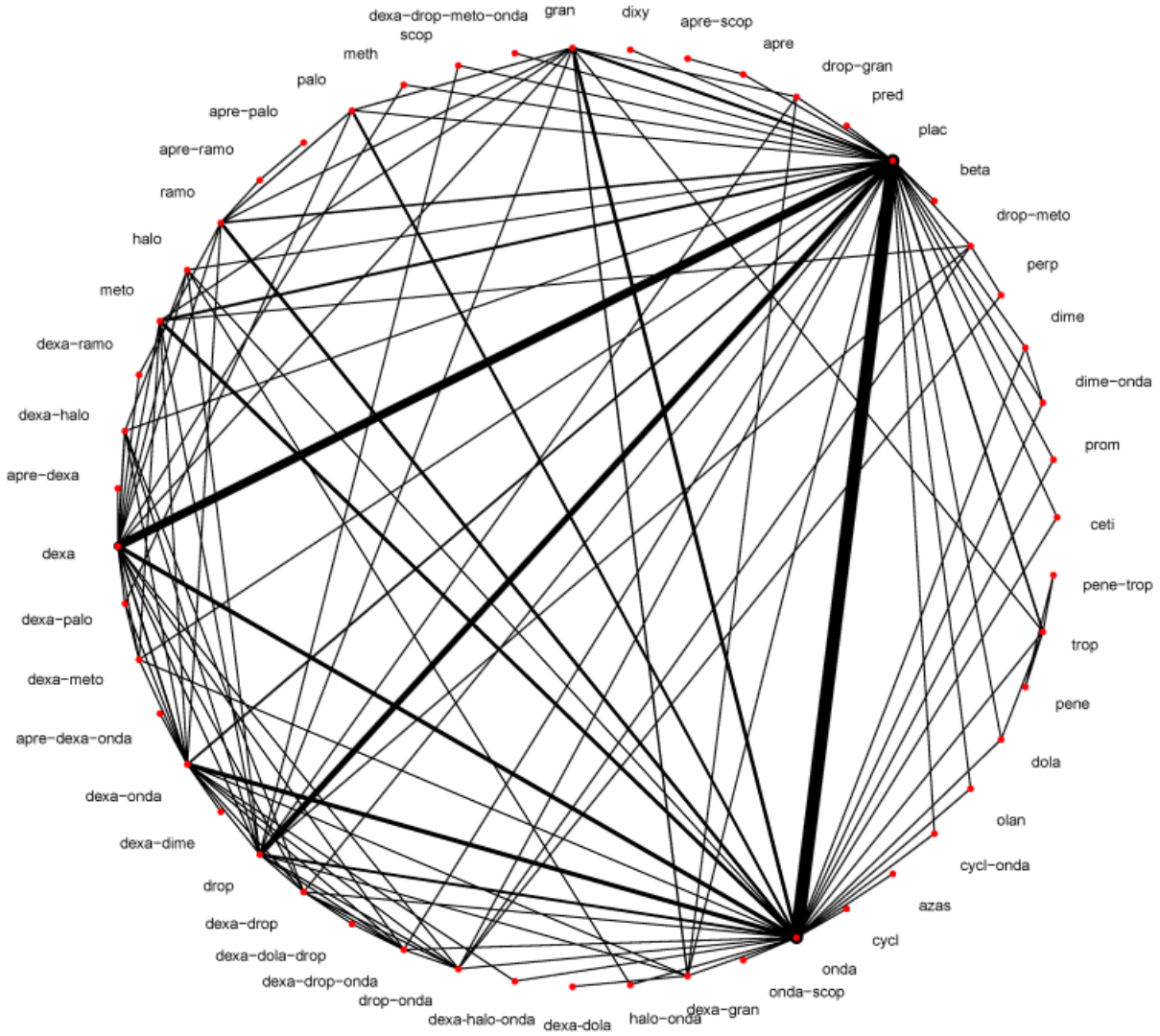
Figure 32. Network geometry of eligible comparisons for late postoperative vomiting. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 51 different treatments, 1275 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 112 of 1275 comparisons, direct and indirect evidence was available, whereas for 18 comparisons, only direct evidence was available, and for 1145 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (RR with 95% CI) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 33. Of the 24 single drugs, eight drugs showed important benefit (95% CI upper boundary < 0.8) compared to placebo, with RRs ranging between 0.06 (95% CI 0.01 to 0.48) for azasetron and 0.57 (95% CI 0.51 to 0.63) for ondansetron. Amongst the most effective single drugs of direct interest with important benefit for late vomiting prophylaxis compared to placebo in decreasing order according to P scores were aprepitant, granisetron, ramosetron, palonosetron, tropisetron, dexamethasone, and ondansetron. Eleven single drugs, eight of direct interest (promethazine, methylprednisolone, perphenazine, dimenhydrinate, dolasetron, haloperidol, scopolamine, droperidol), showed benefit associated with uncertainty (95% CI crossing the range of equivalence). Three single drugs, one of direct interest (metoclopramide), showed little or no effect associated with uncertainty. Penehyclidine and

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prednisolone, both not of direct interest, showed harm associated with uncertainty. Treatment effects of all single drugs compared to placebo ranged between RR 0.06 (95% CI 0.01 to 0.48) for azasetron and RR 1.44 (95% CI 0.68 to 3.03) for prednisolone. Of all 26 drug combinations, 18 combinations showed important benefit compared to placebo, with RRs ranging between 0.01 (95% CI 0.00 to 0.22) for aprepitant-palonosetron and 0.47 (95% CI 0.36 to 0.61) for ondansetron-scopolamine. Eight drug combinations showed benefit associated with uncertainty compared to placebo. Treatment effects of drug combinations compared to placebo ranged between RR 0.01 (95% CI 0.00 to 0.22) for aprepitant-palonosetron and RR 0.57 (95% CI 0.22 to 1.43) for droperidol-metoclopramide.

Figure 33. Forest plot of network meta-analysis of all trials for late postoperative vomiting. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.8 to

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1.25). Treatments are ranked according to efficacy based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.

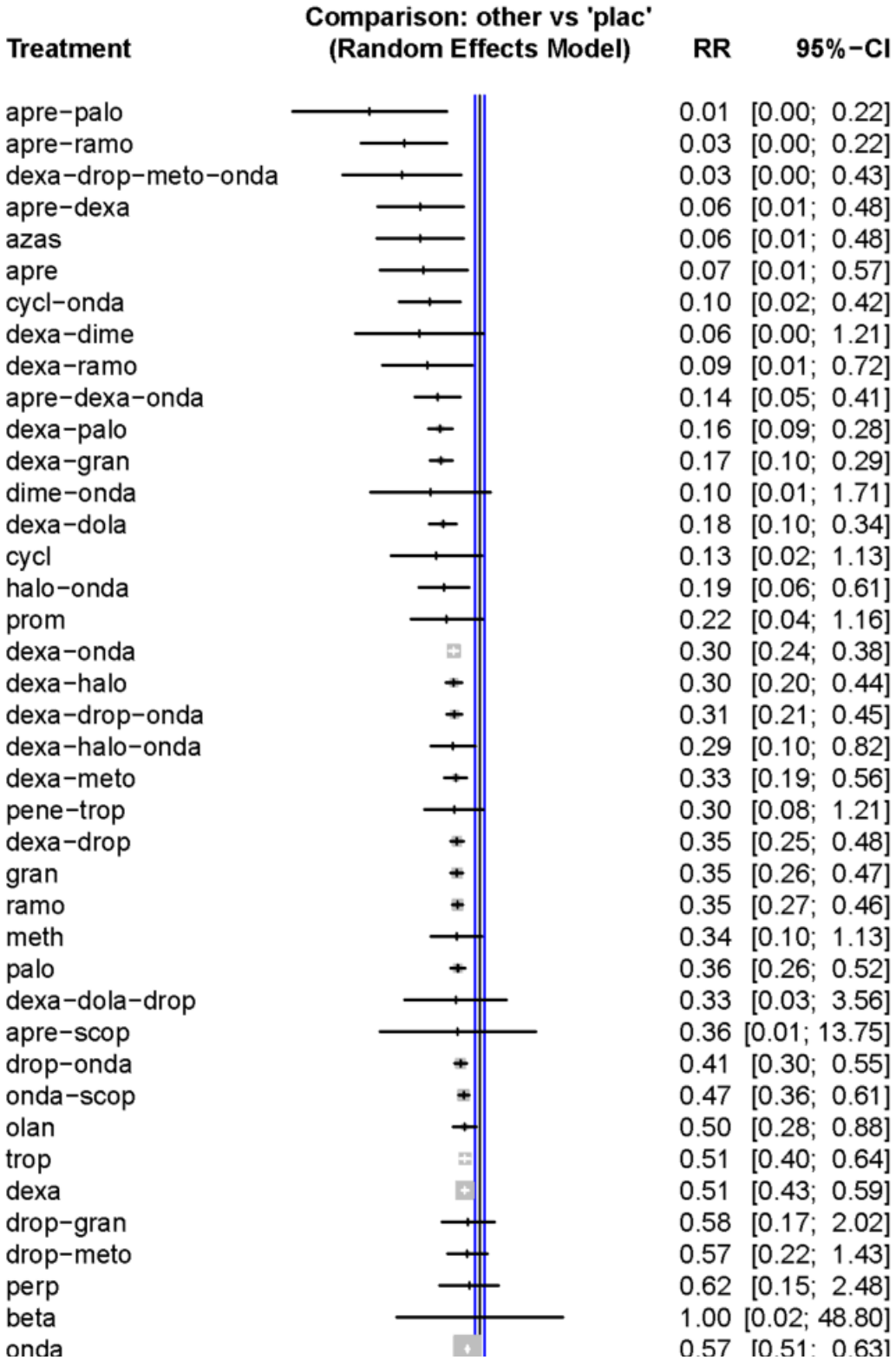

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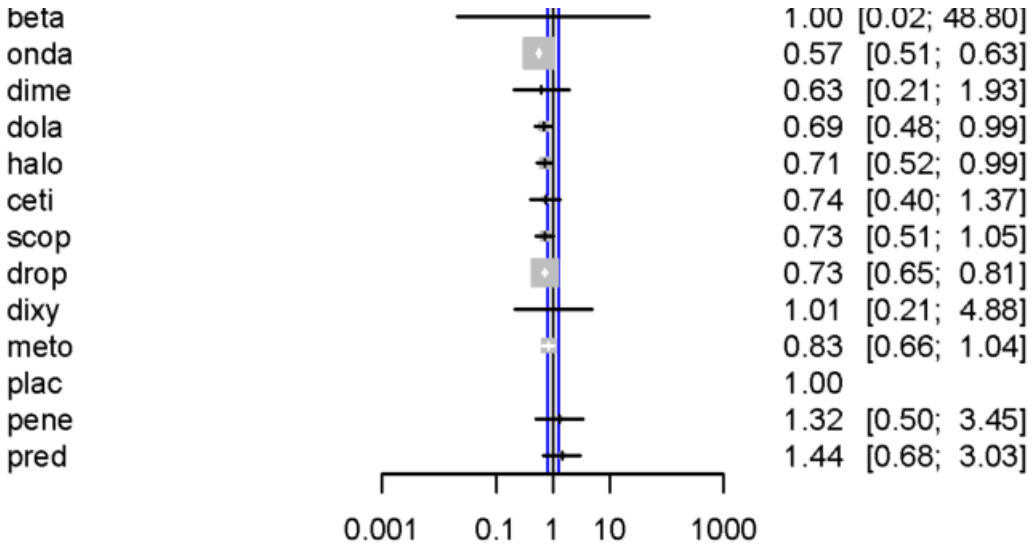
Figure 33. (Continued)



The estimated value of between-study variance for the network meta-analysis of late vomiting was 0 (tau²) (I^2 = 0%). For the random-effects model, there was no heterogeneity within designs (Q = 100.69, df = 114, P = 0.81) and no inconsistency between designs (Q = 145.54, df = 133, P = 0.22). No clinically relevant heterogeneity for comparisons of direct interest (single drugs of direct interest compared to placebo) was detectable because 95% CIs and 95% PIs were compatible with respect to the range of equivalence. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed disagreement (direct versus indirect) for 10 out of 112 comparisons (dexamethasone versus ondansetron (P = 0.03), dexamethasone-droperidol versus dexamethasone-droperidol-ondansetron (P = 0.02), dexamethasone-droperidol versus droperidol (P = 0.03), dexamethasone-droperidol-ondansetron versus dexamethasone-ondansetron (P = 0.002), dexamethasone-ondansetron versus droperidol (P = 0.003), dexamethasone-ondansetron versus droperidol-ondansetron (P = 0.03), dexamethasone-ondansetron versus placebo (P = 0.02), dolasetron versus ondansetron (P = 0.003), dolasetron versus placebo (P = 0.006), droperidol versus placebo (P = 0.001)). Clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo was found for dolasetron and metoclopramide.

Reporting bias (late vomiting)

Nine direct pair-wise comparisons included 10 or more studies for which small-study effects such as reporting or publication bias were investigated: dexamethasone, droperidol, granisetron, and ondansetron, all compared to placebo; and dexamethasone, dexamethasone-ondansetron, granisetron, metoclopramide, and ramosetron, all compared to ondansetron. Results of the funnel plots, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. According to the explorative analyses, we did not suspect publication bias for any of the above mentioned comparisons. A small P value when the arcsine test was used to detect funnel plot asymmetry was found for ondansetron versus placebo (P = 0.002). The contour-enhanced funnel plots suggested asymmetry for dexamethasone versus placebo. However, we did not suspect relevant publication bias for these comparisons because trim and fill sensitivity analysis did not change the conclusion with respect to the range of equivalence.

Nausea (or PONV) within 24 hours postoperatively

Primary analysis of nausea: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome nausea are available in an online repository (Supplementary Files-14-nausea *; including direct and indirect effect estimates to the primary NMA, explorative analyses of reporting bias, and funnel plots).*

In total, 325 RCTs including 55,208 participants were eligible for the network meta-analysis of nausea. All studies have reported events in at least one study arm. One study was not connected to the network and was excluded from the following analysis: Bergese 2016, comparison: aprepitant-dexamethasone-promethazine versus dexamethasone-ondansetron-promethazine. The network of the remaining 324 studies included 65 different treatments (nodes), with 670 pair-wise comparisons due to multi-arm studies (Figure 34). The 65 treatments included 35 drug combinations (30 times: two-fold, four times: three-fold, once: four-fold), 29 single drugs, and placebo or no treatment. The most common comparisons were ondansetron (k = 87 studies), dexamethasone (k = 53), droperidol (k = 50), metoclopramide (k = 30), granisetron (k = 20), and tropisetron (k = 15), all compared to placebo, and metoclopramide (k = 17), dexamethasone-ondansetron (k = 16), droperidol (k = 16), and dexamethasone (k = 14), all compared to ondansetron. Three single drugs of direct interest were poorly connected to the network. Amisulpride was connected only to placebo; aprepitant and fosaprepitant were connected only to ondansetron.

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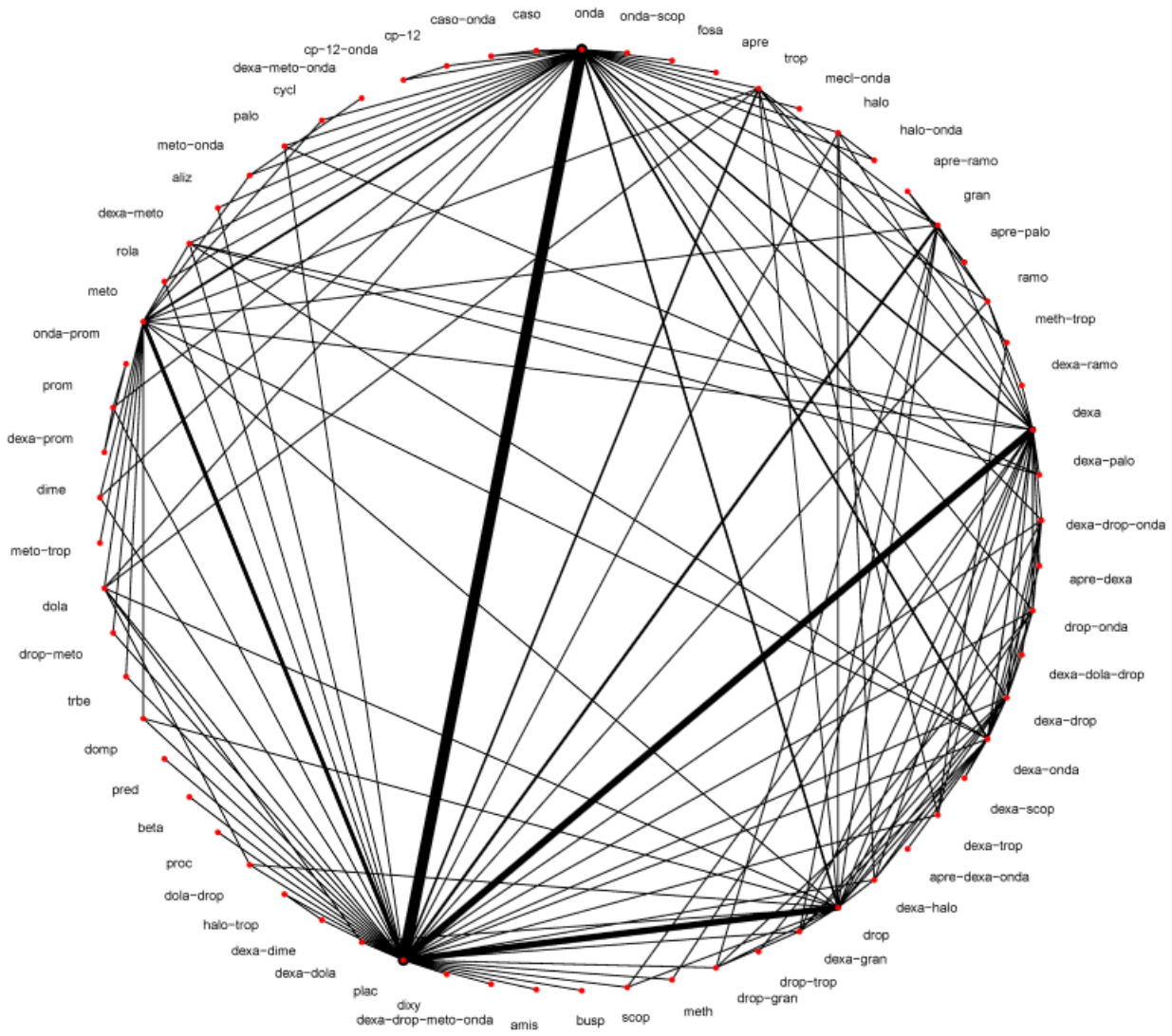
Figure 34. Network geometry of eligible comparisons for postoperative nausea within 24 hours postoperatively. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 65 different treatments, 2080 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 135 of 2080 comparisons, direct and indirect evidence was available, whereas for 24 comparisons, only direct evidence was available, and for 1921 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (RR with 95% CI) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 35. In terms of preventing nausea, of the 29 single drugs, nine showed important benefit (95% CI upper boundary < 0.8) compared to placebo, with RRs ranging between 0.31 (95% CI 0.13 to 0.74) for dixyrazine and 0.69 (95% CI 0.65 to 0.74) for ondansetron. Amongst the most effective single drugs of direct interest with important benefit for nausea prophylaxis compared to placebo in decreasing order according to P scores were methylprednisolone, ramosetron, droperidol, palonosetron, granisetron, dexamethasone, tropisetron, and ondansetron. Eleven single drugs, nine of direct interest

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(dimenhydrinate, aprepitant, promethazine, scopolamine, haloperidol, fosaprepitant, casopitant, amisulpride, dolasetron), showed benefit associated with uncertainty (95% CI crossing the range of equivalence). Nine single drugs, two of direct interest (rolapitant, metoclopramide), showed little or no effect associated with uncertainty. Treatment effects of all single drugs compared to placebo ranged between RR 0.31 (95% CI 0.13 to 0.74) for dixyrazine and RR 1.14 (95% CI 0.74 to 1.74) for cyclizine. Of the 35 drug combinations, 27 combinations showed important benefit compared to placebo, with RRs ranging between 0.05 (95% CI 0.01 to 0.41) for dexamethasone-metoclopramide-ondansetron and 0.53 (95% CI 0.39 to 0.71) for dexamethasone-metoclopramide. Eight drug combinations showed benefit associated with uncertainty compared to placebo. Treatment effects of drug combinations compared to placebo ranged between RR 0.05 (95% CI 0.01 to 0.41) for dexamethasone-metoclopramide-ondansetron and RR 0.72 (95% CI 0.38 to 1.34) for droperidol-metoclopramide.

Figure 35. Forest plot of network meta-analysis of all trials for postoperative nausea within 24 hours postoperatively. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR < 1 favours the intervention, RR > 1 favours placebo. The blue lines indicate the range of equivalence (RR = 0.8 to 1.25). Treatments are ranked according to efficacy based on P scores.

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Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.

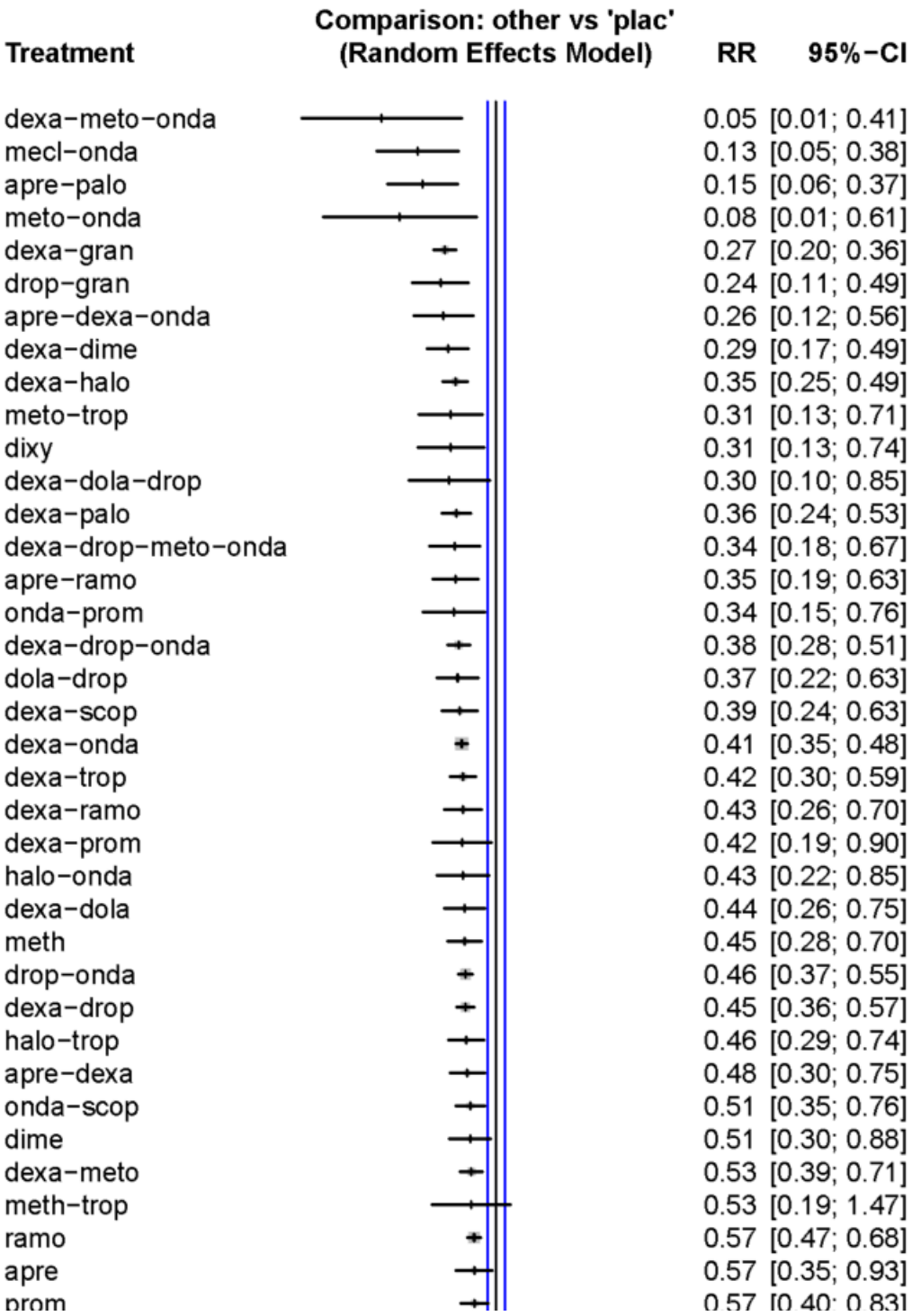

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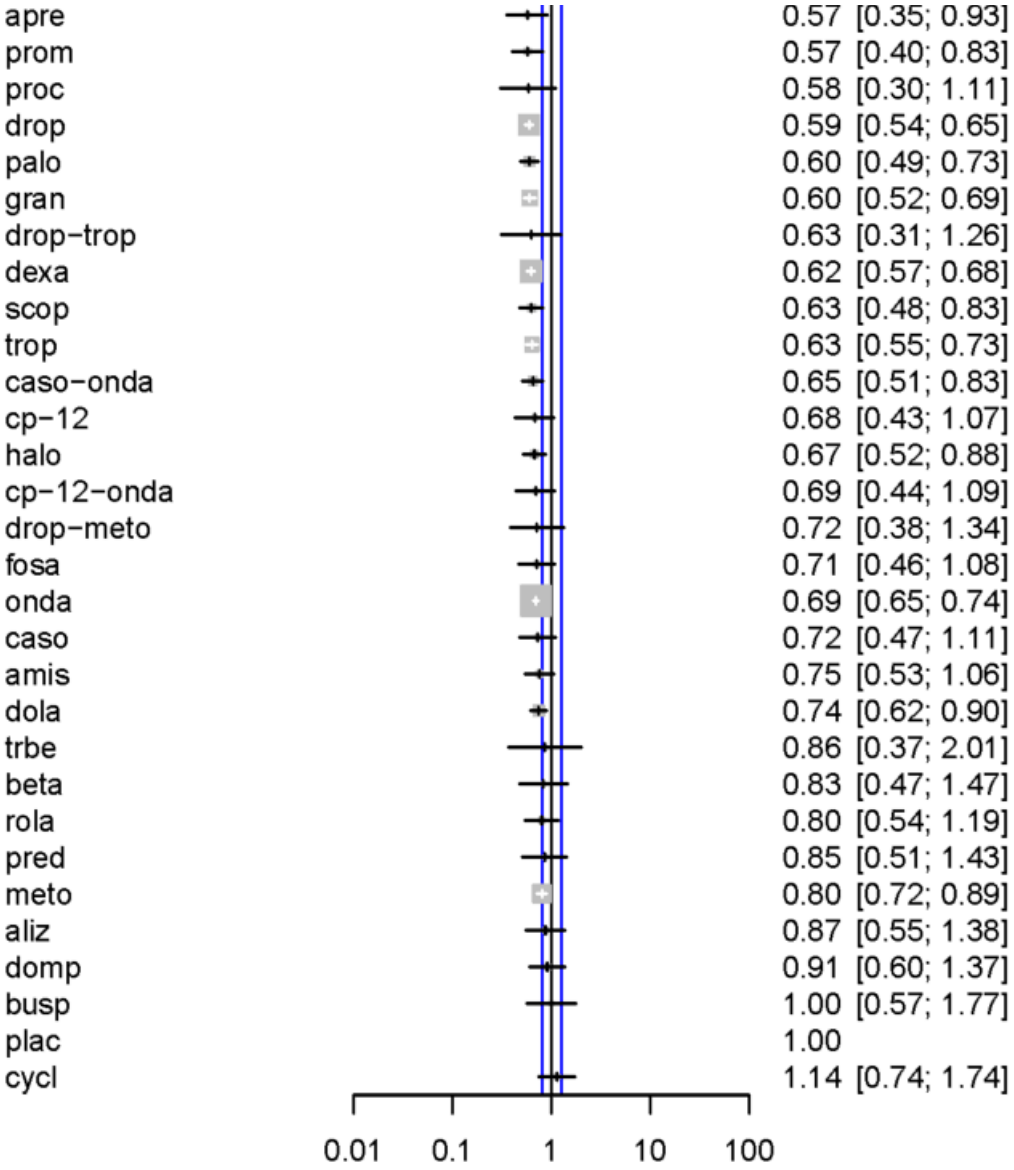
Figure 35. (Continued)



The estimated value of between-study variance for the network meta-analysis of nausea was 0.0524 (tau^2) (I^2 = 55.5%). For the random-effects model, there was heterogeneity within designs (Q = 546.86, df = 234, P < 0.0001) and inconsistency between designs (Q = 356.60, df = 168, P < 0.0001). When the full random-effects design-by-treatment interaction model was used, there was no evidence of residual statistical inconsistency (Q = 180.00, df = 168, P = 0.25). Clinically relevant heterogeneity for comparisons of direct interest (single drugs of direct interest compared to placebo) was detected for amisulpride, casopitant, dexamethasone, droperidol, fosaprepitant, granisetron, methylprednisolone, metoclopramide, ondansetron, palonosetron, ramosetron, rolapitant, and tropisetron. In these cases, 95% PIs of treatment estimates included different clinical implications compared to the 95% CIs. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed disagreement (direct versus indirect) for five out of 135 comparisons (dexamethasone versus dexamethasone-granisetron (P = 0.01), dexamethasone-granisetron versus dexamethasone-ondansetron (P = 0.02), dexamethasone-metoclopramide versus metoclopramide (P = 0.01), droperidol-granisetron versus granisetron (P = 0.02), ondansetron versus palonosetron (P = 0.02)). Clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo

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was found for haloperidol, palonosetron, promethazine, and rolapitant.

Reporting bias (nausea)

Eleven direct pair-wise comparisons included 10 or more studies for which small-study effects such as reporting or publication bias were investigated: dexamethasone, droperidol, granisetron, metoclopramide, ondansetron, and tropisetron, all compared to placebo; dexamethasone, dexamethasone-ondansetron, droperidol, and metoclopramide, all compared to ondansetron; and dexamethasone-ondansetron compared to dexamethasone. Results of the funnel plots, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. According to the explorative analyses, we suspected publication bias for the comparisons tropisetron versus placebo (P = 0.08), dexamethasone-ondansetron versus dexamethasone (P = 0.04), and dexamethasone-ondansetron versus ondansetron (P = 0.37). Small P values when the arcsine test was used to detect funnel plot asymmetry were also found for droperidol versus placebo (P = 0.047) and metoclopramide versus placebo (P = 0.07). The contour-enhanced funnel plots suggested asymmetry for dexamethasone, granisetron, and droperidol versus placebo. However, we did not suspect relevant publication bias for these comparisons because trim and fill sensitivity analysis did not change the conclusion with respect to the range of equivalence. Asymmetry may have been caused by other factors such as heterogeneity.

Complete response (no nausea or vomiting or need for rescue antiemetics) within 24 hours postoperatively

Primary analysis of complete response: network meta-analysis with all single drugs and drug combinations

Raw data of individual studies and all analyses for the outcome complete response are available in an online repository (Supplementary Files-15-complete response ; including direct and indirect effect estimates to the primary NMA, explorative analyses of reporting bias, and funnel plots).

In total, 137 RCTs including 30,254 participants were eligible for the network meta-analysis of complete response. All studies have reported events in at least one study arm. One three-arm study was not connected to the network and was excluded from the following analysis: Gandhi 2009, comparison: promethazine versus dexamethasone-promethazine versus ondansetron-promethazine). The network of the remaining 136 studies included 38 different treatments (nodes), with 278 pair-wise comparisons due to multi-arm studies (Figure 36). The 38 treatments included 20 drug combinations (19 times: two-fold, once: three-fold), 17 single drugs, and placebo or no treatment. The most common comparisons were ondansetron (k = 35 studies), droperidol (k = 19), and dexamethasone (k = 17), all compared to placebo. Four single drugs of direct interest were poorly connected to the network. Amisulpride and scopolamine were connected only to placebo, and aprepitant and fosaprepitant were connected only to ondansetron.

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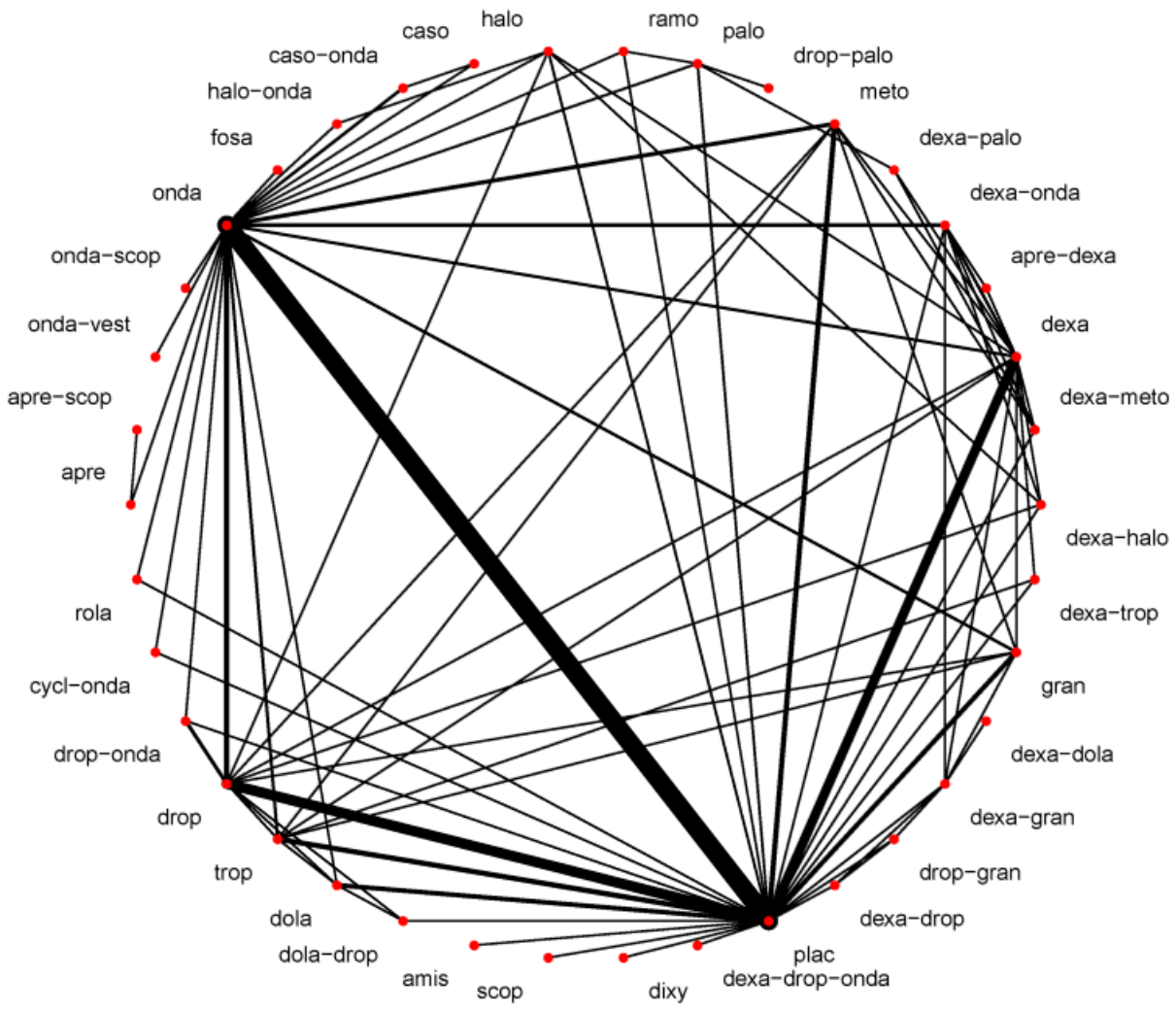
Figure 36. Network geometry of eligible comparisons for complete response within 24 hours postoperatively. The thickness of the edges is proportionate to the number of included studies comparing two treatments. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.



For 38 different treatments, 703 pair-wise comparisons are possible, and the results of all network estimates are available in the online repository. For 76 of 703 comparisons, direct and indirect evidence was available, whereas for 13 comparisons, only direct evidence was available, and for 614 comparisons, only indirect evidence was available.

The relative efficacy presented as summary relative effects (RR with 95% CI) of all drugs or drug combinations compared to placebo (reference compound) ranked according to P scores is shown in Figure 37. In terms of complete response, of the 17 single drugs, 11 showed important benefit (95% CI lower boundary > 1.25) compared to placebo, with RRs ranging between 2.23 (95% CI 1.68 to 2.96) for ramosetron and 1.45 (95% CI 1.29 to 1.64) for dolasetron. Amongst the most effective single drugs of direct interest with important benefit for complete response compared to placebo in increasing order according to P scores were ramosetron, granisetron, fosaprepitant, aprepitant, palonosetron, dexamethasone, haloperidol, tropisetron, droperidol, ondansetron, and dolasetron. Five single drugs, four of direct interest (scopolamine, casopitant, rolapitant, amisulpride), showed benefit associated with uncertainty (95% CI crossing the range of equivalence). One single drug of direct interest (metoclopramide) showed little or

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no effect associated with uncertainty (95% CI crossing the range of equivalence). Treatment effects of all single drugs compared to placebo ranged between RR 11.00 (95% CI 0.64 to 188.18) for scopolamine and RR 1.23 (95% CI 1.06 to 1.43) for metoclopramide. Of the 20 drug combinations, 16 combinations showed important benefit compared to placebo, with RRs ranging between 2.81 (95% CI 1.59 to 4.96) for cyclizine-ondansetron and 1.61 (95% CI 1.31 to 1.97) for dexamethasone-metoclopramide. Four drug combinations showed benefit associated with uncertainty compared to placebo. Treatment effects of drug combinations compared to placebo ranged between RR 2.81 (95% CI 1.59 to 4.96) for cyclizine-ondansetron and RR 1.49 (95% CI 0.93 to 2.37) for aprepitant-scopolamine.

Figure 37. Forest plot of network meta-analysis of all trials for complete response within 24 hours postoperatively. Single drugs and combinations were compared with placebo (reference compound). RR = risk ratio, 95% CI = 95% confidence interval. RR > 1 favours the intervention, RR < 1 favours placebo. The blue lines indicate the range of

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equivalence (RR = 0.8 to 1.25). Treatments are ranked according to efficacy based on P scores. Abbreviations for treatments correspond to the first four letters of the drug name and are listed in the Methods and in Appendix 6.

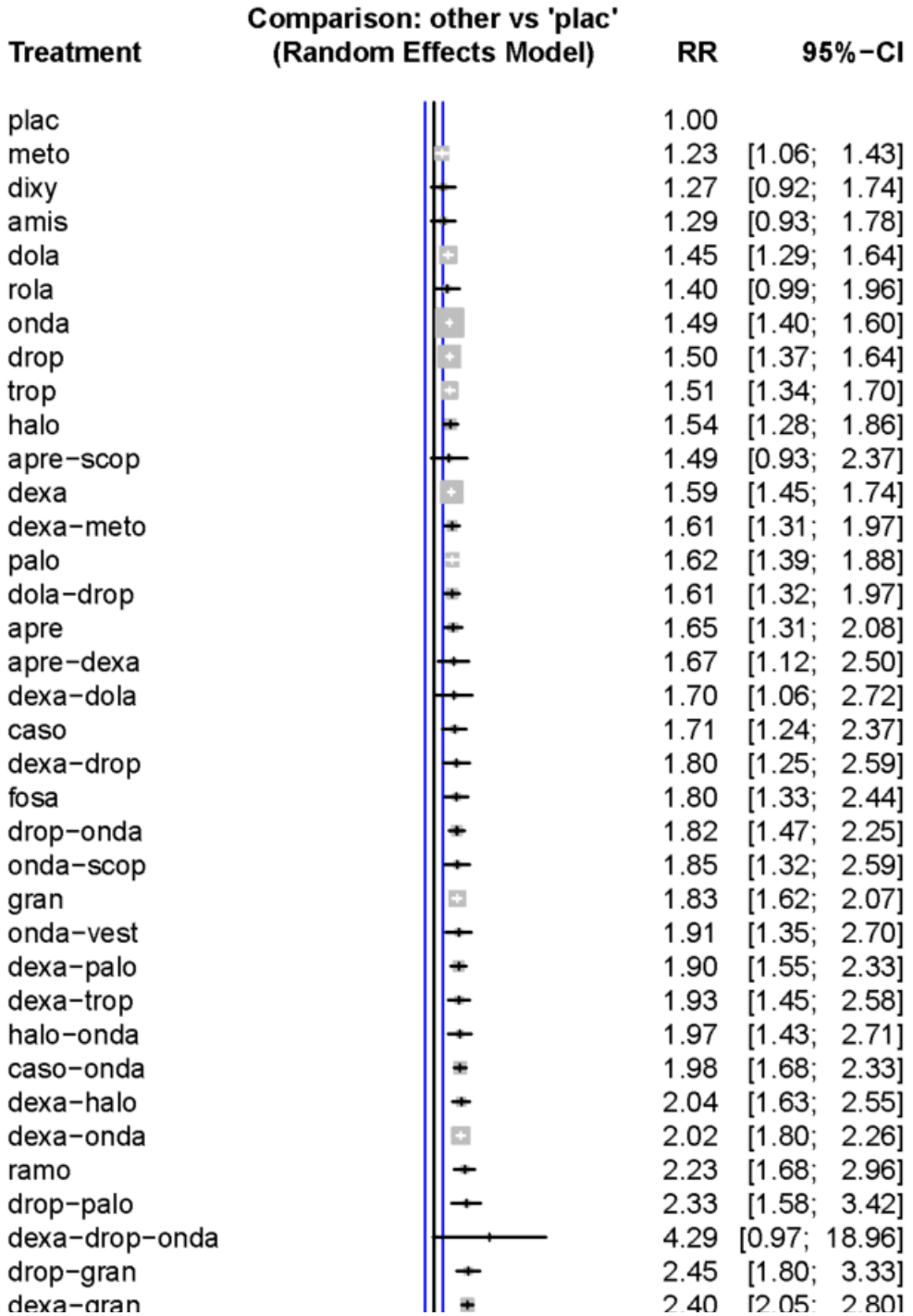

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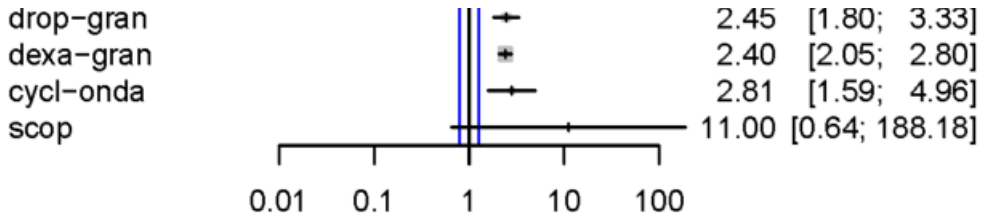
Figure 37. (Continued)



The estimated value of between-study variance for the network meta-analysis of complete response was 0.0196 (tau²) (I^2 = 47.8%). For the random-effects model, there was heterogeneity within designs (Q = 146.39, df = 76, P < 0.0001) and inconsistency between designs (Q = 163.83, df = 86, P < 0.0001). When the full random-effects design-by-treatment interaction model was used, there was no evidence of residual statistical inconsistency (Q = 84.96, df = 86, P = 0.51). Clinically relevant heterogeneity for comparisons of direct interest (single drugs of direct interest compared to placebo) was detected for aprepitant, dexamethasone, dolasetron, droperidol, fosaprepitant, haloperidol, ondansetron, palonosetron, and tropisetron. In these cases, 95% PIs of treatment estimates included different clinical implications compared to the 95% CIs. Splitting of direct and indirect evidence in the network meta-analysis and testing for local inconsistency revealed disagreement (direct versus indirect) for four out of 76 comparisons (dexamethasone versus dexamethasone-palonosetron (P = 0.04), dexamethasone versus placebo (P = 0.008), dexamethasone-palonosetron versus palonosetron (P = 0.03), palonosetron versus placebo (P = 0.04)). Clinically relevant incoherence of direct and indirect treatment estimates for single drugs of direct interest compared to placebo was found for dexamethasone, ondansetron, palonosetron, and tropisetron.

Reporting bias (complete response)

Three direct pair-wise comparisons included 10 or more studies for which small-study effects such as reporting or publication bias were investigated: dexamethasone, droperidol, and ondansetron, all compared to placebo. Results of the funnel plots, the arcsine test for funnel plot asymmetry, and the trim and fill sensitivity analysis are presented in the online repository. According to the explorative analyses, we suspected publication bias for the comparisons droperidol versus placebo (P = 0.10) and ondansetron versus placebo (P = 0.01). The contour-enhanced funnel plots also suggested asymmetry for dexamethasone versus placebo. However, we did not suspect relevant publication bias for this comparison because trim and fill sensitivity analysis did not change the conclusion with respect to the range of equivalence. Asymmetry may have been caused by other factors such as heterogeneity.

DISCUSSION

Summary of main results

This systematic review with network meta-analyses investigated the efficacy and safety of drugs for prevention of postoperative nausea and vomiting (PONV) with focus on postoperative vomiting in adults after general anaesthesia. It included 585 randomized controlled trials (RCTs) with 97,516 participants. A total of 44 single antiemetic drugs belonging to six different substance classes (5-HT_3 receptor antagonists, D_2 receptor antagonists, NK_1 receptor antagonists, corticosteroids, antihistamines, and anticholinergics) and 51 drug combinations were investigated. An overview of the direction and magnitude of effects along with the certainty of evidence for all GRADE-relevant outcomes and all single drugs of direct interest, according to Gan 2014, compared to placebo is summarized in Figure 7.

Primary outcomes

The network meta-analysis (NMA) of the primary efficacy outcome 'vomiting within 24 hours postoperatively' included 282 RCTs, 50,812 participants, and 65 interventions. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to high. High-certainty evidence showed that five drugs (aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron) reduced vomiting, and moderate-certainty evidence indicated that another two single drugs (fosaprepitant and droperidol) probably reduced vomiting compared to placebo (Summary of findings 1; Summary of findings 2). These are the seven most reliable and most effective drugs identified in this review for 'vomiting within 24 hours postoperatively'. All other single drugs of direct interest involved evidence of very low to low certainty (casopitant, tropisetron, and dolasetron), or they were less effective (amisulpride and promethazine), or both (palonosetron, haloperidol, metoclopramide, rolapitant, dimenhydrinate, and scopolamine). In the ranking of treatments with placebo as comparator, single drugs of direct interest with decreasing order according to efficacy were fosaprepitant, casopitant, aprepitant, ramosetron, granisetron, dexamethasone, tropisetron, dimenhydrinate, promethazine, rolapitant, ondansetron, dolasetron, haloperidol, scopolamine, droperidol, palonosetron, amisulpride, and metoclopramide. Drug combinations were generally more effective than most of the single drugs. However, treatment effects of the top three ranked

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single drugs, which belong to the NK_1 receptor antagonist class (fosaprepitant, casopitant, and aprepitant), were comparable to most of the included drug combinations.

The certainty of evidence for single drugs of direct interest in preventing postoperative vomiting applies to recommended and high doses of granisetron, ondansetron, dexamethasone, droperidol, and tropisetron because low doses showed no clinically important effect. Recommended and high doses of these drugs showed similar treatment effects. Thus, recommended doses should be sufficient to prevent postoperative vomiting (Table 3). For all other single drugs of direct interest, there was no clinically relevant difference between the analysed dose categories. Therefore we are best advised to use the most investigated dose, route, and timing of individual drugs as the most reliable current guide (Table 3).

The NMA of the primary safety outcome 'number of participants with SAEs within seven days postoperatively' included 28 RCTs, 10,766 participants, and 22 interventions. A large number of trials (41%) have reported zero events in all study arms, and the baseline risk for serious adverse events (SAEs) with placebo was 1.43%. Only three single drugs of direct interest (aprepitant, dolasetron, and palonosetron) were investigated in large RCTs (> 500 participants/treatment). Thus, the chance to detect rare SAEs was highest for aprepitant, dolasetron, and palonosetron. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to low (Summary of findings 1; Summary of findings 3). In terms of treatment effects, none of the active treatments showed important harm or benefit compared to placebo, and all were associated with uncertainty. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of SAEs were dolasetron, tropisetron, palonosetron, amisulpride, droperidol, ramosetron, scopolamine, dexamethasone, granisetron, aprepitant, ondansetron, and casopitant. Treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty.

The NMA of the primary safety outcome 'number of participants with any AE [adverse event] within seven days postoperatively' included 61 RCTs, 19,423 participants, and 27 interventions. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to moderate (Summary of findings 1; Summary of findings 4). Moderate-certainty evidence shows that granisetron and amisulpride probably had no or little effect on any AE compared to placebo. Two of the 14 single drugs of direct interest, namely, dimenhydrinate and scopolamine, have low-certainty evidence and may increase the number of participants with any AE compared to placebo. None of the other single drugs of direct interest showed important harm. All showed benefit or no effect, but all were associated with only low- or very low-certainty evidence. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of any AE were dexamethasone, aprepitant, dolasetron, casopitant, droperidol, granisetron, metoclopramide, ondansetron, palonosetron, ramosetron, amisulpride, tropisetron, scopolamine, and dimenhydrinate. Of all drug combinations, only ondansetron-scopolamine showed important benefit for any AE compared to placebo. No combinations showed important harm. However, caution is advised, as we have not assessed the certainty of evidence for any of the drug combinations. Treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty. However, in the ranking of treatments, high and recommended doses generally ranked higher than lower doses of the individual drugs in terms of favourable effects on any AE. Thus, contrary to the intuitive assumption that lower doses of drugs produce fewer side effects than higher doses, the opposite seems to be the case here. These findings could be explained by the fact that prevention of PONV generally lowers the risk of other adverse effects (Kranke 2018). Some molecules directly prevent adverse effects, such as headache when droperidol is used, or act as co-analgesics (e.g. valid for dexamethasone).

Secondary outcomes

Substance class-specific side effects

The most investigated secondary safety outcome was headache, with 208 RCTs, 42,445 participants, and 53 interventions. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to moderate (Summary of findings 1; Summary of findings 5). Moderate-certainty evidence shows that droperidol probably reduces and ondansetron probably increases headache—both compared to placebo. None of the other single drugs of direct interest showed important benefit or harm, and all treatment effects were associated with uncertainty, resulting in only low or very low certainty of evidence. However, a tendency toward the well-known substance class-specific increase in headache for $5\text{-}HT_3$ receptor antagonists showed up in the NMA (https://en.wikipedia.org/wiki/5-HT3_antagonist). In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of headache were haloperidol, promethazine, droperidol, casopitant, dexamethasone, aprepitant, metoclopramide, scopolamine, dimenhydrinate, tropisetron, dolasetron, ramosetron, palonosetron, ondansetron, granisetron, and amisulpride. Of all drug combinations, only droperidol-tropisetron showed important benefit for headache compared to placebo. None showed important harm. However, caution is advised because we have not assessed the certainty of evidence for any of the drug combinations. Treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty. However, in the ranking of treatments at different doses, a similar tendency of drug doses was detectable as was found for any AE. Higher doses of drugs produce fewer headache than lower doses.

The secondary safety outcome sedation included 117 RCTs, 21,440 participants, and 44 interventions. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to high (Summary of findings 1; Summary of findings 6). High-certainty evidence shows that dexamethasone has no or little effect on sedation compared to placebo. Moderate-certainty evidence indicates that dimenhydrinate probably increases sedation and ondansetron probably reduces sedation—both compared to placebo. None of the other single drugs of direct interest showed important benefit or harm, and all were assessed with only low- or very low-certainty evidence. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of sedation were perphenazine, tropisetron, ondansetron, aprepitant, ramosetron, haloperidol, metoclopramide, droperidol, amisulpride, dolasetron,

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granisetron, dexamethasone, promethazine, palonosetron, scopolamine, methylprednisolone, and dimenhydrinate. Of all drug combinations, only dexamethasone-metoclopramide showed an important reduction in sedation, and dimenhydrinate-ondansetron showed an important increase in sedation—both compared to placebo. However, caution is advised because we have not assessed the certainty of evidence for any of the drug combinations. According to dose, a clinically relevant difference between doses was found only for high and recommended doses of ondansetron compared to low doses. High and recommended doses probably reduced sedation, and low doses increased sedation. All other treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty.

The secondary safety outcome extrapyramidal symptoms included 64 RCTs, 10,724 participants, and 30 interventions. A large number of trials (75%) have reported zero events in all study arms, and the baseline risk for extrapyramidal symptoms with placebo was 0.79%. Only droperidol was investigated in a large RCT (> 500 participants/treatment). Thus, the chance to detect rare extrapyramidal symptoms was highest for droperidol. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to low (Summary of findings 1; Summary of findings 7). In terms of treatment effects, none of the active treatments showed important harm or benefit compared to placebo, and all were associated with uncertainty. However, a tendency of the well-known substance class-specific increase in extrapyramidal symptoms for D_2 receptor antagonists showed up in the NMA (https://en.wikipedia.org/wiki/Dopamine_antagonist). The currently best D_2 receptor antagonist with no or minimal effect seems to be amisulpride. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of extrapyramidal symptoms were ondansetron, dexamethasone, dolasetron, tropisetron, ramosetron, granisetron, palonosetron, amisulpride, perphenazine, metoclopramide, haloperidol, and droperidol. Treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty.

The secondary safety outcome constipation included 43 RCTs, 11,481 participants, and 23 interventions. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to low (Summary of findings 1; Summary of findings 8). In terms of treatment effects, none of the active treatments showed important harm or benefit compared to placebo, and all were associated with uncertainty. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of constipation were granisetron, ramosetron, casopitant, dexamethasone, ondansetron, aprepitant, palonosetron, tropisetron, amisulpride, and metoclopramide. Treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty.

The secondary safety outcome postoperative wound infection included 32 RCTs, 4369 participants, and 10 interventions. A large number of trials (80%) have reported zero events in all study arms, and the baseline risk for postoperative wound infection with placebo was 0.44%. Most information was available for dexamethasone, but none of the studies investigating dexamethasone or any other drug was of sufficient size (> 500 participants/treatment). Thus, the chance to detect rare postoperative wound infections was strongly limited with this NMA. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to low (Summary of findings 1; Summary of findings 9). In terms of treatment effects, none of the active treatments showed important harm or benefit compared to placebo, and all were associated with uncertainty. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of postoperative wound infection were tropisetron, methylprednisolone, metoclopramide, dexamethasone, and ondansetron. Treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty.

The secondary safety outcome arrhythmia included 25 RCTs, 5067 participants, and 18 interventions. A large number of trials (72%) have reported zero events in all study arms, and the baseline risk for arrhythmia with placebo was 4.25%. Only dolasetron and ondansetron were investigated in large RCTs (> 500 participants/treatment). Thus, the chance to detect rare postoperative arrhythmias was highest for dolasetron and ondansetron. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to low (Summary of findings 1; Summary of findings 10). In terms of treatment effects, none of the active treatments showed important harm or benefit compared to placebo, and all were associated with uncertainty. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of arrhythmia were dolasetron, dexamethasone, droperidol, granisetron, tropisetron, methylprednisolone, haloperidol, metoclopramide, ondansetron, and ramosetron. All treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty.

The secondary safety outcome visual disturbances included 21 RCTs, 3634 participants, and 12 interventions. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to low (Summary of findings 11). In terms of treatment effects, scopolamine and the combination of ondansetron and scopolamine showed important harm compared to placebo. None of the other active treatments showed important harm or benefit compared to placebo, and all were associated with uncertainty. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of visual disturbances were methylprednisolone, droperidol, dexamethasone, tropisetron, metoclopramide, ondansetron, and scopolamine. Treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty.

The secondary safety outcome QT prolongation included 18 RCTs, 4440 participants, and 13 interventions. A large number of trials (44%) have reported zero events in all study arms, and the baseline risk for QT prolongation with placebo was 2.12%. Only aprepitant was investigated in a large RCT (> 500 participants/treatment). Thus, the chance to detect rare postoperative QT prolongations was highest for aprepitant. The certainty of evidence for single drugs of direct interest compared to placebo ranged from very low to low (Summary of findings 1; Summary of findings 12). In terms of treatment effects, none of the active treatments showed important harm or benefit compared to

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placebo, and all were associated with uncertainty. In the ranking of treatments with placebo as comparator, single drugs of direct interest in increasing order according to the risk of QT prolongation were palonosetron, ramosetron, dexamethasone, ondansetron, tropisetron, aprepitant, haloperidol, and droperidol. Treatment effects of different doses of single drugs did not differ in a clinically relevant manner and were associated with uncertainty.

Other secondary outcomes

We have investigated five other secondary outcomes, including mortality within seven days, along with the efficacy outcomes of early and late vomiting, nausea, and complete response within 24 hours. We have not assessed the certainty of evidence for drugs included in the NMAs of these outcomes.

Mortality was reported in only 17 RCTs including 6840 participants. Only one participant with ondansetron died during the study period, and study authors reported that the participant´s death was not drug-related.

The efficacy profile of the seven most effective and most reliable single drugs for the primary outcome 'vomiting within 24 hours' (fosaprepitant, aprepitant, ramosetron, granisetron, dexamethasone, ondansetron, and droperidol) showed a slightly different efficacy profile for other efficacy outcomes such as vomiting (early and late), nausea, and complete response compared to the primary outcome. For early vomiting, the benefit of aprepitant was associated with uncertainty, and the treatment effect of droperidol was slightly better for vomiting within 24 hours, which was comparable to the other 5-HT_3 receptor antagonists. Treatment effects of fosaprepitant, granisetron, ramosetron, ondansetron, and dexamethasone were comparable for early vomiting and vomiting within 24 hours. For late vomiting, no studies investigated fosaprepitant. Aprepitant was the most effective drug for late vomiting. Aprepitant, granisetron, and ramosetron were more effective compared to early vomiting and vomiting within 24 hours. The treatment effect of droperidol was associated with uncertainty and was slightly worse for early vomiting and vomiting within 24 hours. Dexamethasone and ondansetron showed similar treatment effects at all time points investigated for vomiting. For nausea within 24 hours, treatment effects of the NK_1 receptor antagonists, fosaprepitant and aprepitant, were associated with uncertainty and showed less benefit than for vomiting. Ramosetron, droperidol, granisetron, dexamethasone, and ondansetron all showed similarly important benefit for nausea, and their anti-nausea efficacy was comparable to antiemetic efficacy. For the composite outcome ‘complete response’, all seven drugs showed important benefit and were ranked in decreasing order according to efficacy as ramosetron, granisetron, fosaprepitant, aprepitant, dexamethasone, droperidol, and ondansetron.

Overall completeness and applicability of evidence

Types of participants

Most of the studies in the current review included participants at moderate to high risk for PONV based on patient-specific, anaesthesia- and surgery-related risk factors. Most participants were women (83%), received perioperative opioids (88%), were undergoing general anaesthesia using volatile anaesthetics (88%), and were subject to gynaecological or gastrointestinal surgery (53%). The results of the review have limited external validity with respect to the broad population of adults undergoing any surgery with general anaesthesia but are directly transferable to patients at risk for PONV (i.e. women undergoing gynaecological/gastrointestinal surgery with volatile anaesthesia and with the use of perioperative opioids). External validity is further limited in that a majority of trials were conducted in inpatient settings and included healthy participants classified as American Society of Anesthesiologists status ASA I and II (70%). There was at least some geographic variation in study locations, but most of the studies were conducted in Asia (51%), Europe (25%), and North America (16%).

Outcomes

We have chosen vomiting instead of nausea as the primary outcome for this review because vomiting is an objectively measurable outcome and may be associated with higher risk of complications for the postoperative patient compared to nausea. Nevertheless, several other PONV outcomes such as nausea and complete response were also examined as secondary outcomes in this review. However, depending on the outcome of interest, there should be an altered risk/benefit assessment of some antiemetics due to different effect profiles. For example, NK_1 receptor antagonists have a better effect against vomiting than against nausea and therefore do better in this review with a focus on vomiting. In general, the main focus of this review should be on the side effects of antiemetics, as the benefits of antiemetics have been reported much better in the community than their side effects.

Efficacy

With this review, we found sufficient available information to address the review questions on efficacy of antiemetic drugs for prevention of vomiting within 24 hours postoperatively. We found high-certainty evidence showing that five single drugs (aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron) reduce vomiting, and moderate-certainty evidence indicating that two other single drugs (fosaprepitant and droperidol) probably reduce vomiting compared to placebo. Consequently, four of the six substance classes (5-HT_3 receptor antagonists, D_2 receptor antagonists, NK_1 receptor antagonists, and corticosteroids) were represented by at least one single drug with high or moderate certainty of evidence and important benefit for prevention of vomiting. In absolute numbers, for 1000 patients, of whom 300 would vomit after surgery if given placebo, 282 would benefit from fosaprepitant (the most effective drug of the seven most reliable single drugs) and 18 would not, or 117 would benefit from droperidol (the least effective drug of the seven most reliable single drugs) and 183 would not.

Safety and adverse events

In contrast to the large number of studies (89%) reporting relevant efficacy outcomes for this review, just over half of all studies (56%) reported at least one relevant safety outcome. Thus, relevant safety outcomes were highly underrepresented in the included studies. Furthermore, we could not exclude a certain risk of bias, as side effects may be prone to selective outcome reporting and may have been reported more frequently when the findings were generally positive. In this NMA, the risk of selective outcome reporting was difficult to assess, as we found few studies with a prospectively registered protocol. In addition, most of the investigated side effects occurred at a lower rate compared to the rate of PONV (with the exception of the composite safety outcome ‘any AE’, which

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has a similar incidence (38%) in placebo-treated participants after surgery under general anaesthesia as postoperative vomiting in the current review). In general, the lower the event rate, the higher the need for a larger number of study participants to overcome the imprecision of meta-analytic results and to increase the chance of detecting rare events. The most investigated specific side effects in this review were headache (with 208 studies) and sedation (with 117 studies), both with incidences of about 10% in the placebo group. Other side effects were investigated to a much lesser extent and with a much lower baseline risk with placebo. Besides, most of the studies included in NMAs of rare outcomes were small and, therefore, have been unable to detect rare events. Finally, most of the NMA treatment effects were imprecise, which was reflected by only very low- to low-certainty evidence. However, rare adverse effects may be observed only in non-randomized studies such as large cohort studies or case-control studies (Higgins 2019). Therefore, future studies or systematic reviews on adverse events of antiemetic drugs should be or should include non-randomized studies, respectively.

There were two additional issues with adverse events. First, a detailed definition of adverse outcomes such as QT prolongation by study authors often was not available, was difficult to assess, or was different between studies. In addition, the composite outcome 'any AE' was most often given as the total number of participants with any adverse events. However, a detailed definition of which outcomes were finally included often was not provided. Therefore, the separated individual side effects such as headache were more specific and informative. Second, study authors reporting the composite outcome 'any AE' often gave insufficient information on the method of monitoring adverse events. In most studies, it is unclear whether researchers have actively surveyed participants and have asked for the occurrence of any adverse event, or whether they have used only information derived from routinely assessed patient records or have focused only on specific adverse events, lacking relevant side effects.

Interventions

This review compared 44 single drugs belonging to six different substance classes. Twenty-one of the 44 drugs were of direct interest, all of which are listed in the consensus guidelines for management of postoperative nausea and vomiting (Gan 2014), with exception of the two newer drugs, fosaprepitant and amisulpride. An additional 23 drugs were not of direct interest and were used only to supplement the analysis. Drugs not of direct interest were investigated in only 7% of all included studies, limiting the gain of additional information and reflecting the lack of importance of these drugs in clinical practice. The current review is clearly dominated by three single drugs of direct interest: ondansetron (with 246 studies), dexamethasone (with 120 studies), and droperidol (with 97 studies). Of the 21 single drugs of direct interest, only meclizine was not investigated as a single drug for any of the outcomes of interest. It was investigated only in combination with ondansetron. Methylprednisolone and perphenazine, used as single drugs, were not investigated for the primary outcome of vomiting. Fosaprepitant and rolapitant were not investigated for any of the relevant safety outcomes. Dexamethasone, ondansetron, and tropisetron were present in all outcomes investigated in this review. Finally, on the level of substance classes, the 5-HT_3 receptor antagonists were the largest and the best investigated substance class in this review.

Included studies were published between 1965 and 2017. However, most included studies (71%) were published in the last two decades between 2000 and 2017. Despite the large amount of information reported from clinical trials on this topic, the flood of clinical trials was increasing over time, reaching a peak in 2007 with 36 published trials. Since 1996, more than 15 study reports per year were published (Figure 4). On the one hand, there were new substances, such as amisulpride and fosaprepitant, which have been investigated only in recent trials. On the other hand, there were several old and well-known drugs, such as ondansetron, dexamethasone, and droperidol, that have been used extensively in previous studies. However, they have also been studied in recent studies. The use of ondansetron, the gold standard in PONV clinical trials, has its justification in newer studies as an active comparator. However, other recent studies—Zhang 2013-1; Zhang 2013-2—compared ondansetron against placebo and provided no new or additional valuable findings compared to the large IMPACT trial published in 2004 (Apfel 2004-1; Apfel 2004-2). Studies that investigate what we already know and do not add any clinically relevant information are not useful and should be avoided (Ioannidis 2016).

Combination therapy

Combination therapy for PONV prophylaxis is preferable to use of single drugs alone in patients at moderate risk (Gan 2014). Ondansetron, dexamethasone, and droperidol, for example, have similar efficacy for PONV prophylaxis and, when used in combination, they showed additive effects due to independent mechanisms of action (Apfel 2004-1; Apfel 2004-2). In this review, in addition to single drugs, any drug combination was included, and this resulted in the inclusion of 51 different drug combinations. In total, 28% of studies included drug combinations and 72% of all studies investigated single drugs only. Thus, evidence for the effectiveness of drug combinations in this review was based on substantially fewer studies than for single drugs alone. Nevertheless, 29 (81%) of 36 drug combinations investigating the prevention of vomiting within 24 hours showed important treatment effects based on NMA. Dexamethasone-ondansetron (in 54 studies), dexamethasone-granisetron (in 20 studies), and droperidol-ondansetron (in 15 studies) are the only drug combinations included in this review that were investigated in more than 10 studies. Testing the additivity assumption for prevention of vomiting within 24 hours revealed additive effects of single drugs for these three combinations. Altogether, all three combinations were equally effective in preventing vomiting within 24 hours, with comparable effectiveness to aprepitant administered as a single drug.

Combination treatments should include drugs of different substance classes with different mechanisms of action (Gan 2014). This recommendation is based on a strong biological rationale without proof in clinical studies, as combinations of drugs from the same substance class were not investigated in practice. Besides this biological rationale, several findings on NMA treatment effects for other efficacy outcomes (e.g. nausea) and adverse effects of single drugs supported the use of combinations of drugs from different substance classes. First, the NK_1 receptor antagonists showed promising antiemetic efficacy, whereas anti-nausea efficacy was less prominent and was associated with uncertainty. In contrast, the 5-HT_3 receptor antagonists ramosetron and granisetron and the D_2 receptor antagonist droperidol effectively reduced nausea. Therefore, ramosetron, granisetron, and droperidol might

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compensate for the reduced anti-nausea effects of NK_1 receptor antagonists. Second, 5-HT_3 receptor antagonists increased the incidence of headache, whereas the D_2 receptor antagonist droperidol reduced the incidence of headache. A combination of droperidol and ondansetron had an additive effect in reducing postoperative vomiting and might also have reduced the incidence of headache. However, caution is advised because the certainty of evidence was not assessed for other efficacy outcomes nor for combinations of drugs.

Applicability of doses, administration routes, and application time points

For the primary network meta-analyses, different doses, administration routes, and application time points of individual drugs were pooled together. Administration routes and application time points were recorded in the Characteristics of included studies section but were not analysed in detail in this review. Dose effects were investigated in a subgroup analysis for vomiting, splitting doses of drugs into dose categories in accordance with current recommendations (Gan 2014). This review shows that low doses of granisetron, ondansetron, dexamethasone, droperidol, and tropisetron were less effective compared to recommended and high doses. Because recommended and high doses of these drugs were similarly effective, we assume recommended doses to be sufficient to prevent vomiting. No dose effects were detectable for the other drugs, and we are best advised to use the most investigated doses of drugs as the most reliable current guide. With respect to recommendations of the current guideline, casopitant, palonosetron, ramosetron, rolapitant, and tropisetron were most often used at recommended doses according to Gan 2014 in this systematic review. However, most of the studies investigating aprepitant, dolasetron, haloperidol, and promethazine used high doses, and most of the studies investigating dimenhydrinate and metoclopramide used low doses. In these cases, dose recommendations should be reconsidered, or additional studies should investigate dose effects of these drugs. Ongoing debate focuses on the topic of whether metoclopramide is effective for prevention of PONV and whether its limited effectiveness may be caused by low dosing schemes (DeOliveira 2012; Wallenborn 2006). For amisulpride, fosaprepitant, and scopolamine, the current guidelines did not give any dose recommendations (Gan 2014). In the current systematic review, amisulpride was most often used at a dose of 5 mg (IV, at induction of anaesthesia), fosaprepitant at 150 mg (IV, at induction of anaesthesia), and scopolamine at 1.5 mg (TD, at induction of anaesthesia).

Interventions in current practice

The seven most effective single drugs for prevention of postoperative vomiting with at least moderate-certainty evidence found in this review vary by the level of establishment and use in current practice. Ondansetron is the most used gold standard antiemetic drug worldwide developed in the 1980s and approved by the US FDA since January 1991. Dexamethasone was developed in 1957 and was approved for medical use in 1961. It is listed together with ondansetron and metoclopramide as an antiemetic medicine in the World Health Organization List of Essential Medicines reporting the most effective and safe medicines needed in a health system (WHO Model List of Essential Medicines 2019). Droperidol was developed in the 1950s as an antipsychotic and was first approved in Denmark in 1963 for use in anaesthesia, PONV, and psychiatry. In the United States, droperidol was withdrawn from clinical use in 2001 (FDA black box warning) due to accumulating evidence of QT prolongation and concerns about the risk of torsades de pointes (Sneyd 2009). Recently it has been re-licensed in Europe for prevention and treatment of PONV at lower doses of 0.625 to 1.25 mg in adults, and for prevention of nausea and vomiting during postoperative patient-controlled analgesia (PCA) in adults. Granisetron was developed in 1988 and was approved in the UK in 1991 and in the United States in 1994 by the FDA. Ramosetron is approved for use only in Japan and in certain Southeast Asian countries for treatment of nausea and vomiting and diarrhoea-predominant irritable bowel syndrome in males (https://www.drugbank.ca/drugs/DB09290). Aprepitant was approved for medical use in Europe and the United States in 2003. It is listed on the complementary list of antiemetic medicines in the World Health Organization List of Essential Medicines (WHO Model List of Essential Medicines 2019). Fosaprepitant was approved in 2008 by the FDA for use in combination with other antiemetics for prevention of nausea and vomiting caused by chemotherapy. Unlike aprepitant, fosaprepitant is approved by the FDA for prevention of PONV.

Quality of the evidence

Certainty of evidence

This review includes a large number of studies (585 RCTs and 97,516 participants) with a large number of interventions (44 single drugs and 51 drug combinations). Grading the certainty of evidence for all possible combinations of interventions would be difficult to conduct in a reasonable time frame and would be challenging to present in an accessible manner. As an example, for vomiting within 24 hours with 65 different treatments, a total of 2080 pair-wise combinations of treatments were possible. This would equate to 2080 evaluations of the certainty of evidence, which would be an almost unmanageable task and would yield an overload of information. Therefore, we decided to limit the assessment of the certainty of evidence to single drugs of direct interest compared to placebo. As a limitation of this review, an assessment of the certainty of evidence for all drug combinations and all active comparisons is not available.

Study quality based on risk of bias assessments

The overall methodological quality of the primary studies assessed by the Cochrane risk of bias assessment tool 1.0 was limited (Higgins 2011). Only 27% of the studies were assessed as having overall low risk of bias. Most of the studies completely reported their outcome data, which was feasible due to the short follow-up intervals of the study. Major quality concerns were related to selection bias, performance and detection bias, reporting bias, and the other bias domain. About half of all studies did not report the method used for randomization, and 88% of the studies did not specify how allocation of participants was concealed to recruiters. Blinding of participants, personnel, and outcome assessors was not sufficiently described in about 40% of all studies, and about 10% had a non-blinded study design. Selective outcome reporting could be assessed only for studies that had published a prospectively registered study protocol. In total, only 5% of all included studies had a prospectively registered study protocol, and only 2% were judged to have low risk of selective outcome reporting. In the end, we used information from the risk of bias assessment for sensitivity analyses and interpretation of the certainty of evidence for all relevant outcomes. For vomiting within 24 hours, sufficient studies

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at low risk of bias were available to yield a robust NMA treatment effect estimate for at least seven effective single drugs, with high- or moderate-certainty evidence (aprepitant, ramosetron, granisetron, dexamethasone, ondansetron, fosaprepitant, and droperidol). For other safety outcomes, limited study quality was a frequent reason for downgrading the certainty of evidence.

Imprecision

For the primary efficacy outcome postoperative vomiting within 24 hours, high-certainty evidence shows that five single drugs (aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron) reduce vomiting, and moderate-certainty evidence indicates that two other single drugs (fosaprepitant and droperidol) probably reduce vomiting compared to placebo. For most of the primary (SAE, any AE) and secondary safety outcomes (headache, sedation, extrapyramidal symptoms, constipation, wound infection, arrhythmia, QT prolongation, and visual disturbances), we found only very low- to low-certainty evidence for the effects of single drugs of direct interest compared to placebo. Only a few exceptions are listed under Summary of main results. One of the main reasons for the different certainty of evidence levels for drugs in terms of efficacy and safety outcomes was the different amount of underlying information in the NMAs (studies and participants) combined with the lower baseline risks of most safety outcomes. Therefore, the certainty of evidence for safety outcomes is limited for most single drugs of direct interest as a result of imprecision.

We used a clinically relevant size of effects—not statistical significance—to describe and interpret network meta-analysis estimates (Nikolakopoulou 2019; Wasserstein 2019). A risk ratio (RR) of 0.8, which is equivalent to a relative risk reduction (RRR) of 20%, was assumed as a clinically relevant effect for vomiting, and an RR of 0.9 (RRR 10%) was assumed as a clinically relevant effect for all side effects. It is an advantage that precise effect estimates, which are small (and clinically not relevant) but statistically significant in a traditional sense, were not necessarily classified as having a relevant effect. If such small and precise effect estimates were located in the range of equivalence (RR 0.8 to 1.25 for vomiting), they were classified as clinically not important. Only effect estimates that were completely below an RR of 0.8 (benefit) or above an RR of 1.25 (harm) were considered clinically relevant. Moreover, intermediate stages of effect estimates might allow an interpretation of imprecision reflecting the uncertainty associated with effect estimates when 95% confidence intervals (CIs) are broad and include different ranges. Furthermore, retiring statistical significance and focusing on clinically relevant effect sizes helps to solve issues associated with multiple testing in NMA (Efthimiou 2019).

Indirectness

All studies included in this review were relevant for the research question in terms of our defined population, interventions, comparisons, outcomes, and settings of interest. Our PICO criteria are very specific, and all of the conclusions that we have drawn in this review have been directly related to our research question. Consequently, there were no concerns of indirectness in this review, and the certainty of evidence was not downgraded for this item. However, the CINeMA (Confidence in Network Meta-Analysis) approach further considers an imbalance in the distribution of effect-modifying variables among different comparisons for the assessment of indirectness (Nikolakopoulou 2019; Salanti 2014). Effect modifiers are characteristics that impact the relative treatment effect. Comparisons in NMAs will provide direct evidence only if effect modifiers are equally distributed across studies and comparisons. In this case, the assumption of transitivity holds in the NMA. In the protocol, we defined differences in sources of funding, differences in risk of bias, and differences in details of the interventions as effect-modifying variables relevant for this review. In contrast, risk factors for PONV are prognostic variables that directly affect the outcome but not the relative treatment effect on the outcome. In the final review, we accepted heterogeneity (see inclusion criteria of this review) for the effect modifiers 'risk of bias' and 'dose of intervention'. We have, however, assessed the impact of these effect modifiers in sensitivity analyses (risk of bias) and subgroup analyses (dose). Due to the quantity of data and the lack of information for the effect modifier 'funding source' in many studies, an objective and reliable assessment of the distribution of this effect modifier within all comparisons was not possible. In general, we assumed that for all included studies, the study populations, interventions, outcomes, and study settings matched the inclusion criteria of the current systematic review and were sufficiently similar. We have, however, accepted heterogeneity for risk of bias and for intervention details. Thus, we concluded that there was no relevant clinical and methodological heterogeneity within and across treatment comparisons (intransitivity) in the current review.

Heterogeneity and inconsistency/incoherence

In the entire network, there was heterogeneity within designs for the primary efficacy outcome of vomiting. For all other safety outcomes, no heterogeneity between studies of individual comparisons was detectable. At the level of individual comparisons of direct interest (single drugs of direct interest compared to placebo), we assessed heterogeneity using the 95% prediction interval (PI) and considered the impact on clinical conclusions (Nikolakopoulou 2019). In the case of heterogeneity, we investigated the effect-modifier dose in a subgroup analysis and accepted a clinically relevant difference between doses as an explanation for heterogeneity. If there was no explanation by different doses of the intervention, we downgraded due to heterogeneity. In the case of vomiting, heterogeneity was detectable for comparisons of ondansetron, tropisetron, dolasetron, droperidol, amisulpride, and dexamethasone—all compared to placebo. Recommended and high doses of ondansetron, droperidol, and dexamethasone were more favourable compared to low doses. Thus, the certainty of evidence for these comparisons could be applied only to recommended and high doses. Most of the comparisons included in safety outcomes appeared not heterogeneous, as the imprecision of effect estimates was already large.

In the entire network, there was inconsistency between designs for the primary efficacy outcome of vomiting. However, the full random-effects design-by-treatment interaction model revealed that there was no evidence of residual statistical inconsistency, which means that all interventions behave similarly in all comparisons. Other safety outcomes showed no inconsistency between designs. At the level of individual comparisons of direct interest (single drugs of direct interest compared to placebo), we assessed incoherence by comparing direct and indirect effect estimates with respect to impact on the clinical conclusion (Nikolakopoulou 2019). In cases where both estimates have

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resulted in different conclusions, we downgraded this comparison for incoherence. Additionally, we performed a local test using a descriptive Z-statistic for incoherence. Results were reported in the Effects of interventions section, but results were not used for interpretation of incoherence due to the low power of the test.

Publication bias

Publication bias was investigated by explorative analyses for direct comparisons when 10 or more studies were included. Results of the explorative analyses were difficult to interpret because assessment of funnel plots is in general highly subjective, tests for funnel plot asymmetry have low power, and several factors other than publication bias may cause asymmetry in funnel plots. With respect to these limitations, we decided to assume a clinically relevant publication bias if the trim and fill sensitivity analysis changed the clinical conclusion. The trim and fill sensitivity analysis hypothetically estimates the effect based on missing information of the asymmetrical studies. For the primary outcome of vomiting, publication bias was suspected only for droperidol for all single drugs of direct interest compared to placebo. In the cases of dexamethasone, granisetron, and ondansetron (all compared to placebo), the contour-enhanced funnel plots also showed asymmetry. However, trim and fill did not change the conclusion. In cases of granisetron and ondansetron, although estimated effects were overestimated, they were still robust in terms of the range of equivalence. Other primary and secondary safety outcomes included too few studies to test for publication bias, and in cases with enough studies, no publication bias was suspected.

Ranking of treatments

We have reported ranking of treatments in terms of efficacy and safety. The ranking of treatments is based on P scores that measure the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments (Rücker 2015). However, this statistical certainty should not be confused with certainty of evidence. In this review, we have not assessed the certainty of evidence for treatment rankings. In cases where a large number of parameters were independently estimated, the probability increases for finding some extreme results that do not reflect reality (Efthimiou 2019). Thus, the ranking of treatments should be interpreted with caution, and we want to avoid overstated claims. However, comparing the extent of an overlap of 95% CIs of different treatment comparisons may enable us to get a better idea of clinically relevant differences between interventions. In the case of vomiting with placebo as the reference compound, the NK_1 receptor antagonists (fosaprepitant, casopitant, and aprepitant) were the top three ranked single drugs of direct interest. They were comparably effective to most of the drug combinations, and their 95% CIs did not overlap with most of the other single drugs of direct interest. This is a strong indicator that NK_1 receptor antagonists are the most effective single drugs for prevention of vomiting. Differences between all other drugs are of minor importance. In case of most safety outcomes, the ranking of drugs is highly unreliable due to excessive uncertainty in the relative effects.

Potential biases in the review process

The feasibility of conducting an NMA including all available interventions to prevent PONV in adults after surgery strongly correlates with the number of included studies. At the protocol stage, we expected to include more than 1000 studies. Therefore, we carefully planned the best way to narrow down the inclusion criteria of this review to restrict the number of eligible studies in advance. We restricted the review to the population of adults undergoing general anaesthesia only, to pharmacological interventions with direct antiemetic action, and to randomized controlled trials published as full text. Thus we excluded all abstracts and conference proceedings (a total of 84 studies) from the current review. In a currently ongoing project, we used these excluded studies as well as further studies found in an additional search for abstract publications published in conference proceedings to assess the potential for the loss of this information (Hackenbroich (manuscript in preparation)). However, preliminary results indicated that eligibility of most of these abstracts (about 85%) cannot be classified due to missing information. Thus, poor reporting in abstract publications in the field of clinical PONV research seems to be a general limitation preventing inclusion into systematic reviews with narrow inclusion criteria. In contrast to the exclusion of abstract publications, we wanted to include all RCTs independent of their published language. In total, 83 (14%) of all included studies were not published in English. As a strength of this review, we included many local studies that were internationally conducted in non-English-speaking countries. Furthermore, we included full study reports that were not presented as a journal publication. Eligible studies were found in clinical trial registries, and full study reports were either directly linked or found on the companies' websites (e.g. GSK study register). Full study reports are highly valuable and contain detailed information on study details, especially safety assessments.

Several studies had duplicate publications in different journals and were listed in trial registries under different first authors; this complicated the process of data synthesis. By making the dataset fully and freely available, we welcome perusal by outside researchers to identify mistakes in our dataset, our analysis or our interpretation.

A total of 185 studies identified in the first search were listed as awaiting classification; these were either full-text publications (86 studies) or study protocols (99 studies). No full texts for screening and eligibility assessment could be retrieved for 29 studies. Insufficient reporting or lack of reporting of study details relevant for the inclusion/exclusion decision was the main reason for the inability to classify studies. Requests to study authors remained unanswered in these cases. In a worst-case scenario, if we assume that all 86 studies (awaiting classification) published as full text would have been eligible for this review, then we have currently lost about 10% of all available information to date due to poor reporting. However, about half of the studies published as full text and listed as awaiting classification were of older dates (date of publication before 2000). Therefore, we assume that inclusion of these studies would not have substantially altered the conclusions of this review. In contrast, the multitude of studies published only as study protocols and with pending classification were of later publication dates. Future inclusion of these studies could alter the conclusions of the review.

The review team conducting abstract and full-text screening, data extraction, and critical appraisal consisted of 11 persons with different background knowledge in conducting systematic reviews. We held several meetings and training sessions with review authors to ensure a comparable level of knowledge. All new Cochrane

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Review authors had to complete the Cochrane online training (https://training.cochrane.org/interactivelearning). To reduce the risk of errors in data extraction and to reduce the risk of subjective differences in the critical appraisal, data extraction and critical appraisal of all included studies were further checked by one review author (SW, acting as a third author).

Agreements and disagreements with other studies or reviews

A MEDLINE search for 'postoperative nausea and vomiting' AND 'systematic review OR meta-analysis' revealed more than 500 records (November 2019). This snapshot of the literature showed not only that a large number of clinical trials have focused on PONV research but also that a relatively large number of systematic reviews have focused on this topic. In the following discussion, we limit the critical comparison of our most important findings to two large and well-known systematic reviews—the Carlisle Review at Carlisle 2006a, and the Tricco Review at Tricco 2015a and Tricco 2015b.

The previous Cochrane Review on drugs for prevention of PONV by Carlisle and Stevenson included RCTs investigating any drug for prevention of PONV in participants of any age undergoing general anaesthesia, regional anaesthesia, or sedation (Carlisle 2006a). This review searched several databases and included 737 studies involving 103,237 participants. Data were analysed using pair-wise meta-analyses for PONV-related outcomes and side effects comparing a drug with placebo or with another drug. Risk of bias in studies was assessed. However, the certainty of evidence was not evaluated. This review found eight drugs that effectively prevent postoperative nausea and vomiting compared to placebo: droperidol, metoclopramide, ondansetron, tropisetron, dolasetron, dexamethasone, cyclizine, and granisetron. The risk ratio (RR) versus placebo varied between 0.60 and 0.80, depending upon the drug and the outcome. This review concluded that publication bias made the evidence for differences among these drugs unreliable. Evidence for side effects was sparse: droperidol was a sedative (RR 1.32), and headache was more common after ondansetron (RR 1.16). The Carlisle Review on PONV was withdrawn in 2017, in part because this review included several studies that were retracted since publication (Carlisle 2017). Our review on prevention of PONV can be considered, to some extent, as an update to the Carlisle Review. However, to enhance the feasibility and conclusiveness of our review, we narrowed down the inclusion criteria when compared to the Carlisle review and included only adult participants undergoing general anaesthesia who received an antiemetic intervention belonging to one of the six relevant pharmacological substance classes for prevention of PONV. This enabled us to focus the research question and to limit the number of eligible RCTs. In addition, we used NMA to compare all available drugs and combinations against each other, thereby enabling us to generate a ranking of treatment efficacy. Our review included some newer drugs compared to the Carlisle Review, which are drugs of the NK_1 receptor antagonist class (aprepitant, casopitant, fosaprepitant, and rolapitant), and some of the D_2 receptor antagonists (amisulpride and haloperidol). The current review selected the best drugs based on both an important benefit for prevention of vomiting and moderate to high certainty evidence. In contrast, the Carlisle Review selected drugs that had an effect (95% CI < 1) on all four efficacy outcomes (vomiting, nausea, nausea or vomiting, and rescue antiemetic) without knowledge of the certainty of evidence. Four of the eight drugs found to be preventive for PONV in the Carlisle Review were also effective in preventing vomiting (with moderate- to high-certainty evidence) in the current review—dexamethasone, droperidol, granisetron, and ondansetron. We found three more effective drugs with moderate- to high-certainty evidence—aprepitant, fosaprepitant, and ramosetron. However, the other four effective drugs found in the Carlisle Review were not included in our review (cyclizine), were of only low-certainty evidence (dolasetron and tropisetron), or were less effective and of very low-certainty evidence (metoclopramide). The Carlisle Review emphasized that publication bias makes evidence on these drugs unreliable, especially for droperidol, ondansetron, and granisetron. In contrast to the Carlisle Review, we excluded all fraudulent studies and used an alternative strategy to assess publication bias. In our review, we also suggested publication bias for droperidol compared to placebo for vomiting. For granisetron and ondansetron compared to placebo, although estimated NMA treatment effects seem to be overestimated, the estimates were still robust in terms of the clinical conclusion. Thus, we assume that estimated treatment effects for granisetron and ondansetron were overestimated due to publication bias; however, this does not alter the conclusion. The Carlisle Review found sparse evidence for side effects, and we thoroughly underscore this statement more than 10 years later. Evidence for side effects remains limited. We also found an increase in headache for ondansetron compared to placebo with moderate-certainty evidence. We did not, however, find a sedative effect of droperidol compared to placebo found by the Carlisle Review.

A large NMA on the comparative efficacy and safety of 5-HT_3 receptor antagonists compared to each other or placebo and/or combined with other antiemetics for patients undergoing surgical procedures was published in 2015 (Tricco 2015a; Tricco 2015b). Tricco´s review had broader inclusion criteria than our review in terms of the population of interest and the study design. The Tricco Review included RCTs and non-randomized trials investigating participants of any age undergoing any surgery with any type of anaesthesia. However, the interventions of interest were focused on 5-HT_3 receptor antagonists as single interventions and in combination with other antiemetics. Tricco and colleagues searched several databases and included 450 studies with 80,410 participants for efficacy analyses (Tricco 2015a), along with 120 studies with 27,787 participants for safety analyses (Tricco 2015b). The Tricco Review was restricted to trials published in English. Risk of bias was assessed, but certainty of evidence was not evaluated. Significantly fewer patients experienced vomiting with any investigated drug relative to placebo, except for palonosetron plus dexamethasone. Tricco and associates concluded that granisetron plus dexamethasone was the most effective antiemetic. In contrast, our review included many more combinations of 5-HT_3 receptor antagonists with other antiemetics for the outcome of vomiting that were not included in the Tricco Review (aprepitant-palonosetron, aprepitant-ramosetron, CP122,721-ondansetron, aprepitant-ondansetron, casopitant-ondansetron, dexamethasone-ramosetron, haloperidol-ondansetron, ondansetron-promethazine, dexamethasone-tropisetron, droperidol-tropisetron, droperidol-palonosetron, and ondansetron-scopolamine). Estimated NMA treatment effects of single 5-HT_3 receptor antagonists compared to placebo from the Tricco Review were in agreement with our estimates of effects when transformed into odds ratios. However, the negative effect

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of the combination treatment dexamethasone-palonosetron was not detected in our review. Tricco and coworkers investigated arrhythmia, QT prolongation, delirium, and mortality as relevant safety outcomes; headache and constipation as specific side effects of 5-HT_3 receptor antagonists were not included in the Tricco Review. In contrast to our review, trials with zero events in all study arms were excluded from analysis. In the Tricco Review, granisetron plus dexamethasone increased the risk of arrhythmia. This combination, however, was not included in our review, as the two relevant studies investigating this combination were not eligible for our review (El-Deeb 2011: spinal anaesthesia; Riad 2009: children). For QT prolongation, Tricco and colleagues found only two relevant trials with events investigating ondansetron versus placebo and granisetron versus placebo. Tricco and associates found three additional trials with zero events in all arms. As a limitation of the Tricco Review, the review author did not grade the certainty of evidence for the main drugs compared to placebo.

AUTHORS' CONCLUSIONS

Implications for practice

- We found high-certainty evidence showing that compared to placebo, five single drugs (aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron) reduce vomiting, and moderate-certainty evidence indicating that another two single drugs (fosaprepitant and droperidol) probably reduce vomiting. These were the seven most reliable and most effective drugs identified in this review. Therefore, four of the six substance classes (5-HT_3 receptor antagonists, D_2-receptor antagonists, NK_1-receptor antagonists, and corticosteroids) with different mechanisms of action are represented by at least one drug that shows benefit in terms of preventing vomiting.
- In absolute numbers, for every 1000 patients, of whom 300 would vomit after surgery if given placebo, 282 would benefit from fosaprepitant (the most effective drug of the seven most reliable single drugs) and 18 would not. If droperidol were given (the least effective drug of the seven most reliable single drugs), 117 patients would benefit and 183 would not. Aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron were ranked between fosaprepitant and droperidol in terms of their efficacy for prevention of vomiting.
- Recommended and high doses of granisetron, dexamethasone, ondansetron, and droperidol were similarly effective but were more effective than low doses for prevention of vomiting. So far, no dose effects are detectable for aprepitant, ramosetron, and fosaprepitant.
- Ranking of treatments shows that combinations of drugs were generally more effective than the corresponding single drugs in preventing vomiting. However, NK_1 receptor antagonists were the most effective drug class, and single NK_1 receptor antagonists (fosaprepitant, casopitant, aprepitant) were as effective as most of the drug combinations.
- Other single drugs of direct interest for prevention of postoperative vomiting were of uncertain effect due to very low- to low-certainty evidence (casopitant, tropisetron, dolasetron), were less effective (amisulpride, promethazine), or both (palonosetron, haloperidol, metoclopramide, rolapitant, dimenhydrinate, scopolamine), compared to placebo.
- For most of the single drugs of direct interest, we found only very low- to low-certainty evidence for safety assessed by the occurrence of SAEs and any AE. We found only moderate-certainty evidence for granisetron and amisulpride indicating that the drugs probably have little or no effect on any AE compared to placebo, and low-certainty evidence suggesting that dimenhydrinate and scopolamine may increase the number of patients with any AE.
- The certainty of evidence for most of the single drugs of direct interest ranged between very low and low for drug class-specific side effects (headache, constipation, wound infection, extrapyramidal symptoms, sedation, arrhythmia, QT prolongation, visual disturbances). An exception was moderate-certainty evidence showing that ondansetron probably increases headache and probably reduces sedation compared to placebo. The latter effect was limited to recommended and high doses of ondansetron. Droperidol probably reduces headache compared to placebo. Dexamethasone has no effect on sedation compared to placebo. Dimenhydrinate probably increases sedation and scopolamine may increase the risk for visual disturbances, both compared to placebo. No studies considered substance class-specific side effects for fosaprepitant, the most effective drug for prevention of vomiting.
- Results of the review have limited external validity for the broad population of adults undergoing any surgery with general anaesthesia, but they are directly applicable to patients at risk for PONV (i.e. women undergoing gynaecological/gastrointestinal surgery with volatile anaesthesia and patients using perioperative opioids).

Implications for research

We no longer need these types of studies.

- Aprepitant, ramosetron, granisetron, dexamethasone, ondansetron, and droperidol compared with placebo and with different other active comparators in several studies included in the NMA for vomiting. We do not need further RCTs investigating inactive or active comparisons of these six drugs in the investigated population.
- Currently, we have no need for further RCTs comparing other single drugs versus placebo for prevention of postoperative vomiting in the investigated population. Head-to-head comparisons should be the way forward for new drugs.

Here we describe future research needs.

- Fosaprepitant was compared only to ondansetron for prevention of vomiting in three studies. There is limited connectivity within the network of vomiting. Fosaprepitant should be compared to other active drugs such as granisetron, ramosetron, dexamethasone, or aprepitant to further investigate its leading position as the most effective single drug for prevention of vomiting as reported in this review. In addition, no dose-response studies nor safety studies are available for fosaprepitant in this context.
- Data on the NK_1 receptor antagonists casopitant and rolapitant are limited, although this substance class shows promising anti-vomiting effects.
- The conclusions of this review are restricted to patients at risk (women, patients undergoing gynaecological/gastrointestinal surgery, patients given inhalational anaesthesia, and patients using perioperative opioids), most of whom are healthy patients

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(American Society of Anesthesiologists status (ASA) I and II) investigated in inpatient settings. To what extent patients with more severe disease or patients in outpatient settings derive benefit or harm from antiemetic prophylaxis is still unclear.

- Most patients in the general surgical population exposed to prophylactic antiemetics will not benefit because about 70% would not suffer from vomiting. Therefore, we need to understand the risk of side effects. To increase the chances of detecting even rare side effects (e.g. QT prolongation, arrhythmia, extrapyramidal symptoms), non-randomized cohort studies or systematic reviews including non-randomized studies would be useful, in addition to RCTs.
- We do not understand whether higher doses of drugs increase the chances of suffering from certain side effects. Dose-response studies on side effects or observational studies on dose effects would be useful in this regard.
- Future studies should report exact outcome definitions (e.g. QT prolongation, arrhythmia, extrapyramidal symptoms) and should fully report all investigated safety outcomes. Study authors should use online repositories and supplementary material to store detailed information.
- All new studies should prospectively publish a study protocol in an official trial registry. All outcomes of interest including outcome definition, method to measure, and time points should be listed.
- New studies should provide a detailed description of baseline characteristics and the distribution of classical risk factors for PONV in the study population (e.g. in a supplementary table).
- New RCTs should use and clearly describe methods for allocation concealment.
- All studies should declare their funding resources and potential conflicts of interest.
- Negative and non-significant results are also important. We call on all investigators who conducted studies on PONV in the past to please publish their studies, even if time has passed since the study was conducted. Only in this way can we obtain an unbiased picture of the benefits and harms of all relevant drugs.

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Supplementary Files-1-vomiting 24

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Supplementary Files-3-any AE

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Supplementary Files-4-headache

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Supplementary Files-6-extrapyramidal symptoms

Weibel S. Supplementary Files-6-extrapyramidal symptoms (Version 1) [Data set]. Zenodo 2020. [DOI: 10.5281/zenodo.4066442]

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* Indicates the major publication for the study

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Aasboe 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n):* - • *Enrolled (n):* - • *Randomized (n):* 40 • *Received treatment (n):* NA • *Analysed (n):* 40 • *Age (mean ± SD, median (IQR), median (range)):* 45 ± 14 • *Weight (mean ± SD, median (IQR), median (range)):* 64 ± 11 • *BMI (mean ± SD, median (IQR), median (range)):* NA • *ASA I/II/III/IV (n):* NA/NA/NA/0 • *Gender (female in %):* 87.5 • *Non-smoker (%):* NA • *History of PONV/motion sickness (%):* NA • *Type of general anaesthesia: inhalational anaesthesia (isoflurane, N_2O)* • *Duration of anaesthesia or surgery (in min; as mean or median):* 16 (haemorrhoids), 25 (hallux valgus) • *Use of perioperative opioids (if yes, which?):* fentanyl at induction (2 µg/kg), meperidine (10 mg IV) or codeine (30 mg) as rescue analgesic (NA) • *Type of surgery:* haemorrhoids, hallux valgus Betamethasone • *Assessed for eligibility (n):* - • *Enrolled (n):* - • *Randomized (n):* NA • *Received treatment (n):* NA • *Analysed (n):* 38 • *Age (mean ± SD, median (IQR), median (range)):* 44 ± 13 • *Weight (mean ± SD, median (IQR), median (range)):* 65 ± 10 • *BMI (mean ± SD, median (IQR), median (range)):* NA • *ASA I/II/III/IV (n):* NA/NA/NA/0 • *Gender (female in %):* 73.68 • *Non-smoker (%):* NA • *History of PONV/motion sickness (%):* NA • *Type of general anaesthesia: inhalational anaesthesia (isoflurane, N_2O)* • *Duration of anaesthesia or surgery (in min; as mean or median):* 15 (haemorrhoids), 26 (hallux valgus) • *Use of perioperative opioids (if yes, which?):* fentanyl at induction (2 µg/kg), meperidine (10 mg IV) or codeine (30 mg) as rescue analgesic (NA) • *Type of surgery:* haemorrhoids, hallux valgus **Included criteria:** age over 18 years, ASA I to III, no corticosteroids during last week or NSAIDs during the 2 days before operation, scheduled for ambulatory surgery (hallux valgus (Mitchell's operation) or haemorrhoids (Milligan's operation))

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Aasboe 1998 *(Continued)*

	Excluded criteria: known allergy or contraindications to any of the test drugs, pregnancy **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: saline 2 mL • *Time point of administration*: 30 minutes before the start of surgery • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Betamethasone • *Dose*: 12 mg (50% betamethasone disodium phosphate and 50% betamethasone acetate) • *Time point of administration*: 30 minutes before the start of surgery • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Adverse events (general notes in the publication, 4 hours' observation)* • Outcome type: general note on side effects
Identification	**Sponsorship source:** financial support was provided as a research grant before study start from Schering-Plough, Norway, the distributor of Celeston Chronodose (betamethasone) **Country:** Norway **Setting:** outpatient, single-centre **Author's name:** Vidar Aasboe **Institution:** Departments of Anesthesia and Surgery, Ullevaal University Hospital, Oslo, Norway **Email:** NA **Address:** Department of Anesthesia, Oestfold Central Hospital, N-1603 Fredrikstad, Norway **Duration of study:** NA **Language:** English **Study's primary outcome:** postoperative pain **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly assigned to double-blind administration from coded ampoules of 2 mL of the test drug IM 30 min before the start of surgery" Judgement comment: no further information on sequence generation provided

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Aasboe 1998 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the day after surgery, the patients were contacted by telephone and asked to evaluate their pain using the verbal score during rest, ambulation, sitting in a chair (for hemorrhoid patients), and leg movement (for hallux valgus patients). They were also asked about analgesic consumption and the occurrence of PONV. The patients were asked to evaluate their overall experience during the postoperative period as unacceptable, adequate, or good. A similar telephone interview was performed 7 days after the surgery" Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "eighty patients were included in the study. Two patients were excluded because the surgical procedure was changed after inclusion"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the two groups in demographic data (Table 1) or vital signs in the perioperative period" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Abreu 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 (not explicitly stated) • *Age (mean ± SD, median (IQR), median (range))*: 34.53 ± 5.50 • *Weight (mean ± SD, median (IQR), median (range))*: 60.58 ± 10.12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 14/6/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA

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Abreu 2006 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 103.33
- *Use of perioperative opioids (if yes, which?)*: 175 mg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20 (not explicitly stated)
- *Age (mean ± SD, median (IQR), median (range))*: 34.30 ± 7.78
- *Weight (mean ± SD, median (IQR), median (range))*: 64.43 ± 13.15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 16/4/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80.53
- *Use of perioperative opioids (if yes, which?)*: 175 mg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20 (not explicitly stated)
- *Age (mean ± SD, median (IQR), median (range))*: 34.23 ± 9.24
- *Weight (mean ± SD, median (IQR), median (range))*: 62.82 ± 10.04
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 16/4/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93.42
- *Use of perioperative opioids (if yes, which?)*: 190.52 mg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20 (not explicitly stated)
- *Age (mean ± SD, median (IQR), median (range))*: 31.56 ± 5.58
- *Weight (mean ± SD, median (IQR), median (range))*: 59.43 ± 12.75
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 17/3/0/0

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Abreu 2006 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 89.74
- *Use of perioperative opioids (if yes, which?)*: 188.16 mg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20 (not explicitly stated)
- *Age (mean ± SD, median (IQR), median (range))*: 35.60 ± 6.26
- *Weight (mean ± SD, median (IQR), median (range))*: 57.52 ± 9.58
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 16/4/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100.37
- *Use of perioperative opioids (if yes, which?)*: 180.78 mg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Included criteria: patients aged 22 to 62 years, physical status ASA I and II, submitted to diagnostic or surgical gynaecological laparoscopy under general intravenous and inhalational anaesthesia

Excluded criteria: patients with previous history of postoperative nausea and vomiting, those with gastric disorders

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV, perioperative opioids): no; (non-smoker, history of motion sickness): unclear; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: after anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 10 mg • *Time point of administration*: after anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 1.25 mg • *Time point of administration*: after anaesthetic induction • *Route of administration*: IV

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Abreu 2006 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: NA Dexamethasone • *Dose*: 8 mg • *Time point of administration*: after anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Control • *Dose*: no treatment • *Time point of administration*: no treatment • *Route of administration*: no treatment • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting* (PACU or PACU + 4 hours (discharge)) • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Brazil **Setting:** outpatient, single-centre **Author's name:** Múcio Paranhos de Abreu **Institution:** Hospital Centro Médico de Campinas e Instituto Penido Burnier, Campinas, SP **Email:** mpabreu2@gmail.com **Address:** Av. Nossa Senhora de Fátima, 805/J-131 Taquaral13090-000 Campinas, SP **Language:** English/Portuguese **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	Data on incidence of vomiting not plausible when 20 participants per group assumed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly distributed in five groups according to the antiemetic drug, administered immediately after anesthetic induction: group GO: ondansetron (4 mg); group GM: metoclopramide (10 mg); group GD: droperidol (1.25 mg); group GX: dexamethasone (8 mg) and group GC (control) not medicated" Judgement comment: no information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement comment: no statement

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Abreu 2006 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "during PACU stay, the presence of nausea and/or vomiting was periodically evaluated and recorded by an anaesthesiologist" Judgement comment: no statement on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: missing information on number of analysed participants in different groups (incidence of vomiting). Table 1 (demographic data) for all participants We assumed no missing outcome data for incidence of vomiting
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV, perioperative opioids): no; (non-smoker, history of motion sickness): unclear; (duration of anaesthesia): yes

Adducci 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 34 • *Received treatment (n)*: 34 • *Analysed (n)*: 34 • *Age (mean ± SD, median (IQR), median (range))*: 48 (44 to 53) • *Weight (mean ± SD, median (IQR), median (range))*: 66 (62 to 71) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/10/0/0 • *Gender (female in %)*: 67.65 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 72 • *Use of perioperative opioids (if yes, which?)*: 231 µg fentanyl • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 38 • *Received treatment (n)*: 38 • *Analysed (n)*: 38

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Adducci 2002 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 51 (47 to 55)
- *Weight (mean ± SD, median (IQR), median (range))*: 70 (66 to 74)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 25/13/0/0
- *Gender (female in %)*: 71.05
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 83
- *Use of perioperative opioids (if yes, which?)*: 246 µg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: 35
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 45 (40 to 49)
- *Weight (mean ± SD, median (IQR), median (range))*: 66 (62 to 70)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/11/0/0
- *Gender (female in %)*: 77.14
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80
- *Use of perioperative opioids (if yes, which?)*: 225 µg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 37
- *Received treatment (n)*: 37
- *Analysed (n)*: 37
- *Age (mean ± SD, median (IQR), median (range))*: 50 (45 to 55)
- *Weight (mean ± SD, median (IQR), median (range))*: 74 (69 to 80)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 27/10/0/0
- *Gender (female in %)*: 64.86
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80
- *Use of perioperative opioids (if yes, which?)*: 244 µg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -

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Adducci 2002 *(Continued)*

- *Randomized (n)*: 36
- *Received treatment (n)*: 36
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 49 (44 to 53)
- *Weight (mean ± SD, median (IQR), median (range))*: 71 (67 to 74)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 28/8/0/0
- *Gender (female in %)*: 72.22
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88
- *Use of perioperative opioids (if yes, which?)*: 240 µg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: 18 to 75 years of age, ASA physical status I and II, undergoing general anaesthesia for laparoscopic cholecystectomy

Excluded criteria: history of gastrointestinal or neuromuscular disease, known narcotic use or alcohol abuse, patients under 18 or over 75 years of age, patients with nausea and vomiting within 72 hours of surgery or who had received antiemetic therapy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: 2 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: 2 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron + dexamethasone

- *Dose*: ondansetron 8 mg, dexamethasone 8 mg
- *Time point of administration*: 2 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide + dexamethasone

- *Dose*: metoclopramide 10 mg, dexamethasone 8 mg
- *Time point of administration*: 2 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo

- *Dose*: saline
- *Time point of administration*: 2 minutes before induction of anaesthesia

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Adducci 2002 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general note on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** E. Adducci **Institution:** Istituto di Anestrsiologia e Rianimazioiie, Universita Callolica del Sacro Cxiore - Roma **Email:** NA **Address:** Largo Francesco Vito, 1, 00168 Roma RM, Italy **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "using tables of random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "sealed envelope assignment"

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Adducci 2002 *(Continued)*

		Not stated: sequentially numbered, opaque sealed envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "assessment was made by an anaesthesia resident who was blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Agamez Medina 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 33 • *Received treatment (n)*: NA • *Analysed (n)*: 31 • *Age (mean ± SD, median (IQR), median (range))*: 49.29 ± 14.68 • *Weight (mean ± SD, median (IQR), median (range))*: 70.1 ± 14.04 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 71 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl at induction • *Type of surgery*: gynaecological, urological, or orthopaedic surgery Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Agamez Medina 2015 *(Continued)*

- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 52.28 ± 15.57
- *Weight (mean ± SD, median (IQR), median (range))*: 71.41 ± 15.03
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 59.4
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction
- *Type of surgery*: gynaecological, urological, or orthopaedic surgery

Included criteria: age over 18 years, ASA I or II programmed to undergo general, gynaecological, urological, or orthopaedic surgery at the centre, for which informed written consent was requested

Excluded criteria: presence of cardiac pathology, any abnormal finding on ECG or heart rate < 60 beats per minute, concomitant medication with known involvement of QT interval duration, family history of sudden death, arrhythmias or long QT syndrome (SQTL), electrolyte disturbances

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 7 minutes after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 1.25 mg • *Time point of administration*: 7 minutes after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Arrhythmia (*during surgery to immediate postoperative phase*)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this work was financed with funds from the Department of Anesthesia and Reanimation of the University Hospital Foundation-Alcorcón **Country:** Spain **Setting:** inpatient, single-centre **Author's name:** Agámez Medina **Institution:** Department of Anaesthesiology and Resuscitation, University Hospital Foundation Alcorcón, Alcorcón, Madrid, Spain **Email:** agamezgabriela@gmail.com

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Agamez Medina 2015 *(Continued)*

	Address: Calle Budapest, 1, 28922 Alcorcón, Madrid, Spain **Duration of study:** October to December 2011 **Language:** Spanish (Google Translator) **Study's primary outcome:** QT prolongation **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote (translated): "the assignment was made using a table of random numbers generated by computer''
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote (translated): "all the investigators were unaware of the group to which the patient belonged until the end of the analysis''
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote (translated): "EKG analyses were independently performed by two cardiologists blinded to the state of the traces or group allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote (translated): "68 patients were included. Five patients were excluded after the start of the study: four because their surgery was cancelled or postponed (two from each group) and one from the droperidol group due to the use of phenylephrine after induction"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: quote (translated): "the mean age was 50.8 years (SD 15.1), there were no differences between the groups (table 1)" Baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Agarkar 2015

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ramosetron

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Agarkar 2015 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 103
- *Received treatment (n)*: 103
- *Analysed (n)*: 103
- *Age (mean ± SD, median (IQR), median (range))*: 49.0 ± 13.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 84.5
- *Non-smoker (%)*: 92.2
- *History of PONV/motion sickness (%)*: 4.9
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 140.0
- *Use of perioperative opioids (if yes, which?)*: 162.6 µg intraoperative fentanyl, 18.4% morphine, 88.3% perioperative opioids
- *Type of surgery*: breast, parotid, thyroid or gynaecological surgery, TURBT, neck dissection

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 103
- *Received treatment (n)*: 103
- *Analysed (n)*: 103
- *Age (mean ± SD, median (IQR), median (range))*: 47.3 ± 13.8
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 89.3
- *Non-smoker (%)*: 92.2
- *History of PONV/motion sickness (%)*: 2.9
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 135.9
- *Use of perioperative opioids (if yes, which?)*: 163.2 µg intraoperative fentanyl, 19.4% morphine, 93.2% perioperative opioids
- *Type of surgery*: breast, parotid, thyroid or gynaecological surgery, TURBT, neck dissection

Included criteria: ASA I and II patients scheduled to undergo breast, parotid, thyroid, or gynaecological surgeries, with at least 2 of the established risk factors: female sex, `non-smoking` status, history of PONV or motion sickness, perioperative use of opioids

Excluded criteria: pregnant or menstruating patients, those with a history of gastroesophageal reflux, those who had received antiemetic or suffered from nausea or vomiting in the 24 hours preceding the scheduled operation, those undergoing major intra-abdominal, intrathoracic, pelvic, and reconstructive surgeries

Pretreatment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ramosetron • *Dose*: 0.3 mg

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Agarkar 2015 *(Continued)*

- *Time point of administration*: 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 23.3% (metoclopramide 10 mg IV)

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: 30 minutes before the end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 32% (metoclopramide 10 mg IV)

Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general note on side effects
Identification	**Sponsorship source:** ramosetron vials were provided by the company (Cadila Healthcare Ltd.) **Country:** India **Setting:** inpatient, NA **Author's name:** Aparna S Chatterjee **Institution:** Department of Anesthesia, Critical Care and Pain, Tata Memorial Hospital, Parel, Mumbai, Maharashtra, India **Email:** aparnasanjay@hotmail.con **Address:** Department of Anesthesia, Critical Care and Pain, 2nd Floor, Main Building, Tata Memorial Hospital, Dr. E. Borges Marg, Parel, Mumbai-400012, Maharashtra, India **Duration of study:** April to September 2012 **Language:** English **Study's primary outcome:** incidence of PONV during the first 24 hours **Trial registry number:** CTRI/2013/02003357
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Agarkar 2015 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study drugs were drawn in identical syringes with 4ml volume each, labelled 'antiemetic'(ramosetron was diluted to 4 ml in normal saline) by a nurse who was not a part of the study and handed to the respective OT anaesthesiologist. The patient and investigators were blinded to the study medication"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "anaesthesiologist. The patient and investigators were blinded to the study medication"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: CTRI/2013/02003357 (retrospective registration)
Other bias	Unclear risk	Quote: "the mean duration of surgery and anaesthesia and the intraoperative dose of fentanyl in both the groups were comparable" Judgement comment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Agarwal 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 40.2 ± 9.9 • *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 64 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 96 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group II)

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Agarwal 2002 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 41.4 ± 12.3
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: patients of either sex, between 18 and 60 years of age, ASA grade I and II, undergoing laparoscopic cholecystectomy

Excluded criteria: patient's refusal to participate in the study, previous history of PONV and travel sickness, impaired renal function with increased urea and creatinine concentrations, diabetes mellitus, obesity, patients receiving antiemetic medication or a histamine H2-receptor antagonist within 72 hours of surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Ondansetron • *Dose*: 4 mg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Anil Agarwal

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Agarwal 2002 *(Continued)*

Institution: Department of Anesthesia, and Biostatistics, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Email: aagarwal@sgpgi.ac.in

Address: Department of Anesthesia, and Biostatistics, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Type IV / 48, S.G.P.G.I.M.S., Lucknow, 226 014, India

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	2 out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a table of random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "groups I and III patients received normal saline 1 mL iv just before induction of anesthesia to maintain blinding" Judgement comment: no further information about blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "blinded observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients were comparable in all three groups with regard to age, sex, height, weight and duration of surgery (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Agarwal 2006

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis

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Agarwal 2006 *(Continued)*

Participants	**Baseline characteristics** Placebo (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 78 • *Received treatment (n)*: 78 • *Analysed (n)*: 78 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 14.4 • *Weight (mean ± SD, median (IQR), median (range))*: 57.3 ± 11.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 46.15 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (propofol, fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: intraoperative and postoperative fentanyl (NA) • *Type of surgery*: percutaneous nephrolithotomy for renal and upper ureteric stone requiring catheterization of urinary bladder Oxybutynin (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 78 • *Received treatment (n)*: 78 • *Analysed (n)*: 78 • *Age (mean ± SD, median (IQR), median (range))*: 45.6 ± 13.2 • *Weight (mean ± SD, median (IQR), median (range))*: 55.4 ± 12.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 48.72 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (propofol, fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: intraoperative and postoperative fentanyl (NA) • *Type of surgery*: percutaneous nephrolithotomy for renal and upper ureteric stone requiring catheterization of urinary bladder **Included criteria:** 18 to 60 years of age, ASA I or II, of either sex, undergoing elective percutaneous nephrolithotomy for renal and upper ureteric stone requiring catheterization of urinary bladder **Excluded criteria:** patients with a history of overactive bladder (frequency over 3 times in the night or over 8 times in 24 hours) and/or at end-stage renal disease (urine output 500 mL/24 h) **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo (group C)

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Agarwal 2006 *(Continued)*

- *Dose*: placebo
- *Time point of administration*: 1 hour before induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Oxybutynin (group O)

- *Dose*: 5 mg
- *Time point of administration*: 1 hour before induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Outcomes

Arrhythmia (0 to 6 hours (clinically relevant dysrhythmias)

- Outcome type: dichotomous outcome

Visual disturbances (e.g. blurred vision) (at 0, 1, 2, 6 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 6 hours observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: India

Setting: inpatient, single-centre

Author's name: A. Agarwal

Institution: Department of Anaesthesia and, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

Email: aagarwal@sgpgi.ac.in

Address: Department of Anaesthesia and Department of Surgical Urology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Type IV/48, SGPGIMS, Lucknow 226 014, India

Duration of study: NA

Language: English

Study's primary outcome: incidence of urinary catheter-related bladder discomfort

Trial registry number: NA

Notes

2 out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomized with the help of a computer generated table of random numbers into three groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Agarwal 2006 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "this nurse was not aware of the medication contained in these bottles and administered these to patients depending upon the results of the randomization" Quote: "tablets were peeled off from their packing and placed in identical bottles marked 1, 2 and 3, and were handed over to a nursing staff in the preoperative area. This nurse was not aware of the medication contained in these bottles and administered these to patients depending upon the results of the randomization"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "(region) was carried out by one of the investigators (V.S.), who was unaware of the group allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences in the patient characteristics including age, gender and weight between the groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Aghadavoudi 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide (group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 32 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 50.6 ± 15.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26.1 ± 3.9 • *ASA I/II/III/IV (n)*: 0/12/18/0 • *Gender (female in %)*: 46.7 • *Non-smoker (%)*: 76.7 • *History of PONV/motion sickness (%)*: 10/NA • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, morphine) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 254.5

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Aghadavoudi 2008 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (4 µg/kg at induction, 2 µg/kg/h during CPB), intraoperative morphine (0.1 mg/kg), postoperative morphine (9.5 mg)
- *Type of surgery*: cardiac surgery with cardiopulmonary bypass

Granisetron (group G)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 50.8 ± 14.6
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25.1 ± 4.3
- *ASA I/II/III/IV (n)*: 0/14/16/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: 73.3
- *History of PONV/motion sickness (%)*: 3.3/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, morphine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 259.7
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (4 µg/kg at induction, 2 µg/kg/h during CPB), intraoperative morphine (0.1 mg/kg), postoperative morphine (9.5 mg)
- *Type of surgery*: cardiac surgery with cardiopulmonary bypass

Placebo (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 50.8 ± 14.9
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23.3 ± 4.1
- *ASA I/II/III/IV (n)*: 0/13/17/0
- *Gender (female in %)*: 40
- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: 10/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, morphine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 259.1
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (4 µg/kg at induction, 2 µg/kg/h during CPB), intraoperative morphine (0.1 mg/kg), postoperative morphine (9.5 mg)
- *Type of surgery*: cardiac surgery with cardiopulmonary bypass

Included criteria: consecutive patients undergoing elective cardiac surgery with cardiopulmonary bypass: underwent coronary artery bypass grafting, valve-related and combined procedures; adult patients between 18 and 70 years of age with American Society of Anesthesiologists (ASA) physical status of II or III

Excluded criteria: past history of hiatus hernia, heartburn, or previous gastric surgery; those with morbid obesity, mental retardation, or psychiatric illness; patients taking antiemetic medication, H2-receptor antagonist, or proton pump inhibitor; not tracheally extubated within 12 hours after end of surgery; intra-aortic balloon pump (IABP) requirement during surgery, emergency resternotomy

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Aghadavoudi 2008 *(Continued)*

	Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV, anaesthesia, use of perioperative opioids): no; (history of motion sickness, use of intraoperative opioids): unclear
Interventions	**Intervention characteristics** Metoclopramide (group M) • *Dose*: 0.1 mg/kg • *Time point of administration*: after weaning from the ventilator but before tracheal extubation in ICU • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.1 mg/kg: 13.4%; granisetron 0.01 mg/kg: 6.7% Granisetron (group G) • *Dose*: 0.01 mg/kg • *Time point of administration*: after weaning from the ventilator but before tracheal extubation in ICU • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.1 mg/kg: 6.7%; granisetron 0.01 mg/kg: 3.35% Placebo (group P) • *Dose*: 5 mL saline • *Time point of administration*: after weaning from the ventilator but before tracheal extubation in ICU • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.1 mg/kg: 30%; granisetron 0.01 mg/kg: 13.4%
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Omid Aghadavoudi **Institution:** Cardiac Anesthesia Department, Chamran Heart Hospital, Isfahan University of Medical Sciences, Isfahan, Iran **Email:** aghadavoudi@med.mui.ac.ir **Address:** NA **Duration of study:** 2-month period **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA

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Aghadavoudi 2008 *(Continued)*

Notes	3 out of 4 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "based on a computer-generated randomization table 20"
Allocation concealment (selection bias)	Unclear risk	Quote: "the participants were allocated by the anesthesiologist to one of the four groups of antiemetic prophylaxis" Judgement comment: no statement on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "study drug was prepared and administered by an anesthesiologist at the investigative site who was not involved in data collection" Judgement comment: anaesthetists not blinded. No information on blinding of participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the incidence and severity of nausea and vomiting were recorded by a blinded investigator, who was not involved in anesthetic and ICU care"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "128 met inclusion criteria, provided informed consent, and were qualified for the study. Eight patients were excluded from the data; two because of protocol violation, three for prolonged ventilation after the end of surgery, one required intraoperative IABP and two required resternotomy for bleeding. Finally, 120 patients were eligible for the statistical analysis"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients' characteristics, including demographic data and baseline characteristics are described in table 1. There were no significant differences among the four groups in factors that could modify the incidence of PONV as background factors, factors related to the operation or anesthesia. Average risk of PONV, according to simplified risk score by Apfel and colleagues, 23 was not statistically different among the four groups. There were no significant differences in pain intensity and total dose of postoperative opioids among groups in the ICU" Judgement comment: baseline characteristics (age, BMI, ASA): no difference. Potential effect modifiers (gender, non-smoker, history of PONV, anaesthesia, use of perioperative opioids): no difference; (history of motion sickness, use of intraoperative opioids): unclear

Ahmed 2000

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics**

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Ahmed 2000 *(Continued)*

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: NA
- *Analysed (n)*: 59
- *Age (mean ± SD, median (IQR), median (range))*: 34 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25 ± 3
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 36/39
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: alfentanil for induction, morphine, postoperative dihydrocodeine
- *Type of surgery*: gynaecological laparoscopy

Ondansetron + cyclizine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: NA
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 32 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25 ± 4
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 37/38
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: alfentanil for induction, morphine, postoperative dihydrocodeine
- *Type of surgery*: gynaecological laparoscopy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 5
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 4
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 50/40

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Ahmed 2000 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: alfentanil for induction, morphine, postoperative dihydrocodeine
- *Type of surgery*: gynaecological laparoscopy

Included criteria: 18 years of age and over, undergoing day-case gynaecological laparoscopy

Excluded criteria: history of gastro-oesophageal reflux, taking medications with known antiemetic activity, pregnant or breastfeeding

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg, 0.9% saline • *Time point of administration*: after induction of standardized anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM; 15.3% Ondansetron + cyclizine • *Dose*: ondansetron 4 mg, cyclizine 50 mg • *Time point of administration*: after induction of standardized anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM; 3.3% Placebo • *Dose*: 2 × 0,9% saline • *Time point of administration*: after induction of standardized anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM; 35%
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 0 to 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general note on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** outpatient, single-centre **Author's name:** G. J. Hobbs

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Ahmed 2000 *(Continued)*

Institution: University Department of Anaesthesia and Intensive Care, Queen's Medical Centre

Email: NA

Address: University Department of Anaesthesia and Intensive Care, Queen's Medical Centre, Nottingham NG72UH, UK

Duration of study: NA

Language: English

Study's primary outcome: incidence of vomiting

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were allocated randomly, using a closed envelope technique, in blocks of 50 to three groups in a 2:2:1 ratio"
Allocation concealment (selection bias)	Unclear risk	Quote: "using a closed envelope technique" Judgement comment: not stated: "sequentially numbered and opaque" envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "each treatment was given as two 10 ml i.v. injections. These were prepared by a single investigator who took no part in data collection" Judgement comment: insufficient information on blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all data were recorded by a single research nurse who remained blinded to the treatment groups throughout the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one patient who underwent laparotomy (control group) was withdrawn from the study. Data before discharge from 139 patients were analysed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "all groups were comparable for patient characteristics, pain and analgesic requirement. No patient required the administration of atropine or glycopyrrolate for intra-operative bradycardia" Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Ahn 2002

Study characteristics

Methods	**Study design:** randomized controlled trial

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Ahn 2002 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Scopolamine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 22 • *Received treatment (n)*: 22 • *Analysed (n)*: 22 • *Age (mean ± SD, median (IQR), median (range))*: 42.6 ± 11.2 • *Weight (mean ± SD, median (IQR), median (range))*: 60.1 ± 23.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 4.55/13.64 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane 1.0%) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 16.8 • *Use of perioperative opioids (if yes, which?)*: fentanyl 63.6 µg • *Type of surgery*: conization due to cervical intraepithelial neoplasm Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 22 • *Received treatment (n)*: 22 • *Analysed (n)*: 22 • *Age (mean ± SD, median (IQR), median (range))*: 36.9 ± 8.1 • *Weight (mean ± SD, median (IQR), median (range))*: 54.3 ± 11.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 9.09/13.64 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane 1.0%) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 12.1 • *Use of perioperative opioids (if yes, which?)*: fentanyl 54.8 µg • *Type of surgery*: conization due to cervical intraepithelial neoplasm **Included criteria:** conization due to cervical intraepithelial neoplasm, ASA I and II **Excluded criteria:** pregnancy, lactating patients, glaucoma, gastrointestinal obstruction, ureter obstruction; patients taking antiemetic, anticholinergic, antihistamine drugs **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): unclear; (duration of anaesthesia): yes
Interventions	**Intervention characteristics** Scopolamine • *Dose*: 1.5 mg • *Time point of administration*: 1 day before surgery until 24 hours after surgery

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Ahn 2002 *(Continued)*

- *Route of administration*: transdermal
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Placebo

- *Dose*: identical looking patch
- *Time point of administration*: 1 day before surgery until 24 hours after surgery
- *Route of administration*: transdermal
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours (total side effects))* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** outpatient, single-centre **Author's name:** Hyun Joo Ahn **Institution:** Department of Anesthesiology, Samsung Medical Center. Surgkymkwan University Scholl of Modecine, Seoul, Korea **Email:** mallang@hanmir.com **Address:** (06351) 81 Irwon-Ro Gangnam-gu. Seoul, Korea **Duration of study:** NA **Language:** Korean (translated by Woocheol Sim) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: insufficient information on sequence generation ("randomly divided")

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Ahn 2002 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on sequence generation ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on sequence generation ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): unclear; (duration of anaesthesia): yes

Ahsan 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 41.32 ± 12.9 • *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 9.25 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 29/21/0/0 • *Gender (female in %)*: 86 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: nalbuphine 10mg at induction • *Type of surgery*: laparoscopic cholecystectomy Ondansetron + dexamethasone • *Assessed for eligibility (n)*: -

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Ahsan 2014 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 44.48 ± 14.5
- *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 8.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/26/0/0
- *Gender (female in %)*: 82
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: nalbuphine 10 mg at induction
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, 20 to 70 years of age, laparoscopic cholecystectomy

Excluded criteria: ASA III and IV; preoperative emesis or pregnant or taking sedatives, anxiolytics, antihistamines, and antiemetics or with known history of drug allergy, hypersensitivity to antiemetics, or with ear disease and vertigo or menstruation at the time of surgery (because menstruation can provoke nausea and vomiting, which could affect the outcome of the study) or history of postoperative emesis; history of motion sickness

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (perioperative opioids, duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 28% required metoclopramide 10 mg (nausea lasted longer than 15 minutes or vomiting has occurred) Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 12% required metoclopramide 10 mg (nausea lasted longer than 15 minutes or vomiting has occurred)
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Pakistan **Setting:** single centre, no other information provided **Author's name:** Ahsan Khalid **Institution:** Department of Anesthesiology, Aga Khan University

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Ahsan 2014 *(Continued)*

	Email: khalid.ahsan@aku.edu **Address:** Liaquat National Hospital, Karachi **Language:** English **Duration of study:** 23 April 2009 to 22 August 2009 **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "they were randomly divided into Group A and Group B with sealed envelope technique of 50 patients in each group"
Allocation concealment (selection bias)	Unclear risk	Quote: "with sealed envelope technique of 50 patients in each group" Judgement comment: not mentioned SNOSE
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data.
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (perioperative opioids, duration of anaesthesia, non-smoker): unclear

Akcabay 1997

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: -

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Akcabay 1997 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 47.0 ± 8.19
- *Weight (mean ± SD, median (IQR), median (range))*: 62.41 ± 8.12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 110.4
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction, postoperative analgesia (NA)
- *Type of surgery*: thyroidectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 45.0 ± 10.81
- *Weight (mean ± SD, median (IQR), median (range))*: 65.50 ± 9.03
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.4
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction, postoperative analgesia (NA)
- *Type of surgery*: thyroidectomy

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 49.0 ± 9.75
- *Weight (mean ± SD, median (IQR), median (range))*: 67.34 ± 7.25
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115.6
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction, postoperative analgesia (NA)
- *Type of surgery*: thyroidectomy

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Akcabay 1997 *(Continued)*

	Included criteria: ASA I and II, undergoing elective thyroidectomy due to nodular goitre **Excluded criteria:** history of central or peripheral emetic stimulation and laboratory results (full blood chemistry, renal and liver function tests) out of normal range **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (gender, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: saline • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Control • *Dose*: no treatment • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Mehmet Akcabay **Institution:** Gazi University, Faculty of Medicine, Department of Anastesiology and Reanimation, Ankara, Turkey **Email:** NA **Address:** Gazi Universitesi Tip Fakältesi, Anesteziyoloji ve Ranimasyon, Anabilim Dali, Besevler, 06500 Ankara, Tukiye

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Akcabay 1997 *(Continued)*

	Duration of study: NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly allocated into 3 equal groups" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "neither the patients nor the anaesthesiologists who were responsible for the follow-up of the patients were aware of which patients belonged to which groups" No information on anaesthesiologists who are responsible for anaesthesia
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "neither the patients nor the anaesthesiologists who were responsible for the follow-up of the patients were aware of which patients belonged to which groups"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: "no missing outcome data"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (gender, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Akin 2005

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA

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Akin 2005 *(Continued)*

- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 34.4 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 73.3 ± 12.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 57.14
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 181
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl for induction
- *Type of surgery*: tympanomastoid surgery

Tropisetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 33.2 ± 13.8
- *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 173
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl for induction
- *Type of surgery*: tympanomastoid surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 31.2 ± 12.7
- *Weight (mean ± SD, median (IQR), median (range))*: 73.3 ± 14.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 57.14
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 165
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl for induction
- *Type of surgery*: tympanomastoid surgery

Included criteria: ASA I and II, 18 to 65 years of age, scheduled for elective tympanomastoid surgery

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Akin 2005 *(Continued)*

Excluded criteria: gastrointestinal disorders, intake of antiemetics or centrally acting medication within 24 hours before surgery, menstruation, body weight exceeding optimal weight > 50%, therapy with corticosteroids or immunosuppressives

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Tropisetron • *Dose*: 5 mg • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 11.4% (metoclopramide 10 mg IV) Tropisetron + dexamethasone • *Dose*: tropisetron 5 mg, dexamethasone 5 mg • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8.6% (metoclopramide 10 mg IV) placebo • *Dose*: NaCl • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 40% (metoclopramide 10 mg IV)
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Aynur Akin **Institution:** Erciycs Universitcsi Tip Fakultesi Anesteziyoloji ve Reanimasyon Anabilim Dah, Kayseri **Email:** aaynur@erciyes.edu.tr **Address:** Alpaslan Mah. Kandil Sok. Bezciler Sitesi 3. Blok No:6 K:6 D:11.38030-Melikgazi-Kayseri **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA

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Akin 2005 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: no information on sequence generation provided ("randomized")
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blinded manner")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blinded manner")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Akin 2006

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron (group T) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: 35 • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 42.0 ± 11.6 • *Weight (mean ± SD, median (IQR), median (range))*: 70.9 ± 11.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 80 • *Non-smoker (%)*: NA

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Akin 2006 *(Continued)*

- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 122.0
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction
- *Type of surgery*: thyroidectomy

Placebo (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: 35
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 43.1 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 72.0 ± 13.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 82.86
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.5
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction
- *Type of surgery*: thyroidectomy

Included criteria: NA

Excluded criteria: gastrointestinal problems, had used a central-acting drug or an antiemetic in the previous 24 hours, having menstruationl or history of nausea and vomiting

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Interventions

Intervention characteristics

Tropisetron (group T)

- *Dose*: 5 mg
- *Time point of administration*: immediately after anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV; 22.8%

Placebo (group P)

- *Dose*: saline
- *Time point of administration*: immediately after anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV; 71.4%

Outcomes

Vomiting or retching (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

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Akin 2006 *(Continued)*

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Aynur Akin **Institution:** Erciyes University Medical Faculty, Department of Anesthesiology and Intensive Care, Kayseri, Turkey **Email:** aaynur@erciyes.edu.tr **Address:** Erciyes University Medical Faculty, Department of Anesthesiology and Intensive Care, Alpaslan Mah. Kandilli Sok. Bezciler sitesi 3.blok No. 6/11, 38030 Kayseri, Turkey **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	2 out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Akkaya 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 31.7 ± 9.2 • *Weight (mean ± SD, median (IQR), median (range))*: 62.4 ± 15.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 53 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 168 • *Use of perioperative opioids (if yes, which?)*: 8 mg postoperative PCA morphine consumption • *Type of surgery*: mastoidectomy Granisetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 28.1 ± 7.9 • *Weight (mean ± SD, median (IQR), median (range))*: 63.2 ± 13.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 155 • *Use of perioperative opioids (if yes, which?)*: 3 mg postoperative PCA morphine consumption • *Type of surgery*: mastoidectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 30.3 ± 8.7 • *Weight (mean ± SD, median (IQR), median (range))*: 64.3 ± 10.2

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Akkaya 2001 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 47
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 160
- *Use of perioperative opioids (if yes, which?)*: 13 mg postoperative PCA morphine consumption
- *Type of surgery*: mastoidectomy

Included criteria: ASA I or II, mastoidectomy

Excluded criteria: antiemetics within 24 hours before surgery, history of PONV, reflux, pregnancy, menstruation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Granisetron • *Dose*: 3 mg, saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: chlorpromazine 12.5 mg IM (13%) Granisetron + dexamethasone • *Dose*: granisetron 3 mg + dexamethasone 8 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: chlorpromazine 12.5 mg IM (0%) Placebo • *Dose*: saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: chlorpromazine 12.5 mg IM (38%)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects

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Akkaya 2001 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Taylan Akkaya **Institution:** Ankara Egitim Hastanesi Anesteziyoloji ve Reanimasyon Klinigi **Email:** NA **Address:** NA **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "computer-generated random sequence" (translated)
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "random sequence was generated by an independent investigator" (translation) Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "anaesthestists and nurses injecting the study drugs were blinded" (translated)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "outcome assessors were blinded" (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker): unclear; (perioperative opioids): yes

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Alam 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 57 • *Age (mean ± SD, median (IQR), median (range))*: 42.7 ± 1.24 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 56.14 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 57 • *Age (mean ± SD, median (IQR), median (range))*: 44.1 ± 1.05 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 52.63 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** chronic cholecystitis secondary to gallstones, advised laparoscopic cholecystectomy **Excluded criteria:** head injuries, history of motion sickness, preexisting medical illness that can precipitate vomiting **Pretreatment:** baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, history of motion sickness): no; (history of PONV, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Alam 2016 *(Continued)*

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: at time of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 10 mg • *Time point of administration*: at time of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Saudi Arabia **Setting:** inpatient, single-centre **Author's name:** Umar Farooq Dar **Institution:** Community Family Medicine, Aljouf University College of Medicine, Kingdom of Saudi Arabia **Email:** umardar84@gmail.com **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement

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Alam 2016 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, history of motion sickness): no; (history of PONV, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Alexander 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 54 (16 to 80) • *Weight (mean ± SD, median (IQR), median (range))*: 62.8 (35 to 103) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 62.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 37.5 • *Type of general anaesthesia*: combined general (enflurane with nitrous oxide) and epidural anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 114 • *Use of perioperative opioids (if yes, which?)*: epidural infusion with fentanyl 10 mg/mL in saline and bupivacaine 0.1% over 24 hours • *Type of surgery*: major lower limb orthopaedic surgery (joint replacement or long bone resection) Metoclopramide (group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: 42 • *Analysed (n)*: 42

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Alexander 1997 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 57 (19 to 80)
- *Weight (mean ± SD, median (IQR), median (range))*: 68 (46 to 94)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 57.14
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 45.24
- *Type of general anaesthesia*: combined general (enflurane with nitrous oxide) and epidural anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 121
- *Use of perioperative opioids (if yes, which?)*: epidural infusion with fentanyl 10 mg/mL in saline and bupivacaine 0.1% over 24 hours
- *Type of surgery*: major lower limb orthopaedic surgery (joint replacement or long bone resection)

Ondansetron (group O)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 42
- *Analysed (n)*: 42
- *Age (mean ± SD, median (IQR), median (range))*: 57 (18 to 79)
- *Weight (mean ± SD, median (IQR), median (range))*: 67.6 (38 to 99)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 64.29
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 40.48
- *Type of general anaesthesia*: combined general (enflurane with nitrous oxide) and epidural anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 109
- *Use of perioperative opioids (if yes, which?)*: epidural infusion with fentanyl 10 mg/mL in saline and bupivacaine 0.1% in mL over 24 hours
- *Type of surgery*: major lower limb orthopaedic surgery (joint replacement or long bone resection)

Included criteria: ASA I and II, 16 to 80 years of age, scheduled to undergo major lower limb orthopaedic surgery

Excluded criteria: had taken antiemetic, antidopaminergic, or dopaminergic medication in previous 24 hours; had history of chronic alcohol ingestion or renal failure or sensitivity to study drugs

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: placebo • *Time point of administration*: 90 minutes preoperatively • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg given intramuscularly on request (68%) Metoclopramide (group M) • *Dose*: 10 mg

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Alexander 1997 *(Continued)*

- *Time point of administration*: 90 minutes preoperatively
- *Route of administration*: oral
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg given intramuscularly on request (57%)

Ondansetron (group O)

- *Dose*: 8 mg
- *Time point of administration*: 90 minutes preoperatively
- *Route of administration*: oral
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg given intramuscularly on request (38%)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** inpatient, single-centre **Author's name:** R. Alexander **Institution:** Shackleton Department of Anaesthetics, Southampton General Hospital **Email:** NA **Address:** Southampton General Hospital, Tremona Road, Southampton SO9 4XY, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated using a computer generated table"
Allocation concealment (selection bias)	Unclear risk	Quote: "the study drugs were supplied by the hospital pharmacy in coded dark identical bottles" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	Quote: "the anaesthetists, nurses and patients were unaware as to which group the patients were allocated"

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Alexander 1997 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the recovery room staff, ward nursing staff and the patient were unaware of the identity of the study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "forty-two patients received ondansetron, 42 metoclopramide and 40 placebo. Fourteen patients were removed from the study because they declined further participation in the trial or due to the premature termination of the epidural infusion"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Alghanem 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 13.3 • *Weight (mean ± SD, median (IQR), median (range))*: 76.4 ± 13.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 73.33 • *Non-smoker (%)*: 93.33 • *History of PONV/motion sickness (%)*: 1.67/0 • *Type of general anaesthesia*: TIVA (propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 57.9 • *Use of perioperative opioids (if yes, which?)*: 1.5 mg/kg tramadol at induction • *Type of surgery*: laparoscopic cholecystectomy Dexamethasone (group D) • *Assessed for eligibility (n)*: . • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 45.1 ± 14.1

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Alghanem 2010 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 76.1 ± 12.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 83.33
- *Non-smoker (%)*: 96.67
- *History of PONV/motion sickness (%)*: 8.33/0
- *Type of general anaesthesia*: TIVA (propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 59.9
- *Use of perioperative opioids (if yes, which?)*: 1.5 mg/kg tramadol at induction
- *Type of surgery*: laparoscopic cholecystectomy

Placebo (group P)

- *Assessed for eligibility (n)*: .
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 44.0 ± 14.9
- *Weight (mean ± SD, median (IQR), median (range))*: 76 ± 15.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 88.33
- *Non-smoker (%)*: 96.67
- *History of PONV/motion sickness (%)*: 5/0
- *Type of general anaesthesia*: TIVA (propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 60.3
- *Use of perioperative opioids (if yes, which?)*: 1.5 mg/kg tramadol at induction
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, 18 to 70 years of age, scheduled for elective laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: had received antiemetics or cortisone within 48 hours before surgery; required opioids before and after surgery; pregnant or breastfeeding; BMI > 34 kg/m^2; gastrointestinal, hepatic, renal, mental, or psychiatric illness; history of motion sickness; if postoperatively, VAS persisted at > 4; subsequent 2 mg dose of morphine given

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Ondansetron (group O)

- *Dose*: 4 mg
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 7% (metoclopramide 10 mg)

Dexamethasone (group D)

- *Dose*: 8 mg
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 8% (metoclopramide 10 mg)

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Alghanem 2010 *(Continued)*

	Placebo (group P) • *Dose*: saline • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 12% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Jordan **Setting:** inpatient, single-centre **Author's name:** Subhi M. Alghanem **Institution:** Department of Anesthesia and Intensive Care, Jordan University Hospital, Jordan **Email:** alghanem@ju.edu.jo **Address:** Department of Anesthesia and Intensive Care, Jordan University Hospital, P.O. Box 13046, Amman 11492, Jordan **Duration of study:** November 2007 to March 2008 **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NCT00825071
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "table of randomized numbers" Quote: "patients were randomly assigned to one of three groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "a table of randomized numbers. The anesthetists, surgeons, and nurses managing these patients were blinded to the study drugs. The same anesthetics and techniques"
Blinding of outcome assessment (detection bias)	Low risk	Quote: "the postoperative data collection was performed by an anesthesia resident blinded to the study groups"

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Alghanem 2010 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 196 patients who consented to participate in the study, 180 (60 in each group; 147 females and 33 males) completed the study, and 16 who received morphine for postoperative analgesia were excluded. Data from the 180 study patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00825071 (retrospective registration)
Other bias	Low risk	Quote: "there were no significant statistical differences in demographic data among the groups (Table 1). The patient-related risk factors, Apfel score, and surgically related risk factors (duration of surgery and gas insufflation) for PONV were similar between the groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Alia 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + dexamethasone (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 82 • *Received treatment (n)*: NA • *Analysed (n)*: 82 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: standardized anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 82 • *Received treatment (n)*: NA • *Analysed (n)*: 82

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Alia 2015 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: standardized anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: patients of either sex and age ranging from 20 to 60 years, undergoing laparoscopic cholecystectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (ASA): no; (weight, BMI, age): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron + dexamethasone (group A) • *Dose*: ondansetron 4 mg, dexamethasone 4 mg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (group B) • *Dose*: 4 mg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Pakistan **Setting:** inpatient, single-centre **Author's name:** Umar Farooq Dar **Institution:** Community Medicine, Gujranwala Medical College, Gujranwala **Email:** umardar84@gmail.com **Address:** NA **Duration of study:** 1st February 2015 to 30th September 2015 **Language:** English **Study's primary outcome:** NA

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Alia 2015 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "using lottery method" Judgement comment: insufficient information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (ASA): no; (weight, BMI, age): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Ali Melkkila 1996

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 45.4 ± 15.5 • *Weight (mean ± SD, median (IQR), median (range))*: 73.4 ± 17.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Ali Melkkila 1996 *(Continued)*

- *ASA I/II/III/IV (n)*: 23/6/11/0
- *Gender (female in %)*: 32.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 25/NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 1.58
- *Use of perioperative opioids (if yes, which?)*: induction fentanyl 2 µg/kg, maintenance 1 µg/kg to clinical parameters
- *Type of surgery*: ophthalmic surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 18.1
- *Weight (mean ± SD, median (IQR), median (range))*: 73.2 ± 12.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 19/11/10/0
- *Gender (female in %)*: 42.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 32.5/NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 1.78
- *Use of perioperative opioids (if yes, which?)*: induction fentanyl 2 µg/kg, maintenance 1 µg/kg to clinical parameters
- *Type of surgery*: ophthalmic surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 44.7 ± 14.9
- *Weight (mean ± SD, median (IQR), median (range))*: 70.9 ± 14.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/9/9/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 25/NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 1.82
- *Use of perioperative opioids (if yes, which?)*: induction fentanyl 2 µg/kg, maintenance 1 µg/kg to clinical parameters
- *Type of surgery*: ophthalmic surgery

Included criteria: between 18 and 75 years of age, scheduled for elective ophthalmic surgery under general anaesthesia and studied over a period of 12 months

Excluded criteria: childbearing potential or lactation, taking concomitant medication that could influence gastrointestinal motility or vomiting, coexisting conditions that could interfere with evaluation of

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Ali Melkkila 1996 *(Continued)*

	study drugs, or putting the patient at risk (e.g. congestive heart failure, liver disease, renal failure, hypersensitivity to study drugs, history of drug/alcohol abuse) **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Tropisetron • *Dose*: 0.1 mg/kg • *Time point of administration*: at end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (17.5%) droperidol 2.5 mg IV Metoclopramide • *Dose*: 0.25 mg/kg • *Time point of administration*: at end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (15%) droperidol 2.5 mg IV Placebo • *Dose*: saline • *Time point of administration*: at end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (27.5%) droperidol 2.5 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatient, single-centre **Author's name:** T. Ali-Melkkilä **Institution:** Department of Anaesthesia, Paijat-Hame Central Hospital, Lahti, Finland **Email:** NA **Address:** Department of Anaesthesia, Paijat-Hame Central Hospital, ST-15850 Lahti, Finland **Duration of study:** NA **Language:** English **Study's primary outcome:** the primary endpoints were the number of emetic episodes (nausea or vomiting/retching) during the first 24 hours after surgery

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Ali Melkkila 1996 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly allocated" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "anaesthesia; the investigators and the observers were blinded as to the agent given"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "anaesthesia; the investigators and the observers were blinded as to the agent given"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the three groups were comparable with regard to age, weight, height, gender distribution and ASA physical status. The number of patients who had been anaesthetised previously was higher in the placebo group, but there was no statistically significant difference between the three groups on the occurrence of PONV after previous general anaesthesia" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Alkaissi 2004

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 165 • *Received treatment (n)*: 165

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Alkaissi 2004 *(Continued)*

- *Analysed (n)*: 165
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 4
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 73
- *History of PONV/motion sickness (%)*: 41/43
- *Type of general anaesthesia*: inhalational anaesthesia (iso-/des-/sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 45
- *Use of perioperative opioids (if yes, which?)*: 41% intraoperative alfentanil, 58% intraoperative fentanyl, 3 mg postoperative morphine
- *Type of surgery*: gynaecological surgery, such as abortion, dilatation curettage, conization, hysterectomy, prolapse, or laparoscopic surgery

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 165
- *Received treatment (n)*: NA
- *Analysed (n)*: 165
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23 ± 4
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 78
- *History of PONV/motion sickness (%)*: 42/43
- *Type of general anaesthesia*: inhalational anaesthesia (iso-/des-/sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 35
- *Use of perioperative opioids (if yes, which?)*: 46% intraoperative alfentanil, 52% intraoperative fentanyl, 4 mg postoperative morphine
- *Type of surgery*: gynaecological surgery, such as abortion, dilatation curettage, conization, hysterectomy, prolapse, or laparoscopic surgery

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 165
- *Received treatment (n)*: NA
- *Analysed (n)*: 165
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 15
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25 ± 5
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 81
- *History of PONV/motion sickness (%)*: 43/42
- *Type of general anaesthesia*: inhalational anaesthesia (iso-/des-/sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 40
- *Use of perioperative opioids (if yes, which?)*: 46% intraoperative alfentanil, 54% intraoperative fentanyl, 4 mg postoperative morphine

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Alkaissi 2004 *(Continued)*

- *Type of surgery*: gynaecological surgery, such as abortion, dilatation curettage, conization, hysterectomy, prolapse, or laparoscopic surgery

Included criteria: women undergoing gynaecological surgery, such as abortion, dilatation curettage, conization, hysterectomy, prolapse, or laparoscopic surgery; risk > 30% for postoperative vomiting (PV) according to a score based on gender, age, smoking, history of motion sickness or PONV, and duration of anaesthesia

Excluded criteria: nausea and vomiting during last 24 hours before surgery, had taken antiemetics within 24 hours before surgery or were breastfeeding

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Droperidol • *Dose*: 1.25 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dixyrazine 5 mg IV, droperidol 1.25 mg IV, granisetron 1 mg IV Granisetron • *Dose*: 3 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dixyrazine 5 mg IV, droperidol 1.25 mg IV, granisetron 1 mg IV Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: dixyrazine 5 mg IV, droperidol 1.25 mg IV, granisetron 1 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** financial support was provided by the Health Research Council in the South-East of Sweden (project F2000-222) **Country:** Sweden **Setting:** NA, multi-centre

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Alkaissi 2004 *(Continued)*

Author's name: Aidah Alkaissi

Institution: Departments of Anesthesiology and Intensive Care, University Hospital in Linköping, Sweden

Email: aidah.alkaissi@lio.se

Address: Department of Anesthesiology and Intensive Care, University Hospital in Linköping S-581 85 Linköping, Sweden

Duration of study: May 2000 to January 2001

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the study, the patients were randomised according to a randomisation list, generated by the pharmacy. Block randomization was used for nine patients in each group. Twelve patients were lost to..."
Allocation concealment (selection bias)	Low risk	Judgement comment: central allocation Replacement of 12 participants who were lost to follow-up by sealed envelopes (minority of study population; 2%)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the two groups treated with antiemetic were blinded to all involved in administration and anaesthesia. The control group was not blinded to the anaesthetist but to all other personnel" Judgement comment: high risk of bias for the 2 groups treated with antiemetics vs control Low risk of bias for the droperidol vs granisetron
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "during analysis the treatment groups were concealed and only the labels provided by the pharmacy identified which group the patient belonged to" Quote: "the two groups treated with antiemetic were blinded to all involved in administration and anaesthesia. The control group was not blinded to the anaesthetist but to all other personnel"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "out of the 495 patients were lost to follow-up. Another 12 patients were added at the end of the study. Response rate was 98%"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

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Alon 1982

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Domperidone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: 15 • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, ether) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 72 ± 39 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: NA Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: 15 • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, ether) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 72 ± 39 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: NA **Included criteria:** NA **Excluded criteria:** liver or renal disease, diabetes mellitus **Pretreatment:** baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Alon 1982 *(Continued)*

Interventions	**Intervention characteristics** Domperidone • *Dose*: 0.2 mg/kg • *Time point of administration*: approximately 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Switzerland **Setting:** NA, single-centre **Author's name:** E. Alon **Institution:** Institut für Anaesthesiologie, Universitätsspital, Zürich **Email:** NA **Address:** Institut für Anaesthesiologie, Universitätsspital, CH-8091 Zürich **Duration of study:** NA **Language:** German **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "während die nach randomisierter Liste gewählte Kontrollgruppe prophylaktisch keine antiemetische Medikation erhielt" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Alon 1982 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no statement. Anesthesiologists were not blinded because no placebo treatment in control group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Alon 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 32 (17 to 72) • *Weight (mean ± SD, median (IQR), median (range))*: 62 (41 to 101) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 13/NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 37 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (17 patients), nicomorphine sc as rescue analgesic (NA) • *Type of surgery*: gynaecological surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Alon 1996 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 36 (20 to 62)
- *Weight (mean ± SD, median (IQR), median (range))*: 63 (42 to 120)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 20/NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 45
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (18 patients), nicomorphine sc as rescue analgesic (NA)
- *Type of surgery*: gynaecological surgery

Included criteria: ASA I and II, 17 to 72 years of age, scheduled to undergo general anaesthesia for gynaecological surgery

Excluded criteria: clinical or laboratory evidence of severe renal, haematologic, or hepatic abnormalities, metabolic disorders accompanied by increased incidence of nausea and vomiting such as diabetes mellitus; history of drug abuse; previous allergic reactions to serotonin antagonists; any antiemetic therapy within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Tropisetron • *Dose*: 5 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (Itinerol B6, containing a combination of 50 mg meclozine, 50 mg piridoxine, 20 mg caffeine) Placebo • *Dose*: matching placebo • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (Itinerol B6, containing a combination of 50 mg meclozine, 50 mg piridoxine, 20 mg caffeine)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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Alon 1996 *(Continued)*

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Switzerland **Setting:** NA, single-centre **Author's name:** Eli Alon **Institution:** Departments of Anesthesiology and Gynecology, Zurich University Hospital, Zurich, and Sandoz-Wander Pharma Ltd., Berne, Switzerland **Email:** NA **Address:** Department of Anesthesiology, Zurich University Hospital, Raemistrasse 100, 8091 Zurich Switzerland **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind manner" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an investigator, a physician blind to the study group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "0.05 was considered significant. Results of the 84 patients in the study, four (two per group) had to be excluded from efficacy analysis. One woman erroneously received metoclopramide during induction of general anesthesia after the study medication; one woman was excluded because of postoperative

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Alon 1996 *(Continued)*

		communication problems. In one patient the medication vial was accidentally broken, and the case report form of one patient was lost. Among the 80 analyzable patients..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "and 40 the matching placebo. The two groups were similar with respect to demographic variables-age, weight and height, history of previous PONV-as well as duration of study medication injection, duration of operation, duration of anesthesia, total anesthetics, additional analgesics during and after surgery, and the type of surgical procedures (Table 1). The IV injection of tropisetron" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Alonso Damian 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Aprepitant (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 37.13 ± 11.84 • *Weight (mean ± SD, median (IQR), median (range))*: 70.6 ± 7.83 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 19/11/0/0 • *Gender (female in %)*: 70 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 101.93 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl • *Type of surgery*: open cholecystectomy Ondansetron (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 37.93 ± 9.53

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Alonso Damian 2012 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 71.7 ± 13.29
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 15/15/0/0
- *Gender (female in %)*: 90
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 109
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: open cholecystectomy

Included criteria: ASA I or II, older than 18 years of age, weighing more than 40 kg and less than 100 kg, undergoing open cholecystectomy on a scheduled basis under general anaesthesia, with surgery lasting longer than 30 minutes and anaesthesia longer than 40 minutes

Excluded criteria: surgical techniques other than open; pregnant or lactating; regional or combined anaesthetic technique; ASA III or higher; emergency department patients; full stomach; episode of nausea, vomiting, or receiving antiemetics in the 24 hours before the surgical event; use of drugs capable of inducing the CYP3A4 isoenzyme; known hypersensitivity to aprepitant or ondansetron; alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) values 2.5 times above normal; total bilirubin values 1.5 times higher than normal; serum creatinine values greater than 1 above normal; transoperative bleeding > 500 mL, use of drugs different from those established for induction and maintenance of anaesthesia; refusal to participate in the study; discharge of patient to intensive care unit or to any other specialized care unit; use of opioid antagonists or benzodiazepines; presence of postoperative mechanical ventilatory support; death

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear; (gender = 20% more females in the ondansetron group): yes

Interventions	**Intervention characteristics** Aprepitant (group A) • *Dose*: 80 mg • *Time point of administration*: 3 hours before anaesthetic induction • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (group B) • *Dose*: 4 mg • *Time point of administration*: 20 minutes before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*QT prolongation (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Mexico **Setting:** inpatient, single-centre

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Alonso Damian 2012 *(Continued)*

Author's name: Edmundo Román Alonso-Damián

Institution: Department of Anesthesiology of the General Hospital of Ticomán of the Secretary of Health of the Federal District

Email: dextroerad@hotmail.com

Address: Cerrada de José Loreto Fabela Núm. 6 BIS,Colonia San Juan de Aragón,Delegación Gustavo A. Madero, Distrito Federal, 07950

Duration of study: March to June 2011

Language: Spanish (Google Translator)

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "patients were randomly assigned in 2 groups" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: blinding of personnel and participants not possible because of different ways and times of administration without sham treatment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear; (gender = 20% more females in the ondansetron group): yes

Altorjay 2011

Study characteristics

Methods	**Study design:** randomized controlled trial

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Altorjay 2011 *(Continued)*

Study grouping: 2 groups, monoprophylaxis and combination prophylaxis

Participants

Baseline characteristics

Ondansetron (cohort A)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 242
- *Received treatment (n)*: NA
- *Analysed (n)*: 229
- *Age (mean ± SD, median (IQR), median (range))*: 44.8 ± 12.44
- *Weight (mean ± SD, median (IQR), median (range))*: 70.6 ± 17.05
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 94/145/2/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 100
- *Type of general anaesthesia*: balanced general anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 92.1
- *Use of perioperative opioids (if yes, which?)*: yes
- *Type of surgery*: hysterectomy, cholecystectomy, breast operation, thyroid operation, bilateral salpingo-oophorectomy

Ondansetron + casopitant (cohort B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 242
- *Received treatment (n)*: NA
- *Analysed (n)*: 227
- *Age (mean ± SD, median (IQR), median (range))*: 44.4 ± 12.19
- *Weight (mean ± SD, median (IQR), median (range))*: 72.3 ± 17.55
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 87/152/1/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 100
- *Type of general anaesthesia*: balanced general anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 87.7
- *Use of perioperative opioids (if yes, which?)*: yes
- *Type of surgery*: hysterectomy, cholecystectomy, breast operation, thyroid operation, bilateral salpingo-oophorectomy

Included criteria: 18 years of age or older; ASA I and II; 4 Apfel risk factors for PONV (female sex, history of PONV and/or motion sickness, non-smoker status, and anticipated to receive opioids postoperatively); scheduled to undergo one of the following surgical procedures: breast surgery, orthopaedic shoulder surgery, or thyroid surgery; laparoscopic or laparotomy procedures for cholecystectomy, hysterectomy, or other gynaecological surgery; anticipated to involve general anaesthesia of at least 1 hour; anaesthetic regimens not specified but investigators required to adhere to a balanced general anaesthetic regimen (propofol was permitted for induction of anaesthesia, TIVA was not allowed in this study)

Excluded criteria: anticipated to require a nasogastric or oral gastric tube with intermittent or continuous suctioning postoperatively; had received medication with potential antiemetic activity in the 24-

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Altorjay 2011 *(Continued)*

	hour period before surgery; scheduled to receive antiemetics not included in the study dosing scheme during the evaluation period **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Ondansetron (cohort A) • *Dose*: 4 mg • *Time point of administration*: placebo 60 minutes before induction of anaesthesia, ondansetron immediately before induction of anaesthesia • *Route of administration*: placebo oral, ondansetron IV • *Rescue antiemetics (if yes, which?)*: 31.0% (NA, at physician discretion) Ondansetron + casopitant (cohort B) • *Dose*: casopitant 50 mg, ondansetron 4 mg • *Time point of administration*: casopitant 60 minutes before induction of anaesthesia, ondansetron immediately before induction of anaesthesia • *Route of administration*: casopitant oral, ondansetron IV • *Rescue antiemetics (if yes, which?)*: 26.0% (NA, at physician discretion)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 48 hours)* • Outcome type: dichotomous outcome *Mortality (0 to 48 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** funding for this study was provided by GlaxoSmithKline, Sponsor's Protocol Code Number: NKT102553 **Country:** international **Setting:** multi-centre (43) **Author's name:** Joseph Pergolizzi Jr **Institution:** Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, Maryland, and Department of Anesthesiology and Pain Medicine, Georgetown University School of Medicine, Washington, DC, USA

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Altorjay 2011 *(Continued)*

Email: jpjmd@msn.com

Address: Department of Medicine, The Johns Hopkins University, 1830 E Monument St, Ninth Fl, Baltimore, MD 21205

Duration of study: 20 March to 31 August 2006

Language: English

Study's primary outcome: proportion of patients who achieved a complete response, defined as no vomiting, retching, or rescue therapy

Trial registry number: NCT00326248, EUCTR2005-005856-42

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized to 1 of 2 treatment arms" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "in total, 456 patients (94.2%) completed the study: 229 (94.6%) in cohort A and 227 (93.8%) in cohort B. The reasons for the premature withdrawal of the 28 patients were as follows: 7 were lost to follow-up (3 [1.3%] in cohort A and 4 [1.8%] in cohort B), 3 had protocol violations (2 [0.9%] in cohort A and 1 [0.4%] in cohort B), 5 decided to withdraw (1 [0.4%] in cohort A and 4 [1.8%] in cohort B), and 13 withdrew because of other reasons (7 [3.1%] in cohort A and 6 [2.6%] in cohort B), including cancelled surgery (4 in cohort A and 3 in cohort B), closed to recruitment (1 in each group), and treatment failure (1 in cohort A)"
Selective reporting (reporting bias)	Low risk	Judgement comment: NCT00326248 (retrospective registration), EUCTR2005-005856-42 (prospective registration). The prospectively registered primary outcome (complete response) was reported in the prespecified way in the final study report
Other bias	Low risk	Quote: "demographic characteristics were well balanced among the treatment groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

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Altunkaya 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 41.05 ± 8.6 • *Weight (mean ± SD, median (IQR), median (range))*: 69.5 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: Inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 195.6 • *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg, postoperative meperidine 1 mg/kg IM for rescue pain • *Type of surgery*: hemi-thyroidectomy or total thyroidectomy Placebo (group S) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 45.5 ± 6.1 • *Weight (mean ± SD, median (IQR), median (range))*: 72.8 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 55 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 193.8 • *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg, postoperative meperidine 1 mg/kg IM for rescue pain • *Type of surgery*: hemi-thyroidectomy or total thyroidectomy **Included criteria:** ASA I or II, 18 to 60 years of age, elective hemi-thyroidectomy or total thyroidectomy **Excluded criteria:** intrathoracic goiter, gastrointestinal disease, travel sickness, taking antiemetics 48 hours before surgery

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Altunkaya 2003 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear
Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 8 mg • *Time point of administration*: 30 seconds before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10 mg metoclopramide IV, second-line ondansetron 8 mg Placebo (group S) • *Dose*: saline 2 mL • *Time point of administration*: 30 seconds before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10 mg metoclopramide IV, second-line ondansetron 8 mg
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Hanife Altunkaya **Institution:** NA **Email:** haltunkaya@hotmail.com **Address:** Fatih Sitesi Ev.Ko Konutlan F:66 No:8, Kozlu, Zonguldak, Turkey **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "patients were randomly divided" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Low risk	Judgement comment: quote (translated): "the study drugs were numbered and prepared by an independent investigator"

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Altunkaya 2003 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote (translated): "nausea, vomiting, and postoperative pain were reported by an independent staff member during the 48 h postoperative period"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

Amer 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Metoclopramide (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 32 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 50/0/0/0 • *Gender (female in %)*: 76 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide + dexamethasone (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 4.5 • *Weight (mean ± SD, median (IQR), median (range))*: NA

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Amer 2012 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 50/0/0/0
- *Gender (female in %)*: 64
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: 25 to 40 years of age, ASA physical status I, scheduled for laparoscopic cholecystectomy

Excluded criteria: received antiemetic or steroid; history of allergy to metoclopramide or dexamethasone

Pretreatment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide (group A) • *Dose*: 10 mg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide + dexamethasone (group B) • *Dose*: metoclopramide 5 mg, dexamethasone 4 mg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Pakistan **Setting:** inpatient, single-centre **Author's name:** Muhammad Amer **Institution:** Department of Anaesthesia, Quaid-e-Azam Medical College, B. V. Hospital, Bahawalpur **Email:** amir_anas@hotmail.com **Address:** NA **Duration of study:** May 2010 to May 2011 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA

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Amer 2012 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was done by envelope draw method"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not stated: "sequentially numbered, opaque and sealed" envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the patients were divided randomly into two groups to receive metoclopramide 10mg alone or dexamethasone 4mg plus metoclopramide 5 mg in a double blind fashion from coded syringes of 3 ml IV" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were visited 1, 2, 4, 6, 12, 18 and 24 hours after operation by one of the investigators blinded for the type of intervention for data collection"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "0.05 regarded as significant. RESULTS: there were no significant differences between the two groups with respect to age and gender distribution. (Table 1) In the first 6 hours" Judgement comment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Ansari 2010

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 65 • *Age (mean ± SD, median (IQR), median (range))*: 39.18 ± 4.7 (31 to 42) • *Weight (mean ± SD, median (IQR), median (range))*: 52.6 ± 4.3 (49 to 57)

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Ansari 2010 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 70.1
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Ramosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 65
- *Age (mean ± SD, median (IQR), median (range))*: 39.63 ± 4.74 (32 to 43)
- *Weight (mean ± SD, median (IQR), median (range))*: 53.1 ± 2.7 (51 to 60)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 68.8
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: women between 30 and 50 years of age (ASA I and II) undergoing elective standard 4-port laparoscopic cholecystectomy at J.N. Medical College Hospital, A.M.U., Aligarh

Excluded criteria: history of motion sickness, gastrointestinal disease; receiving antiemetics within 24 hours before surgery; receiving long-term steroid therapy; diabetes mellitus or cardiovascular disease

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: before shifting of patient from operating room to postoperative unit • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 41.5 (metoclopramide 10 mg IV) Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: before shifting of patient from operating room to postoperative unit • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 27.7 (metoclopramide 10 mg IV)
Outcomes	*Vomiting (0 to 24 hours)*

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Ansari 2010 *(Continued)*

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 48 hours)

- Outcome type: dichotomous outcome

Headache (0 to 48 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 48 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Maulana M. Ansari **Institution:** Departments of Surgery and Anaesthesiology, J. N. Medical college, Aligarh Muslim University, Uttar Pradesh, India **Email:** mma_amu@yahoo.com **Address:** B-27, Silver Oak Avenue, Street No. 4, Dhorra Mafi, Aligarh - 202 002, UP, India **Duration of study:** January 2010 to March 2011 **Language:** English **Study's primary outcome:** complete response **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated randomization list"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "medications were prepared by a blinded paramedic not involved in the study in identical 5-ml syringes and were administered according to the randomization list"
Blinding of outcome assessment (detection bias)	Low risk	Quote: "by an independent observer (usually a Resident Officer) who was blinded to the study"

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Ansari 2010 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the control group (Ondansetron) and the study group (Ramosetron) were comparable (P >0.05) with respect to the patients' demographic data and the durations of anesthesia, CO 2 insufflation, and surgery [Table 1]" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Aouad 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Haloperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 32 • *Received treatment (n)*: 29 • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 38.4 ± 9.9 • *Weight (mean ± SD, median (IQR), median (range))*: 70.9 ± 10.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 68.97 • *History of PONV/motion sickness (%)*: 24.13/20.69 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 86.1 • *Use of perioperative opioids (if yes, which?)*: 154.3 µg intraoperative fentanyl, 20 mg postoperative meperidine • *Type of surgery*: laparoscopy, hysteroscopy, open myomectomy/abdominal hysterectomy, vaginal hysterectomy Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30

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Aouad 2007 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 37.9 ± 8.8
- *Weight (mean ± SD, median (IQR), median (range))*: 65.3 ± 10.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 70.00
- *History of PONV/motion sickness (%)*: 26.67/26.67
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 98.4
- *Use of perioperative opioids (if yes, which?)*: 163.3 µg intraoperative fentanyl, 31.6 mg postoperative meperidine
- *Type of surgery*: laparoscopy, hysteroscopy, open myomectomy/abdominal hysterectomy, vaginal hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 31
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 37.9 ± 11.2
- *Weight (mean ± SD, median (IQR), median (range))*: 65.8 ± 12.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 76.67
- *History of PONV/motion sickness (%)*: 6.67/10
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 84.6
- *Use of perioperative opioids (if yes, which?)*: 137.1 µg intraoperative fentanyl, 28.6 mg postoperative meperidine
- *Type of surgery*: laparoscopy, hysteroscopy, open myomectomy/abdominal hysterectomy, vaginal hysterectomy

Included criteria: ASA I and II, women 23 to 64 years of age, scheduled for gynaecological surgery under general anaesthesia

Excluded criteria: pregnancy, breastfeeding, psychiatric illness, previous intolerance to ondansetron or haloperidol, preexisting nausea or intake of antiemetics 24 hours before the study, morbid obesity, major organ disease

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness): no; (perioperative opioids, history of PONV > 20%): yes

Interventions	**Intervention characteristics**

Haloperidol

- *Dose*: 1 mg
- *Time point of administration*: haloperidol following induction of anaesthesia, saline 10 minutes before end of surgery
- *Route of administration*: I.
- *Rescue antiemetics (if yes, which?)*: 22.2% (promethazine 12.5 mg)

Ondansetron

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Aouad 2007 *(Continued)*

- *Dose*: 4 mg
- *Time point of administration*: saline following induction of anaesthesia, ondansetron 10 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 44.4% (promethazine 12.5 mg)

Placebo

- *Dose*: saline
- *Time point of administration*: following induction of anaesthesia and 10 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 40.7% (promethazine 12.5 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Arrhythmia (0 to 2 hours (dysrhythmias))* • Outcome type: dichotomous outcome *QT prolongation (0 to 2 hours (> 470 ms))* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 2 hours)* • Outcome type: dichotomous outcome *Headache (0 to 2 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, PACU)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this project was funded by the Department **Country:** Lebanon **Setting:** inpatient and outpatient, NA **Author's name:** Marie T. Aouad **Institution:** American University of Beirut, Department of Anesthesiology, Medical Center, Beirut, Lebanon **Email:** mm01@aub.edu.lb

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Aouad 2007 *(Continued)*

Address: Department of Anesthesiology, American University of Beirut Medical Center, P.O. Box 11 0236, Beirut, Lebanon

Duration of study: NA

Language: English

Study's primary outcome: complete absence of nausea and vomiting

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer generated table of random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study drugs were mixed with 0.9% saline to a final volume of 5 ml by personnel not involved in the study and were administered in a double-blind fashion"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "in the postanaesthesia care unit, patients were observed by the same nurse who was blinded to study group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of 93 patients enrolled, four were excluded (3 loss to follow-up, 1 protocol violation). Therefore, data from 89 patients were analyzed in the postanaesthesia care unit: 29 haloperidol, 30 ondansetron and 30 controls (see Fig. 1). In addition, two patients in the haloperidol group and three patients each in the ondansetron and the placebo group were lost to longterm follow-up. Thus, 27 patients in each group were analyzed for 24 h following discharge from the postanaesthesia care unit. There were no differences among"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there were no differences among the groups with respect to patients' characteristics, type of surgery, duration of anaesthesia, emergence time, average fentanyl consumption and average Lactated Ringer received (Table 1). No difference among the groups was noted with respect to risk factors predisposing to PONV (Table 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness): no; (perioperative opioids, history of PONV > 20%): yes

Apfel 2004-1

Study characteristics

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Apfel 2004-1 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 8 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 174 • *Age (mean ± SD, median (IQR), median (range))*: 47 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 81.5 • *Non-smoker (%)*: 81.2 • *History of PONV/motion sickness (%)*: 54.5 • *Type of general anaesthesia*: inhalational anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific) Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 166 • *Age (mean ± SD, median (IQR), median (range))*: 47 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 81.5 • *Non-smoker (%)*: 81.2 • *History of PONV/motion sickness (%)*: 54.5 • *Type of general anaesthesia*: inhalational anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific) Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 172

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Apfel 2004-1 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 174
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Dexamethasone + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 176
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA

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Apfel 2004-1 *(Continued)*

- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Ondansetron + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 178
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Ondansetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 171
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Ondansetron + dexamethasone + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 169
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA

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Apfel 2004-1 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Included criteria: elective surgery during general anaesthesia that was expected to last at least 1 hour, risk of postoperative nausea and vomiting that exceeded 40% (presence of at least 2 of the following risk factors: female sex, non-smoker status, previous history of postoperative nausea and vomiting or motion sickness, anticipated use of postoperative opioids)

Excluded criteria: contraindication to any of the study drugs, had taken emetogenic or antiemetic drugs within the 24 hours before surgery, expected to require postoperative mechanical ventilation, pregnant or lactating

Pretreatment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Control

- *Dose*: no treatment
- *Time point of administration*: -
- *Route of administration*: -
- *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: within 20 minutes after start of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added

Dexamethasone

- *Dose*: 4 mg
- *Time point of administration*: within 20 minutes after start of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: during the last 20 minutes of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added

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Apfel 2004-1 *(Continued)*

	Dexamethasone + droperidol • *Dose*: dexamethasone 4 mg, droperidol 1.25 mg • *Time point of administration*: both within 20 minutes after start of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added Ondansetron + droperidol • *Dose*: ondansetron 4 mg, droperidol 1.25 mg • *Time point of administration*: droperidol within 20 minutes after start of anaesthesia, ondansetron during the last 20 minutes of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 4 mg • *Time point of administration*: dexamethasone within 20 minutes after start of anaesthesia, ondansetron during the last 20 minutes of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added Ondansetron + dexamethasone + droperidol • *Dose*: ondansetron 4 mg, dexamethasone 4 mg, droperidol 1.25 mg • *Time point of administration*: droperidol and dexamethasone within 20 minutes after start of anaesthesia, ondansetron during the last 20 minutes of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this study was supported by the Department of Anaesthesiology, University of Würzburg, Grant 1518 TG 72, Josef-Schneider Str. 2, D-97080 Würzburg, Germany; Helsinki University Hospital, HUS-EVO Grants TYH0324, TKK 2120, and TKK 3120; University of Helsinki, Helsinki, Finland; Biomedicum Helsinki Foundation, Haartmaninkatu 8, FIN-00029 HUCH, Finland; Finnish Medical Foundation, Kalevankatu 11 A, FIN-00100, Helsinki, Finland; Maud Kuistila Foundation, Manner-heimintie 12 B, FIN-00101, Helsinki, Finland; Paulo Foundation, Tiistinniityntie 4, FIN-02231, Espoo, Finland; Research Foundation of Orion Corporation, Orionintie 1, FIN-02200, Espoo, Finland; NIH Grant GM 061655 (Bethesda, MD, USA); Gheens Foundation (Louisville, KY, USA); Joseph Drown Foundation (Los Angeles, CA, USA); Commonwealth of Kentucky Research Challenge Trust Fund (Louisville, KY, USA)

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Apfel 2004-1 *(Continued)*

Country: Germany, Finland, England, Turkey, Slovakia, Spain, UK, Austria

Setting: multi-centre (28)

Author's name: Christian C. Apfel

Institution: Julius-Maximilians Universität, Würzburg, Germany

Email: apfel@ponv.org

Address: Outcomes Research Institute, 501 East Broadway, Suite 210, Louisville, KY 40202, USA

Duration of study: 2 February 2000 to 30 July 2002

Language: English, German

Study's primary outcome: incidence of any nausea, vomiting, or both during first 24 hours after surgery.

Trial registry number: Controlled Clinical Trials 24 (2003), 736-751

Notes	Factorial trial design. Used as 2 sub-studies (propofol, inhalational anaesthesia), each with 8 groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "therefore, permuted blocks of 96 (2 3 ¬3¬2 2) patients were generated. Each center received four blocks with a unique computerized randomization"
Allocation concealment (selection bias)	Low risk	Quote: "stored in sequentially numbered, sealed, opaque envelopes" Quote: "the envelopes were opened after consent was obtained, just before the induction of general anesthesia"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the anesthesiologists responsible for intraoperative management were not blinded to the treatment, but they were not involved in the postoperative assessment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "after the 2nd and 24th postoperative hours, trained investigators who were fully blinded to the intraoperative management and random treatment assignments recorded the number of emetic episodes and the time each one occurred"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "outcome data were incomplete for 38 patients, leaving 5161 patients (99 percent) for whom complete outcome data were available. One center each did not randomize with respect to carrier gas (424 patients), use of remifentanil or fentanyl (191 patients), or both of these factors (181 patients). Three centers randomly assigned a total of 280 patients to 80 percent oxygen in nitrogen (as a third alternative to 30 percent oxygen in nitrogen or in nitrous oxide). A total of 4123 patients were thus randomly assigned with respect to all six primary factors, and outcome data were incomplete in 37 of them (1 patient with incomplete data was among those not randomly assigned with respect to carrier gas), leaving 4086 patients (99 percent) for whom complete outcome data could be analyzed (Fig. 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: study protocol published in Controlled Clinical Trials 24 (2003) 736-751 (retrospective registration)

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Apfel 2004-1 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Apfel 2004-2

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 8 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 345 • *Age (mean ± SD, median (IQR), median [range])*: 47 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 81.5 • *Non-smoker (%)*: 81.2 • *History of PONV/motion sickness (%)*: 54.5 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific) Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 335 • *Age (mean ± SD, median (IQR), median (range))*: 47 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 81.5 • *Non-smoker (%)*: 81.2 • *History of PONV/motion sickness (%)*: 54.5 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA

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Apfel 2004-2 *(Continued)*

- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 340
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 338
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Dexamethasone + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 341
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA

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Apfel 2004-2 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Ondansetron + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 330
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Ondansetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 33
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Ondansetron + dexamethasone + droperidol

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Apfel 2004-2 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 341
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 81.5
- *Non-smoker (%)*: 81.2
- *History of PONV/motion sickness (%)*: 54.5
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery, hysterectomy, head and neck surgery, cholecystectomy, thyroid surgery, hernia repair, breast surgery, hip replacement, arm or hand surgery, knee arthroscopy, others (overall information on type of surgery, not group specific)

Included criteria: elective surgery during general anaesthesia that was expected to last at least 1 hour, risk of postoperative nausea and vomiting that exceeded 40% (presence of at least 2 of the following risk factors: female sex, non-smoker status, previous history of postoperative nausea and vomiting or motion sickness, anticipated use of postoperative opioids)

Excluded criteria: contraindication to any of the study drugs, those who had taken emetogenic or antiemetic drugs within the 24 hours before surgery, those who were expected to require postoperative mechanical ventilation, those who were pregnant or lactating

Pretreatment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Control

- *Dose*: no treatment
- *Time point of administration*: -
- *Route of administration*: -
- *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: within 20 minutes after start of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added

Dexamethasone

- *Dose*: 4 mg
- *Time point of administration*: within 20 minutes after start of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added

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Apfel 2004-2 *(Continued)*

	Ondansetron • *Dose*: 4 mg • *Time point of administration*: during the last 20 minutes of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added Dexamethasone + droperidol • *Dose*: dexamethasone 4 mg, droperidol 1.25 mg • *Time point of administration*: both within 20 minutes after start of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added Ondansetron + droperidol • *Dose*: ondansetron 4 mg, droperidol 1.25 mg • *Time point of administration*: droperidol within 20 minutes after start of anaesthesia, ondansetron during the last 20 minutes of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 4 mg • *Time point of administration*: dexamethasone within 20 minutes after start of anaesthesia, ondansetron during the last 20 minutes of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added Ondansetron + dexamethasone + droperidol • *Dose*: ondansetron 4 mg, dexamethasone 4 mg, droperidol 1.25 mg • *Time point of administration*: droperidol and dexamethasone within 20 minutes after start of anaesthesia, ondansetron during the last 20 minutes of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4 mg ondansetron; if symptoms persisted, 4 mg of dexamethasone and 1.25 mg of droperidol were added
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this study was supported by the Department of Anaesthesiology, University of Würzburg, Grant 1518 TG 72, Josef-Schneider Str. 2, D-97080, Würzburg, Germany; Helsinki University

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Apfel 2004-2 *(Continued)*

Hospital, HUS-EVO Grants TYH0324, TKK 2120, and TKK 3120, University of Helsinki, Helsinki, Finland; Biomedicum Helsinki Foundation, Haartmaninkatu 8, FIN-00029, HUCH, Finland; Finnish Medical Foundation, Kalevankatu 11 A, FIN-00100, Helsinki, Finland; Maud Kuistila Foundation, Manner-heimintie 12 B, FIN-00101, Helsinki, Finland; Paulo Foundation, Tiistinniityntie 4, FIN-02231, Espoo, Finland; Research Foundation of Orion Corporation, Orionintie 1, FIN-02200, Espoo, Finland; NIH Grant GM 061655 (Bethesda, MD, USA), Gheens Foundation (Louisville, KY, USA), Joseph Drown Foundation (Los Angeles, CA, USA), Commonwealth of Kentucky Research Challenge Trust Fund (Louisville, KY, USA)

Country: Germany, Finland, England, Turkey, Slovakia, Spain, UK, Austria

Setting: multi-centre (28)

Author's name: Christian C. Apfel

Institution: Julius-Maximilians Universität, Würzburg, Germany

Email: apfel@ponv.org

Address: Outcomes Research Institute, 501 East Broadway, Suite 210, Louisville, KY 40202, USA

Duration of study: 2 February 2000 to 30 July 2002

Language: English, German

Study's primary outcome: incidence of any nausea, vomiting, or both during first 24 hours after surgery

Trial registry number: Controlled Clinical Trials 24 (2003), 736-751

Notes	Factorial trial design. Used as 2 sub-studies (propofol, inhalational anaesthesia), each with 8 groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "therefore, permuted blocks of 96 (2 3 ¬3¬2 2) patients were generated. Each center received four blocks with a unique computerized randomization"
Allocation concealment (selection bias)	Low risk	Quote: "stored in sequentially numbered, sealed, opaque envelopes" Quote: "the envelopes were opened after consent was obtained, just before the induction of general anesthesia"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the anesthesiologists responsible for intraoperative management were not blinded to the treatment, but they were not involved in the postoperative assessment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "after the 2nd and 24th postoperative hours, trained investigators who were fully blinded to the intraoperative management and random treatment assignments recorded the number of emetic episodes and the time each one occurred"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "outcome data were incomplete for 38 patients, leaving 5161 patients (99 percent) for whom complete outcome data were available. One center each did not randomize with respect to carrier gas (424 patients), use of remifentanil or fentanyl (191 patients), or both of these factors (181 patients). Three centers randomly assigned a total of 280 patients to 80 percent oxygen in nitrogen (as a third alternative to 30 percent oxygen in nitrogen or in nitrous oxide). A total of 4123 patients were thus randomly assigned with respect to all six primary factors, and outcome data were incomplete in 37 of them (1 pa-

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Apfel 2004-2 *(Continued)*

		tient with incomplete data was among those not randomly assigned with respect to carrier gas), leaving 4086 patients (99 percent) for whom complete outcome data could be analyzed (Fig. 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: study protocol published in Controlled Clinical Trials 24 (2003) 736-751 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Areeruk 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 43.40 ± 9.28 • *Weight (mean ± SD, median (IQR), median (range))*: 55.65 ± 10.15 • *BMI (mean ± SD, median (IQR), median (range))*: 22.99 ± 4.23 • *ASA I/II/III/IV (n)*: 11/14/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 142.20 • *Use of perioperative opioids (if yes, which?)*: fentanyl 0.5 µg/kg for induction, intraoperative morphine 0.1 mg/kg, postoperatively morphine via PCA at 24 hours (15.88mg) • *Type of surgery*: gynaecological laparotomy surgery Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 41.67 ± 10.05 • *Weight (mean ± SD, median (IQR), median (range))*: 56.49 ± 8.84 • *BMI (mean ± SD, median (IQR), median (range))*: 23.50 ± 3.47 • *ASA I/II/III/IV (n)*: 12/12/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Areeruk 2016 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.83
- *Use of perioperative opioids (if yes, which?)*: fentanyl 0.5 µg/kg for induction, intraoperative morphine 0.1 mg/kg, postoperative morphine via PCA at 24 hours (24.25 mg)
- *Type of surgery*: gynaecological laparotomy surgery

Included criteria: ASA I or II, 18 to 65 years of age, undergoing elective gynaecological laparotomy surgery with Pfannenstiel incision under general anaesthesia consented to participate in the study

Excluded criteria: patients with diabetic mellitus, treatment with steroids, obesity, use of opioid or analgesic drug within 1 month before the study, history of alcohol or drug abuse, pregnancy, undergoing surgical staging surgery, history of chronic pain, history of peptic ulcer or gastritis, those who refused the study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids, duration of anaesthesia -> significant P values): yes

Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 8 mg • *Time point of administration*: after intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo (group P) • *Dose*: saline • *Time point of administration*: after intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Postoperative wound infection (0 to 7 days)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Thailand **Setting:** inpatient, single-centre **Author's name:** Pornpatra Areeruk **Institution:** Department of Anesthesiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand **Email:** pornpatra.are@mahidol.ac.th **Address:** Department of Anesthesiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand **Duration of study:** NA **Language:** English **Study's primary outcome:** total morphine consumption at six hours and 24 hours postoperatively **Trial registry number:** TCTR20151116001

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Areeruk 2016 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "based on computer generated random number list (nQuery program)"
Allocation concealment (selection bias)	Unclear risk	Quote: "the study solution was prepared by a nurse not involved in the perioperative and postoperative care of the patient three hours before surgery. Then it was given to the patient in a sealed envelope, which was handed over to the anesthesiologist who was not involved in the study" Judgement comment: not mentioned: opaque, sequentially numbered envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, anesthesiologists, and the follow-up team were blinded to the administered drugs"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all patients, anesthesiologists, and the follow-up team were blinded to the administered drugs"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "fifty-two patients undergoing gynecological laparotomy surgery were recruited. Three patients were excluded due to receiving succinylcholine for induction, operative time more than three hours, and having paracoxib for pain relief in the postanesthesia care unit"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: TCTR20151116001 (retrospective registration)
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids, duration of anaesthesia -> significant P values): yes

Argiriadou 2002

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 29 • *Received treatment (n)*: 29 • *Analysed (n)*: 29

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Argiriadou 2002 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 43.9 ± 13.6
- *Weight (mean ± SD, median (IQR), median (range))*: 71.5 ± 14.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 21/8/0/0
- *Gender (female in %)*: 79.31
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 67.4
- *Use of perioperative opioids (if yes, which?)*: 3 to 5 µg/kg fentanyl at induction, dextropropoxyphene or meperidine as rescue analgesic
- *Type of surgery*: laparoscopic cholecystectomy

Tropisetron (group B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 31
- *Received treatment (n)*: 31
- *Analysed (n)*: 31
- *Age (mean ± SD, median (IQR), median (range))*: 47.9 ± 16.7
- *Weight (mean ± SD, median (IQR), median (range))*: 73.4 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 19/12/0/0
- *Gender (female in %)*: 74.19
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 75
- *Use of perioperative opioids (if yes, which?)*: 3 to 5 µg/kg fentanyl at induction, dextropropoxyphene or meperidine as rescue analgesic
- *Type of surgery*: laparoscopic cholecystectomy

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 27
- *Received treatment (n)*: 27
- *Analysed (n)*: 27
- *Age (mean ± SD, median (IQR), median (range))*: 41.3 ± 13.6
- *Weight (mean ± SD, median (IQR), median (range))*: 68.5 ± 8.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 17/10/0/0
- *Gender (female in %)*: 74.07
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 69
- *Use of perioperative opioids (if yes, which?)*: 3 to 5 µg/kg fentanyl at induction, dextropropoxyphene or meperidine as rescue analgesic
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II patients scheduled for elective laparoscopic cholecystectomy

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Argiriadou 2002 *(Continued)*

	Excluded criteria: patients who had a history of PONV, motion sickness, gastrointestinal disorders, or receipt of antiemetic within 24 hours before surgery **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Ondansetron (group A) • *Dose*: 4 mg • *Time point of administration*: at anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 24.1% (metoclopramide 10 mg IV) Tropisetron (group B) • *Dose*: 5 mg • *Time point of administration*: at anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16.1% (metoclopramide 10 mg IV) Placebo (group C) • *Dose*: saline • *Time point of administration*: at anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Headache (0 to 12 hours)* • Outcome type: dichotomous outcome *Sedation/ drowsiness (0 to 12 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Greece **Setting:** inpatient, single-centre **Author's name:** B. Papaziogas **Institution:** 2nd Surgical Clinic of the Aristotle University of Thessaloniki, G. Gennimatas Hospital, Ethnikis Aminis 41, 546 35 Thessaloniki, Greece **Email:** NA **Address:** Bl. Gabriilidis str. 29, 546 55 Thessaloniki, Greece **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

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Argiriadou 2002 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated randomized list"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the syringes containing each drug were identical and were prepared by personnel not involved in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "these parameters were measured immediately after surgery (0 h), and at 3 h, 6 h, and 12 h postoperatively by anesthesia residents blinded to which antiemetic the patient had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "were enrolled in the study. Patients' demographics were similar in all study groups (Table 1). Both groups A" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Arslan 2011

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 9.9 • *Weight (mean ± SD, median (IQR), median (range))*: 72.8 ± 10.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/6/0/0 • *Gender (female in %)*: 76.7

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Arslan 2011 *(Continued)*

- *Non-smoker (%)*: 63.3
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105.5
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil infusion 0.2 µg/kg
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 41.5 ± 7.8
- *Weight (mean ± SD, median (IQR), median (range))*: 70.5 ± 8.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 25/5/0/0
- *Gender (female in %)*: 83.3
- *Non-smoker (%)*: 70.0
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 110.5
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil infusion 0.2 µg /kg
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: patients scheduled for laparoscopic cholecystectomy (25 to 55 years of age; 48 women) with an American Society of Anesthesiologists (ASA) physical status classification system risk of I or II

Excluded criteria: history of hepatic, renal, or cardiovascular disease; chronic obstructive pulmonary disease; haematological or gastrointestinal disorders, or both; hypersensitivity to propofol or to any other drug; history of vertigo or motion sickness; previous postoperative emesis; pregnant or breastfeeding or menstruating women; use of an antiemetic agent within 24 hours before surgery; laparoscopy replaced by laparotomy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 2 × 8 mg • *Time point of administration*: at induction of anaesthesia and at time to skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (metoclopramide 10 mg) Metoclopramide • *Dose*: 0.2 mg/kg • *Time point of administration*: at time to skin closure (metoclopramide) • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 46.7% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome

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Arslan 2011 *(Continued)*

Vomiting (4 to 12 hours))

- Outcome type: dichotomous outcome

PONV (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Mustafa Arslan **Institution:** Gazi University Faculty of Dentistry, Anesthesiology and Reanimation Specialist, Department of Oral and Maxillofacial Surgery **Email:** mustarslan@gmail.com **Address:** Gazi University Faculty of Dentistry, Anesthesiology and Reanimation Specialist, Department of Oral and Maxillofacial Surgery, Emek 06510 Ankara, Turkey **Duration of study:** NA **Language:** English **Study's primary outcome:** primary end point of this study was total PONV rate up to 24 hours post anaesthesia **Trial registry number:** NA
Notes	None&&

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, the anesthesiologist attending during surgery, and the anesthesiologist who collected postoperative data were all blinded to the randomization process and the identity of the study drugs"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients, the anesthesiologist attending during surgery, and the anesthesiologist who collected postoperative data were all blinded to the randomization process and the identity of the study drugs"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 64 patients were approached for study inclusion, 4 of whom were excluded based on criteria described previously"

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Arslan 2011 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "no statistically significant between-group differences were found in the patients' demographic and clinical characteristics" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Asadollah 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 44 • *Received treatment (n)*: NA • *Analysed (n)*: 43 • *Age (mean ± SD, median (IQR), median (range))*: 31.3 ± 4.0 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 10.1 • *BMI (mean ± SD, median (IQR), median (range))*: 27.2 ± 4.9 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 74.2 • *Use of perioperative opioids (if yes, which?)*: fentanyl 2 mg/kg for induction, fentanyl 0.4 µg/kg/min for maintenance • *Type of surgery*: gynaecological laparoscopic surgery such as tubal ligation, myomectomy, or ovarian cystectomy Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 47 • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 32.3 ± 3.6 • *Weight (mean ± SD, median (IQR), median (range))*: 69.5 ± 9.6 • *BMI (mean ± SD, median (IQR), median (range))*: 28.4 ± 4.6 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Asadollah 2014 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 72.9
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 mg/kg for induction, fentanyl 0.4 µg/kg/min for maintenance
- *Type of surgery*: gynaecological laparoscopic surgery such as tubal ligation, myomectomy, or ovarian cystectomy

Included criteria: women classified as American Society of Anesthesiology (ASA) physical status I or II, lack of allergy to metoclopramide, no use of antidepressants or antiemetics in 24 hours before surgery

Excluded criteria: pregnant or lactating women; weight over 90 kg; conditions such as malignant hypertension, hepatic dysfunction, pheochromocytoma, and seizure; symptoms of extrapyramidal mechanical ileus; need for post-operation ventilator or NG tube

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: after intubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 9.3% (metoclopramide 10 mg IM/PRN or promethazine 25 mg IM/PRN)

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: after intubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 22.2% (metoclopramide 10 mg IM/PRN or promethazine 25 mg IM/PRN)

Outcomes

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Iran

Setting: inpatient, single-centre

Author's name: Sara Asadollah

Institution: Tehran University of Medical Sciences Rasool-E-Akram Hospital, Clinic of Obstetrics and Gynecology, Tehran, Iran

Email: sara_asadolla@yahoo.com

Address: Tehran Province, Tehran, District 6, Tehran, Iran

Duration of study: December 2012 to January 2014

Language: English

Study's primary outcome: primary outcome variable of this study was the incidence of PONV

Trial registry number: NA

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Asadollah 2014 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients and anesthesiologist were blinded to the study groups"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "postoperative nausea and vomiting results: from 91 patients who entered the study, 3 individuals underwent laparotomy due to adhesions; so 88 patients were analyzed (Figure 1). Mean age..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "mean age of these patients was 31.7 (±3.8) years. There was no significant difference in age, weight, BMI, operation duration, type of surgery and duration of anesthesia between two groups of our study (P value > 0.05)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Ascaso 1997

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 84 • *Received treatment (n)*: 84 • *Analysed (n)*: 84 • *Age (mean ± SD, median (IQR), median (range))*: 70 ± 9

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Ascaso 1997 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 74/10/0/0
- *Gender (female in %)*: 53.57
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 65
- *Use of perioperative opioids (if yes, which?)*: alfentanil for intraoperative analgesia
- *Type of surgery*: extracapsular cataract surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 51
- *Received treatment (n)*: 51
- *Analysed (n)*: 51
- *Age (mean ± SD, median (IQR), median (range))*: 68 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 45/6/0/0
- *Gender (female in %)*: 45.10
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 72
- *Use of perioperative opioids (if yes, which?)*: alfentanil for intraoperative analgesia
- *Type of surgery*: extracapsular cataract surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 116
- *Received treatment (n)*: 116
- *Analysed (n)*: 116
- *Age (mean ± SD, median (IQR), median (range))*: 68 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 102/14/0/0
- *Gender (female in %)*: 46.55
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 67
- *Use of perioperative opioids (if yes, which?)*: alfentanil for intraoperative analgesia
- *Type of surgery*: extracapsular cataract surgery

Included criteria: ASA physical status I or II; 5 to 89 years of age; scheduled to undergo extracapsular cataract surgery under general anaesthesia

Excluded criteria: predisposed to nausea and vomiting secondary to gastrointestinal reflux, gastroparesis, motion sickness, inner ear disorders, or CNS disorders; use of antiemetics in the 24 hours preceding administration of study drug; use of intragastric tubes after operation

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Ascaso 1997 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: over 2 to 5 minutes just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 10 mg • *Time point of administration*: over 2 to 5 minutes just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 4 mg • *Time point of administration*: over 2 to 5 minutes just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Spain **Setting:** NA, single-centre **Author's name:** F.J. Ascaso **Institution:** Department of Ophthalmology, University Clinic Hospital, Zaragoza, Spain **Email:** NA **Address:** Department of Ophthalmology, University Clinic Hospital, San Juan Bosco 15, E-50009, Zaragoza, Spain **Duration of study:** NA **Language:** English

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Ascaso 1997 *(Continued)*

	Study's primary outcome: number of patients who did not report nausea or vomiting during the first 24 hours after recovery from anaesthesia compared with those who did **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly assigned". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "data concerning nausea and vomiting were collected by trained nursing staff. All observations were made without knowledge of which treatment the patient had received"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: group imbalances in number of participants per group (84/51/116). Reasons not described
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Awad 2002

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: 30 • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 49 ± 18 • *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 12

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Awad 2002 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 81.48
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 97
- *Use of perioperative opioids (if yes, which?)*: 21 mg morphine
- *Type of surgery*: laparoscopic cholecystectomy

Droperidol + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 34
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 51 ± 15
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 87.50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 96
- *Use of perioperative opioids (if yes, which?)*: 21 mg morphine
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA physical status I or II, 18 to 80 years of age, scheduled for elective laparoscopic cholecystectomy

Excluded criteria: history of PONV or motion sickness, antiemetic therapy within 24 hours of surgery, concurrent steroid therapy, gastrointestinal disease

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Droperidol • *Dose*: 1.25 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 48% (prochlorperazine 12.5 mg IM) Droperidol + ondansetron • *Dose*: droperidol 1.25 mg, ondansetron 4 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 34% (prochlorperazine 12.5 mg IM)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome

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Awad 2002 *(Continued)*

Vomiting (3 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Constipation (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Ireland **Setting:** inpatient, single-centre **Author's name:** George D. Shorten **Institution:** Cork University Hospital **Email:** shorteng@shb.ie **Address:** Department of Anesthesia and Intensive Care Medicine, Cork University Hospital, Cork, Republic of Ireland **Duration of study:** NA **Language:** English **Study's primary outcome:** no nausea or vomiting **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "according to random allocation" Judgement comment: no statement on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Awad 2002 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an investigator who was unaware of the group to which each patient belonged interviewed the patients at 1, 3, and 24 hours after arrival at the recovery room"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 64 patients recruited, 59 patients completed the study. In five patients, the procedure was converted to open cholecystectomy and data obtained from these patients were eliminated from final analysis"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic data were similar in the two groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): unclear

Bacic 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 24 (secondary publication) • *Age (mean ± SD, median (IQR), median (range))*: 32.9 ± 3.1 (all groups combined) • *Weight (mean ± SD, median (IQR), median (range))*: 65.5 ± 2.6 (all groups combined) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: Balanced anaesthesia (fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 52.8 ± 6.2 (all groups combined) • *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia • *Type of surgery*: unilateral thyroid surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Bacic 1998 *(Continued)*

- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 21 (secondary publication)
- *Age (mean ± SD, median (IQR), median (range))*: 32.9 ± 3.1 (all groups combined)
- *Weight (mean ± SD, median (IQR), median (range))*: 65.5 ± 2.6 (all groups combined)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (fentanyl, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 52.8 ± 6.2 (all groups combined)
- *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia
- *Type of surgery*: unilateral thyroid surgery

Included criteria: female patients, 18 to 45 years of age, regular menstrual periods, scheduled for elective unilateral thyroid surgery

Excluded criteria: patients with irregular cycles, those using oestrogen or progestogen drugs, persons with a positive history of earlier postoperative nausea and vomiting or motion sickness

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 8 mg • *Time point of administration*: 30 minutes before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: saline • *Time point of administration*: 30 minutes before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Croatia

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Bacic 1998 *(Continued)*

Setting: inpatient, single-centre

Author's name: Zvonko Rumboldt

Institution: Department of Medicine, University of Split School of Medicine, Croatia

Email: NA

Address: Department of Medicine, University of Split School of Medicine, 21000 Split, Spinciceva 1, Croatia

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	Two studies. Only 1 study was randomized. Secondary publication available (data inconsistent with the primary report)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "these women received randomly" No information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "...following instructions in sealed envelopes" Not stated sequentially numbered, opaque, sealed envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: 5 dropouts (1 in the ondansetron group and 4 in the placebo group; refused to gauge postoperative nausea and vomiting intensity). Data from the secondary publication were used because data are consistent but are different from the primary reference (Bacic 2000)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Backes 2013

Study characteristics

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Backes 2013 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 66.3 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 34.0 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: general endotracheal anaesthesia without adjuvant neuraxial analgesia was used for all patients • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 59.9 mg equivalent hydrocodone • *Type of surgery*: unilateral, total hip or knee arthroplasty Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 46 • *Received treatment (n)*: 46 • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 65.1 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 32.0 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: general endotracheal anaesthesia without adjuvant neuraxial analgesia was used for all patients • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 24.4 mg equivalent hydrocodone • *Type of surgery*: unilateral, total hip or knee arthroplasty Dexamethasone + ondansetron (+ dexamethasone 24 hours postoperatively) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 44 • *Received treatment (n)*: 44 • *Analysed (n)*: 42 • *Age (mean ± SD, median (IQR), median (range))*: 66.0 • *Weight (mean ± SD, median (IQR), median (range))*: NA

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Backes 2013 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 31.2
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: general endotracheal anaesthesia without adjuvant neuraxial analgesia was used for all patients
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 15.1 mg equivalent hydrocodone
- *Type of surgery*: unilateral, total hip or knee arthroplasty

Included criteria: patients undergoing elective unilateral total hip or knee arthroplasty

Excluded criteria: patients with a history of poorly controlled diabetes (HgbA1c > 7.5 on pre-admission testing); steroid or immunosuppressive drug use within 6 months of surgery; renal failure, hepatic failure, or previous adverse effects from medications utilized in this study

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: approximately 15 minutes before skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, prochlorperazine 5 mg IV Dexamethasone + ondansetron • *Dose*: dexamethasone 10 mg, ondansetron 4 mg • *Time point of administration*: dexamethasone immediately before induction of anaesthesia, ondansetron approximately 15 minutes before skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, prochlorperazine 5 mg IV Dexamethasone + ondansetron (+ dexamethasone 24 hours postoperatively) • *Dose*: dexamethasone 2 × 10 mg, ondansetron 4 mg • *Time point of administration*: dexamethasone immediately before induction of anaesthesia and 24 hours postoperatively, ondansetron approximately 15 minutes before skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, prochlorperazine 5 mg IV
Outcomes	*Postoperative wound infection (6-month follow-up)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, at a minimum of 6-month follow-up)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre

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Backes 2013 *(Continued)*

Author's name: Joel R. Politi

Institution: Cardinal Orthopedic Institute, Columbus, OH, USA

Email: NA

Address: Cardinal Orthopedic Institute, 170 Taylor Station Road, Columbus, OH 43213, USA

Duration of study: September 2011 to February 2012

Language: English

Study's primary outcome: primary outcome measures included (1) length of hospital stay (measured as number of calendar days patient was hospitalized), (2) duration of ambulation, (3) knee ROM, (4) cumulative hydromorphone PCA use, (5) daily hydrocodone consumption, (6) patient pain scores, (7) daily rescue antiemetic consumption, (8) patient nausea/vomiting scores

Trial registry number: NA

Notes	Repetitive dose of dexamethasone in 1 group after 24 hours. Data for adverse effects not eligible for the third group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer based random integer generator"
Allocation concealment (selection bias)	Unclear risk	Quote: "patients were randomized into one of three study groups by a research assistant who was not involved with outcome assessment" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "patients, physical therapists, and orthopedic surgeons were blinded to study group allocation. The anesthesiologists responsible for intra-operative management were not blinded to treatment, but were not involved in any outcome assessment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients, physical therapists, and orthopedic surgeons were blinded to study group allocation. The anesthesiologists responsible for intra-operative management were not blinded to treatment, but were not involved in any outcome assessment. Nurses that administered the IV dexamethasone push at 24 hours to patients in group 3 were also not blinded, but no other study group identifiers were present to nursing staff thereafter"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "ten patients had incomplete data available, leaving 120 patients for final analysis"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the amount of milligram equivalents of hydrocodone consumed for breakthrough analgesia was significantly more in the control group; those receiving dexamethasone at the time of operation received less than half that of controls on PODs 0, 1, and 2 (15.9 vs 4.2 P = 0.003, 47.4 vs 20.2 P = 0.000, 59.9 vs 18.7 P = 0.003, respectively). Furthermore, a continued effect was seen with administering dexamethasone at 24 hours, as group 3 consumed less total mg equivalents of hydrocodone on POD 2 than group 2 (24.4 vs 15.1 P = 0.015)"

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Backes 2013 *(Continued)*

	Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Badaoui 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 53 ± 19 • *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 19 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 15/7/3/0 • *Gender (female in %)*: 56 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 61 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 0.1 mg bolus • *Type of surgery*: laparoscopic cholecystectomy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 19 • *Age (mean ± SD, median (IQR), median (range))*: 54 ± 16 • *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 9/9/1/0 • *Gender (female in %)*: 73.7 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 75 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 0.1 mg bolus • *Type of surgery*: laparoscopic cholecystectomy Ondansetron

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Badaoui 1998 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: 54 ± 17
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 20
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 14/8/2/0
- *Gender (female in %)*: 70.8
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 0.1 mg bolus
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: age over 18 years, laparoscopic cholecystectomy, ASA I to III

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 125 mL saline • *Time point of administration*: 1 hour before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 1 mg • *Time point of administration*: 1 hour before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 4 mg • *Time point of administration*: 1 hour before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** France

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Badaoui 1998 *(Continued)*

Setting: inpatient, single-centre

Author's name: R. Badaoui

Institution: Department of Anesthesia Resuscitation B, CHU Nord

Email: NA

Address: Département d'Anesthésie-Réanimation B, CHU Nord, Place Victor-Pauchet, 80054, Amiens Cedex 01

Duration of study: NA

Language: French (2 reviewers: MSS, AA)

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote "randomized" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "double-blind" Insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "double-blind" Insufficient information on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear

Badaoui 1999

Study characteristics

Methods	**Study design:** randomized controlled trial

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Badaoui 1999 *(Continued)*

Study grouping: 3 groups, monoprophylaxis

Participants

Baseline characteristics

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 51 ± 19
- *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 30/15/5/0
- *Gender (female in %)*: 56
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 62
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 0.1 mg bolus as required
- *Type of surgery*: cholecystectomy, parotid, proctologic surgery, thyroidectomy, mastectomy, varicosectomy

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 49 ± 16
- *Weight (mean ± SD, median (IQR), median (range))*: 76.5 ± 16
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 26/20/3/1
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 0.1 mg bolus as required
- *Type of surgery*: cholecystectomy, parotid, proctologic surgery, thyroidectomy, mastectomy, varicosectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 52 ± 15
- *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 27/16/2/0

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Badaoui 1999 *(Continued)*

- *Gender (female in %)*: 53.3
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 61
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 0.1 mg bolus as required
- *Type of surgery*: cholecystectomy, parotid surgery, proctologic surgery, thyroidectomy, mastectomy, varicosectomy

Included criteria: age over 18 years, elective surgery that "was considered emetogenic", ASA I to III

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 125 ml NaCl • *Time point of administration*: 30 minutes before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 1 mg • *Time point of administration*: 30 minutes before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 4 mg • *Time point of administration*: 30 minutes before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** France **Setting:** inpatient, single-centre **Author's name:** D.R. Badaoui **Institution:** Department of Anesthesia Resuscitation B, Chu Nord **Email:** NA **Address:** Départment d'Anesthésie-Réanimation B, CHU Nord, place Victor-Pauchet, 80054 Amiens Cedex 01

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Badaoui 1999 *(Continued)*

	Duration of study: February to July 1997 **Language:** French (2 reviewers: MSS, AA) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" (translated). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "double-blind" (translated) Insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "double-blind" (translated) Insufficient information on blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: it is stated that 150 participants have been included and 145 CRFs were analysable. No reasons/further information for exclusion of the 5 participants, which apparently have been all in the ondansetron arm, are provided
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Bailey 1990

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA

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Bailey 1990 *(Continued)*

- *Analysed (n)*: 68
- *Age (mean ± SD, median (IQR), median (range))*: 32.1 ± 5.7
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 61/7/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 72
- *Use of perioperative opioids (if yes, which?)*: fentanyl 0.5 to 2 µg/kg for induction
- *Type of surgery*: laparoscopy

Scopolamine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 70
- *Age (mean ± SD, median (IQR), median (range))*: 32 ± 5.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 62/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 73
- *Use of perioperative opioids (if yes, which?)*: fentanyl 0.5 to 2 µg/kg for induction
- *Type of surgery*: laparoscopy

Included criteria: ASA physical status I or II, women scheduled for outpatient laparoscopy under general anaesthesia

Excluded criteria: participants who were pregnant or nursing; medical history of narrow-angle glaucoma, gastrointestinal obstruction, urinary tract obstruction; using antiemetics, anticholinergics, or antihistamines

Pretreatment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Placebo

- *Dose*: placebo patch
- *Time point of administration*: placed on the night before surgery or at least 8 hours before scheduled start time of surgery
- *Route of administration*: transdermal patch
- *Rescue antiemetics (if yes, which?)*: 32% (0.625 mg droperidol IV)

Scopolamine

- *Dose*: 1.5 mg, delivered on a constant rate of 5 µg/h

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Bailey 1990 *(Continued)*

- *Time point of administration*: placed on the night before surgery or at least 8 hours before scheduled start time of surgery
- *Route of administration*: transdermal patch
- *Rescue antiemetics (if yes, which?)*: 13% (0.625 mg droperidol IV)

Outcomes	*Subjects with any SAE (0 to 48 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 48 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported in part by the Stanley Research Foundation and Ciba-Geigy Pharmaceuticals **Country:** USA **Setting:** outpatient, single-centre **Author's name:** P.L. Bailey **Institution:** Department of Anesthesiology, University of Utah School of Medicine, Salt Lake City, UT, USA **Email:** NA **Address:** Department of Anesthesiology, University of Utah School of Medicine, 50 North Medical Drive, Salt Lake City, UT 84132, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Transdermal scopolamine for 3 days

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized fashion" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Bailey 1990 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: quote: "one hundred ninety-one patients were enrolled into the study; 53 patients were excluded from analysis because of a breach in the study protocol. Reasons for the removal of these subjects from evaluation included failure to apply the patch (n=17), patch removal either before surgery (n=5) or within 6 h after surgery (n=2), drugs with potential antiemetic effect given intraoperatively (n= 21), epidural instead of general anesthesia (n=1), non-abdominal surgery (n=3), and cancellation of surgery (n=3). In addition, one patient received no fentanyl. There was no difference between active (n=27) and placebo (n=26) groups with respect to subject removal from analysis. When appropriate, data from these patients were included in the analysis of side effects" Dropouts 27.74% (> 15%), but reasons reported. Participants seem to have problems applying the patch
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Bajwa 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 33.46 ± 1.86 • *Weight (mean ± SD, median (IQR), median (range))*: 54.32 ± 3.66 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 21/9/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: TIVA

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Bajwa 2011 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 36.42
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: bilateral laparoscopic tubal ligation

Palonosetron (group 2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 32.22 ± 1.58
- *Weight (mean ± SD, median (IQR), median (range))*: 55.12 ± 3.14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 19/11/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 38.26
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: bilateral laparoscopic tubal ligation

Included criteria: ASA I or II; patients between the ages of 25 and 40 years who underwent bilateral laparoscopic tubal ligation surgery, lived in the vicinity of 10 to 15 km radii from the institute, and had communication (mobile and land line phones) and personal transportation modes

Excluded criteria: ASA III or IV; psychiatric disease, diabetes, history of drug abuse, duration of surgery longer than 1 hour, chronic obstructive pulmonary disease, previous history of motion sickness and PONV; patients in premenstrual phase and with body mass index > 35 kg/m^2

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioid): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron (group 1) • *Dose*: 8 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg with maximum dose of 12 mg/d Palonosetron (group 2) • *Dose*: 0.075 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg with maximum dose of 12 mg/d
Outcomes	*Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Headache (0 to 72 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 72 hours)*

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Bajwa 2011 *(Continued)*

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 72 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 72 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** nil **Country:** India **Setting:** outpatient, single-centre **Author's name:** Sukhminderjit Singh Bajwa **Institution:** Gian Sagar Medical College Hospital **Email:** sukhminder_bajwa2001@yahoo.com **Address:** Department of Anaesthesiology and Intensive Care, Gian Sagar Medical College Hospital, Ram Nagar, Banur, Punjab, India **Duration of study:** January 2010 to May 2010 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated codes"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "these syringes were prepared by an anesthesia technician who was given a written set of instructions and was unaware of the procedure in the operation room"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Bajwa 2011 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioid): no; (non-smoker): unclear

Bala 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Palonosetron (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 42 • *Received treatment (n)*: NA • *Analysed (n)*: 42 • *Age (mean ± SD, median (IQR), median (range))*: 42.26 ± 11.60 • *Weight (mean ± SD, median (IQR), median (range))*: 62.02 ± 10.70 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 28/14/0/0 • *Gender (female in %)*: 76.19 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 58.33 • *Use of perioperative opioids (if yes, which?)*: fentanyl for induction • *Type of surgery*: laparoscopic cholecystectomy Palonosetron + dexamethasone (group DP) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 42 • *Age (mean ± SD, median (IQR), median (range))*: 41.26 ± 11.71 • *Weight (mean ± SD, median (IQR), median (range))*: 58.67 ± 8.05 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 32/10/0/0 • *Gender (female in %)*: 85.71 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 61.29 • *Use of perioperative opioids (if yes, which?)*: fentanyl for induction • *Type of surgery*: laparoscopic cholecystectomy

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Bala 2014 *(Continued)*

	Included criteria: ASA physical status I or II, between 19 and 60 years of age, scheduled to undergo elective laparoscopic cholecystectomy **Excluded criteria:** patients with gastrointestinal disease, BMI > 30 kg/m^2, smokers, history of PONV or motion sickness, those who had allergy to the study drugs or received antiemetics within 24 hours before surgery **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Palonosetron (group P) • *Dose*: 0.075 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 42.9% (metoclopramide 10 mg IV) Palonosetron + dexamethasone (group DP) • *Dose*: palonosetron 0.075 mg, dexamethasone 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 14.3% (metoclopramide 10 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** study authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript **Country:** India **Setting:** inpatient, single-centre **Author's name:** N. Bharti **Institution:** Department of Anesthesia and Intensive Care, PGIMER, 160012, Chandigarh, India

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Bala 2014 *(Continued)*

Email: bhartineerja@yahoo.com

Address: Department of Anesthesia and Intensive Care, PGIMER, 160012, Chandigarh, India

Duration of study: NA

Language: English

Study's primary outcome: postoperative vomiting

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated random number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "the person who enrolled the patient in groups and prepared the study drugs was not involved in the patient management or data collection" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the person who enrolled the patients in groups and prepared the study drugs was not involved in the patient management or data collection"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "blinded observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "the groups were well matched with respect to age, height, weight, PONV risk factors and ASA status. There was no significant difference in duration of surgery and CO 2 insufflations time among groups (Table I). The intraoperative hemodynamic parameters and fluid requirements were also comparable" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Bang 2016

Study characteristics

Methods	**Study design:** randomized controlled trial

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Bang 2016 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 59.4 ± 7.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 38/12/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 92 • *History of PONV/motion sickness (%)*: 50/92 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 123 • *Use of perioperative opioids (if yes, which?)*: 536.8 µg fentanyl • *Type of surgery*: gynaecological laparoscopic surgery Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 59.8 ± 7.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 38/12/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 86 • *History of PONV/motion sickness (%)*: 56/86 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 126 • *Use of perioperative opioids (if yes, which?)*: 540.9 µg fentanyl • *Type of surgery*: gynaecological laparoscopic surgery **Included criteria:** women 20 to 60 years of age with American Society of Anesthesiologists physical status I or II **Excluded criteria:** patients who experienced vomiting or retching in the 24-hour period before surgery; patients who underwent emetogenic radiotherapy within 8 weeks or cancer chemotherapy within 4 weeks before study entry; patients who had received steroids, antiemetics, or psychoactive medications 24 hours before study initiation **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Placebo

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Bang 2016 *(Continued)*

- *Dose*: saline 1.5 mL
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 12% (metoclopramide 10 mg)

Palonosetron

- *Dose*: 0.075 mg
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 4% (metoclopramide 10 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** there are no financial or other relationships to disclose that might lead to a conflict of interest regarding this article **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Soo Kyoung Park **Institution:** Department of Anesthesiology and Pain Medicine, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Gyeonggi, Korea **Email:** hardmong@naver.com **Address:** Department of Anesthesiology and Pain Medicine, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, 7 Keun Jaebong Road, Hwaseong, Gyeonggi, Korea **Duration of study:** June to October 2015 **Language:** English

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Bang 2016 *(Continued)*

	Study's primary outcome: the primary outcome was the overall incidence of nausea and vomiting during the first 24 hours after anaesthesia **Trial registry number:** NCT01478165
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "trained nurses, who were not involved in the study, prepared the study drugs before induction of anesthesia, according to directions in an envelope containing the allocation groups" Judgement comment: not stated sequentially numbered, opaque, and sealed envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "trained nurses, who were not involved in the study, prepared the study drugs before induction of anesthesia, according to directions in an envelope containing the allocation groups"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "every assessment and interview was performed by doctors blinded to treatment group enrolment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred patients were enrolled (50 per group) and all completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01478165 (retrospective registration)
Other bias	Low risk	Quote: "patient demographic data, risk factors and operative data were comparable between the two groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Bang 2017

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Palonosetron (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Bang 2017 *(Continued)*

- *Randomized (n)*: 29
- *Received treatment (n)*: 29
- *Analysed (n)*: 29
- *Age (mean ± SD, median (IQR), median (range))*: 40.00 ± 9.60
- *Weight (mean ± SD, median (IQR), median (range))*: 59.21 ± 9.54
- *BMI (mean ± SD, median (IQR), median (range))*: 23.40 ± 3.51
- *ASA I/II/III/IV (n)*: 19/10/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 111.03
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, fentanyl 1 µg/kg 30 minutes before end of surgery, PCA fentanyl 20 µg/kg
- *Type of surgery*: gynaecological laparoscopic

Ramosetron (group B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 29
- *Received treatment (n)*: 29
- *Analysed (n)*: 29
- *Age (mean ± SD, median (IQR), median (range)*: 37.00 ± 8.65
- *Weight (mean ± SD, median (IQR), median (range))*: 58.53 ± 12.16
- *BMI (mean ± SD, median (IQR), median (range))*: 22.82 ± 4.00
- *ASA I/II/III/IV (n)*: 19/10/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 116.21
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, fentanyl 1 µg/kg 30 minutes before end of surgery, PCA fentanyl 20 µg/kg
- *Type of surgery*: gynaecological laparoscopic

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 29
- *Received treatment (n)*: 29
- *Analysed (n)*: 29
- *Age (mean ± SD, median (IQR), median (range))*: 37.97 ± 9.05
- *Weight (mean ± SD, median (IQR), median (range))*: 58.53 ± 7.62
- *BMI (mean ± SD, median (IQR), median (range))*: 22.87 ± 3.76
- *ASA I/II/III/IV (n)*: 20/9/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 106.21
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, fentanyl 1 µg/kg 30 minutes before end of surgery, PCA fentanyl 20 µg/kg

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Bang 2017 *(Continued)*

- *Type of surgery*: gynaecological laparoscopic

Included criteria: ASA I or II, women 20 to 49 years of age, non-smoker, requested intravenous patient-controlled analgesia (PCA) for pain control after gynaecological laparoscopic surgery

Excluded criteria: patients who had an allergy reaction or hypersensitivity to selective serotonin receptor antagonists, smokers, patients who did not want PCA, those of ASA III or higher

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Palonosetron (group A) • *Dose*: 0.075 mg • *Time point of administration*: before induction, saline 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg, ramosetron 0.3 mg Ramosetron (group B) • *Dose*: 0.3 mg • *Time point of administration*: saline before induction, ramosetron 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg, ramosetron 0.3 mg Placebo (group C) • *Dose*: normal saline • *Time point of administration*: before induction and 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg, ramosetron 0.3 mg
Outcomes	*Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** CJ Healthcare **Country:** Korea **Setting:** NA **Author's name:** Jae-Wook Jung **Institution:** Departments of Anesthesiology and Pain Medicine and Obstetrics and Gynecolocy, Seoul Pail Hospital and Haeundae Paik Hospital of InjeUniversity, Seoul, Korea **Email:** jjwooks@naver.com **Address:** Departments of Anesthesiology and Pain Medicine and Obstetrics and Gynecolocy, Seoul Pail Hospital and Haeundae Paik Hospital of InjeUniversity, Seoul, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV

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Bang 2017 *(Continued)*

	Trial registry number: KCT0001930
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized study" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "medications were prepared by a nurse who was not involved in this study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "all assessments were done by anaesthesiologists who were blinded to the study assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: KCT0001930 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Bano 2008

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 41.4 ± 8.2 • *Weight (mean ± SD, median (IQR), median (range))*: 68.9 ± 5.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 33/16/0/0

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Bano 2008 *(Continued)*

- *Gender (female in %)*: 89.80
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88.0
- *Use of perioperative opioids (if yes, which?)*: nalbuphine 0.2 mg/kg for induction
- *Type of surgery*: laparoscopic cholecystectomy

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 48
- *Age (mean ± SD, median (IQR), median (range))*: 39.3 ± 8.6
- *Weight (mean ± SD, median (IQR), median (range))*: 69.02 ± 6.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 29/19/0/0
- *Gender (female in %)*: 85.42
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88.2
- *Use of perioperative opioids (if yes, which?)*: nalbuphine 0.2 mg/kg for induction
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: male or female, 20 to 50 years of age, ASA physical status I and II, scheduled for elective laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: ASA physical status III and IV, ASA I or II with history of hypertension or diabetes, history of allergic reaction to any drug or food, body mass index > 25 kg/m^2, history of motion sickness, history of previous nausea and vomiting, history of alcohol or drug abuse, history of taking any antiemetic agent within 24 hours, history of smoking, conversion to open cholecystectomy, associated pregnancy and chronic cough

Pretreatment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no, (history of motion sickness): unclear

Interventions	**Intervention characteristics** Dexamethasone + ondansetron • *Dose*: dexamethasone 8 mg, ondansetron 4 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 6.12% (metoclopramide 10 mg IV) Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 22.92% (metoclopramide 10 mg IV)
Outcomes	*Vomiting (0 to 24 hours)*

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Bano 2008 *(Continued)*

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Pakistan **Setting:** inpatient, single-centre **Author's name:** Fauzia Bano **Institution:** Department of Anaesthesiology, Surgical Intensive Care Unit Pain Management, Dow University of Health Sciences, Karachi **Email:** sanganifauzia@yahoo.com **Address:** 353 Navan Road, Dublin 7, Republic of Ireland **Duration of study:** March 2007 to September 2007 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomly allocated into two groups (50 patients in each) by ballotting"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "assessed by anaesthetist, who had no knowledge of drug given to patient; similarly, patients were also blind to drug given to them"

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Bano 2008 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred patients, 50 in each group, were initially selected for this study. However, one patient in group A and 2 patients in group B were not included in statistical analysis because of conversion to open cholecystectomy, leaving the study sample to 97 patients"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "both groups were comparable with regards to age (p=0.240), gender (p=0.553), ASA physical status (0.530) and weight (p=0.548), duration of surgeries (p=0.544), and duration of anaesthesia (p=0.872)" Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no, (history of motion sickness): unclear

Barbone 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, dose-finding study, monoprophylaxis
Participants	**Baseline characteristics** Dolasetron (group MD2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 23 • *Received treatment (n)*: NA • *Analysed (n)*: 23 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 80 to 220 • *Use of perioperative opioids (if yes, which?)*: at induction 100 µg fentanyl, intraoperative remifentanil 0.10 to 0.15 µg/kg/min, postoperative 30 mg morphine • *Type of surgery*: general, plastic reconstructive, and vertebral surgery Dolasetron (group MD3) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 23 • *Received treatment (n)*: NA • *Analysed (n)*: 23 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA

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Barbone 2004 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80 to 220
- *Use of perioperative opioids (if yes, which?)*: at induction 100 µg fentanyl, intraoperative remifentanil 0.10 to 0.15 µg/kg/min, postoperative 30 mg morphine
- *Type of surgery*: general, plastic reconstructive, and vertebral surgery

Ondansetron (group MO)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 24
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80 to 220
- *Use of perioperative opioids (if yes, which?)*: at induction 100 µg fentanyl, intraoperative remifentanil 0.10 to 0.15 µg/kg/min, postoperative 30 mg morphine
- *Type of surgery*: general, plastic reconstructive, and vertebral surgery

Dolasetron (group TKD2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 24
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80 to 220
- *Use of perioperative opioids (if yes, which?)*: at induction 100 µg fentanyl, intraoperative remifentanil 0.10 to 0.15 µg/kg/min, postoperative 300 mg tramadol
- *Type of surgery*: general, plastic reconstructive, and vertebral surgery

Dolasetron (group TKD3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -

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Barbone 2004 *(Continued)*

- *Randomized (n)*: 22
- *Received treatment (n)*: NA
- *Analysed (n)*: 22
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80 to 220
- *Use of perioperative opioids (if yes, which?)*: at induction 100 µg fentanyl, intraoperative remifentanil 0.10 to 0.15 µg/kg/min, postoperative 300 mg tramadol
- *Type of surgery*: general, plastic reconstructive, and vertebral surgery

Ondansetron (group TKO)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80 to 220
- *Use of perioperative opioids (if yes, which?)*: at induction 100 µg fentanyl, intraoperative remifentanil 0.10 to 0.15 µg/kg/min, postoperative 300 mg tramadol
- *Type of surgery*: general, plastic reconstructive, and vertebral surgery

Included criteria: ASA I to III, scheduled for elective surgical procedures (general, plastic-reconstructive and vertebral surgery), age from 17 to 78 years, weight 50 to 120 kg

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, BMI, ASA): unclear. Potential effect modifiers (perioperative opioids): no; (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): unclear

Interventions	**Intervention characteristics**

Dolasetron (group MD2)

- *Dose*: 25 mg
- *Time point of administration*: before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: as used in the department

Dolasetron (group MD3)

- *Dose*: 37.5 mg

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Barbone 2004 *(Continued)*

- *Time point of administration*: before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: as used in the department

Ondansetron (group MO)

- *Dose*: 4 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: as used in the department

Dolasetron (group TKD2)

- *Dose*: 25 mg
- *Time point of administration*: before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: as used in the department

Dolasetron (group TKD3)

- *Dose*: 37.5 mg
- *Time point of administration*: before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: as used in the department

Ondansetron (group TKO)

- *Dose*: 4 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: as used in the department

Outcomes	*Vomiting (*early vomiting, after awakening from anaesthesia*)* • Outcome type: dichotomous outcome *Vomiting (late vomiting, next 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, NA **Author's name:** Giuseppe Barbone **Institution:** U.O. Anestesia e Rianimazione Azienda Ospedaliera Policlinico Bari **Email:** g.barbone@libero.it **Address:** Centro di Rianimazione, Policlinico di Bari-Piazza Giulio Cesare, 11-70124 Bari **Duration of study:** NA **Language:** English **Study's primary outcome:** NA

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Barbone 2004 *(Continued)*

	Trial registry number: NA
Notes	Postoperative analgesia: 3 arms with tramadol plus ketorolac as postoperative analgesia (TKO, TKD2, TKD3), 3 arms with morphine as postoperative analgesia (MO, MD2, MD3). TKO and MO, TKD2 and MD2, TKD3 and MD3 were pooled for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly allocated" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "registered by an operator (nurse or anaesthesiologist) who did not know which anti-emetic the patients had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, BMI, ASA): unclear. Potential effect modifiers (perioperative opioids): no; (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): unclear

Barros 2013

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 17 • *Age (mean ± SD, median (IQR), median (range))*: 49 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 9

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Barros 2013 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 9/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative tramadol via PCA
- *Type of surgery*: thyroidectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 17
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 5/11/1/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative tramadol via PCA
- *Type of surgery*: thyroidectomy

Included criteria: female patients between 18 and 75 years of age, ASA (American Society of Anesthesiologists) physical status I to III, undergoing thyroidectomy under general balanced anaesthesia and postoperative analgesia by PCA for 22 hours

Excluded criteria: allergy to tramadol, dexamethasone, or other glucocorticoids; pregnant and lactating women; current systemic infection; inability to use or understand PCA; history of epilepsy, renal or hepatic severe impairment, diabetes mellitus, gastric or duodenal ulcer, inflammatory bowel disease, glaucoma, tuberculosis, myasthenia gravis, or glucocorticoid-induced myopathy; history of alcohol or drug abuse in use of analgesic, antidepressant, antipsychotic, antiepileptic, antifungal, antineoplastic or antiviral drugs, or in use of rifampicin, barbiturates, methotrexate, ephedrine, or antiemetic medications; history of PONV or motion sickness

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, postoperative opioids): no; (non-smoker, intraoperative opioids): unclear

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Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 4 mg
- *Time point of administration*: immediately after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, and if events persisted, propofol 20 mg IV

Placebo

- *Dose*: 0.9% saline

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Barros 2013 *(Continued)*

- *Time point of administration*: immediately after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, and if events persisted, propofol 20 mg IV

Outcomes	*Adverse events (general notes in the publication, 22 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this work had neither financial support nor sponsorship **Country:** Portugal **Setting:** inpatient, single-centre **Author's name:** Frederico C. Pereira **Institution:** Laboratory of Pharmacology and Experimental Therapeutics/Biomedical Institute for Research on Light and Image (IBILI), Faculty of Medicine, University of Coimbra, Coimbra, Portugal **Email:** fredcp@ci.uc.pt **Address:** Laboratory of Pharmacology and Experimental Therapeutics/Biomedical Institute for Research on Light and Image (IBILI) Faculty of Medicine, University of Coimbra, PT–3000-354 Coimbra, Portugal **Duration of study:** NA **Language:** English **Study's primary outcome:** tramadol consumption **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated randomization list"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "both solutions were prepared in a 2-ml syringe, according to the randomization plan, by a nurse not involved in patient care"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "staff members involved in patient care, as well as investigators and patients, were blinded to patient assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "six of these 40 patients were excluded for incorrect data registration. Therefore, 34 women were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Barros 2013 *(Continued)*

Other bias	Unclear risk	Quote: "34 women were analyzed and presented similar demographic and anesthetic-surgical data (Table 2). Tramadol consumption (primary outcome) and postoperative" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, postoperative opioids): no; (non-smoker, intraoperative opioids): unclear

Barrow 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 40.5 (32 to 52) • *Weight (mean ± SD, median (IQR), median (range))*: 61.8 (47 to 87) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: standard general anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 74 • *Use of perioperative opioids (if yes, which?)*: 69.3 mg morphine, 1.5 µg/kg fentanyl • *Type of surgery*: abdominal hysterectomy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 18 • *Age (mean ± SD, median (IQR), median (range))*: 43.9 (29 to 60) • *Weight (mean ± SD, median (IQR), median (range))*: 67.3 (47 to 115) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: standard general anaesthesia

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Barrow 1994 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77
- *Use of perioperative opioids (if yes, which?)*: 59 mg morphine, 1.5 µg/kg fentanyl
- *Type of surgery*: abdominal hysterectomy

Included criteria: ASA I to II, undergoing abdominal hysterectomy under general anaesthesia

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 6.25 mg Droperidol • *Dose*: 1.25 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 6.25 mg
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** England **Setting:** inpatient, single-centre **Author's name:** P.M. Barrow **Institution:** Department of Anaesthesia, Newcastle General Hospital, Newcastle upon Tyne **Email:** NA **Address:** Department of Anaesthesia, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne NE4 6BE **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (1 group with continuous postoperative infusion of antiemetic)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were allocated randomly to one of the following three groups: group 1"

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Barrow 1994 *(Continued)*

		Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "the hospital pharmacy department prepared the study drugs and patients were allocated randomly to one of the following three groups" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: 3 of 60 patients were not analysed No information on reason for missing outcome data provided
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the groups were similar in age, weight, duration of surgery and consumption of morphine" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Basu 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 37 (30 to 45) • *Weight (mean ± SD, median (IQR), median (range))*: 52 (35 to 75) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 64 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 16/4 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O)

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Basu 2011 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 230
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl
- *Type of surgery*: tympanoplasty, mastoidectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 36 (30 to 45)
- *Weight (mean ± SD, median (IQR), median (range))*: 50 (34 to 71)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 68
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 20/0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 240
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl
- *Type of surgery*: tympanoplasty, mastoidectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 37 (30 to 45)
- *Weight (mean ± SD, median (IQR), median (range))*: 50 (39 to 69)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 68
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 4/8
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 235
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl
- *Type of surgery*: tympanoplasty, mastoidectomy

Included criteria: ASA I and II, scheduled for middle ear surgery, 30 to 45 years of age

Excluded criteria: patients with gastrointestinal disorders, pregnant or menstruating females

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Palonosetron • *Dose*: 0.25 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV

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Basu 2011 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: metoclopramide; none

Granisetron

- *Dose*: 3.0 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide; 0 to 6 hours: 20%; 6 to 24 hours: 20%

Ondansetron

- *Dose*: 8.0 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide; 0 to 6 hours: 36%; 6 to 24 hours: 24%

Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Anjana Basu **Institution:** Department of Anaesthesiology, RG Kar Medical College, Kolkata 700004, India **Email:** NA **Address:** Department of Anaesthesiology, RG Kar Medical College, Kolkata 700004, India **Duration of study:** September 2007 to February 2009 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "patients were randomly allocated" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Basu 2011 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "recorded postoperatively by the nursing staff without knowledge of which group of anti-emetic was administered to the patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Bataille 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + ondansetron (group DO) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 61 • *Received treatment (n)*: 58 • *Analysed (n)*: 58 • *Age (mean ± SD, median (IQR), median (range))*: 41 (35 to 52) • *Weight (mean ± SD, median (IQR), median (range))*: 115 (107 to 130) • *BMI (mean ± SD, median (IQR), median (range))*: 42 (40 to 45) • *ASA I/II/III/IV (n)*: 0/27/31/0 • *Gender (female in %)*: 86 • *Non-smoker (%)*: 74 • *History of PONV/motion sickness (%)*: 7 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 96 • *Use of perioperative opioids (if yes, which?)*: 0.10 mg/kg/min remifentanil, 13 mg morphine • *Type of surgery*: laparoscopic sleeve gastrectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 61 • *Received treatment (n)*: 59

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Bataille 2016 *(Continued)*

- *Analysed (n)*: 59
- *Age (mean ± SD, median (IQR), median (range))*: 40 (35 to 48)
- *Weight (mean ± SD, median (IQR), median (range))*: 120 (109 to 136)
- *BMI (mean ± SD, median (IQR), median (range))*: 44 (39 to 47)
- *ASA I/II/III/IV (n)*: 0/28/31/0
- *Gender (female in %)*: 71
- *Non-smoker (%)*: 75
- *History of PONV/motion sickness (%)*: 14
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93
- *Use of perioperative opioids (if yes, which?)*: 0.10 mg/kg/min remifentanil, 13 mg morphine
- *Type of surgery*: elective laparoscopic sleeve gastrectomy

Included criteria: obese patients scheduled for elective laparoscopic sleeve gastrectomy, between 18 and 75 years of age, American Society of Anesthesiologists' physical status I to III, had at least 2 of the following risk factors for developing PONV according to the simplified risk score from Apfel et al: female sex, non-smoker, prior history of PONV or motion sickness, expected to receive postoperative opioid analgesia

Excluded criteria: pregnant or breastfeeding women; psychiatric illness (limiting use of BIS); supraspinal neurological disorders; patients fitted with a pacemaker; symptomatic gastro-oesophageal reflux; contraindication to use of dexamethasone, ondansetron, propofol, remifentanil, or morphine; patients with expected difficult airway management or with planned awake fibreoptic intubation

Pretreatment: baseline characteristics (age, weight, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

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Interventions

Intervention characteristics

Dexamethasone + ondansetron (group DO)

- *Dose*: dexamethasone 4 mg, ondansetron 4 mg
- *Time point of administration*: after tracheal intubation, during skin closure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 55% (ondansetron 4 mg followed by droperidol 0.625 mg)

Placebo

- *Dose*: 2 × 0.9% saline
- *Time point of administration*: after tracheal intubation, during skin closure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 63% (ondansetron 4 mg followed by droperidol 0.625 mg)

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification

Sponsorship source: supported by the Department of Anaesthesiology (Hôpital Foch, Suresnes, France), Vaincre la Mucoviscidose (Paris, France), and Alaris Medical (Hampshire, UK), who loaned the Asena GH infusion pumps for the study

Country: France

Setting: inpatient, single-centre

Author's name: Marc Fischler

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Bataille 2016 *(Continued)*

Institution: Department of Anaesthesiology, Hôpital Foch, Suresnes, France

Email: m.fischler@hospital-foch.org

Address: Department of Anaesthesiology, Hôpital Foch, 40 rue Worth, 92151 Suresnes, France

Duration of study: June 2013 to January 2014

Language: English

Study's primary outcome: overall incidence of PONV during first 24 hours, defined as any episode of vomiting or nausea

Trial registry number: NCT01876290

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the sequence of treatment with dexamethasone and ondansetron (DO group) or placebo (Placebo group) was determined in blocks of 10 (five DO and five Placebo group) using an internet-based randomisation system in a 1:1 ratio"
Allocation concealment (selection bias)	Low risk	Quote: "the sequence of treatment with dexamethasone and ondansetron (DO group) or placebo (Placebo group) was determined in blocks of 10 (five DO and five Placebo group) using an internet-based randomisation system in a 1:1 ratio. The randomisation system gave the assignment to the pharmacy 1 h prior to induction of anaesthesia" Quote: "written informed consent was obtained during the preoperative visit performed by the investigators"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the drugs or placebo [was] prepared in the pharmacy in a volume of 10 ml and [was] colourless and indistinguishable"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: no statement on outcome assessors Blinding of outcome assessors assumed due to the central allocation system and indistinguishable appearance of syringes
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "among 130 obese patients who were approached, 122 were recruited between June 2013 and January 2014. Usable data were obtained from 58 patients in the DO group and 59 patients in the Placebo group (Fig. 1)" Judgement comment: reasons for missing outcome data described and unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01876290 (retrospective registration)
Other bias	Low risk	Quote: "baseline characteristics and risk factors for PONV were similar between the two groups; median of BMI was greater than 40 kg/m^2 in both the groups (Table 1)"

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Bataille 2016 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Baxendale 1993

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + hyoscine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 23.7 (18 to 45) • *Weight (mean ± SD, median (IQR), median (range))*: 66.0 (46 to 102) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 62.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 13.7 • *Use of perioperative opioids (if yes, which?)*: no participants required postoperative morphine 10 mg IM • *Type of surgery*: extraction of 3 or 4 impacted third molar teeth Placebo + hyoscine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 21.9 (18 to 28) • *Weight (mean ± SD, median (IQR), median (range))*: 64.3 (46 to 83) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60.0 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 13.4 • *Use of perioperative opioids (if yes, which?)*: 9 participants required postoperative morphine 10 mg IM • *Type of surgery*: extraction of 3 or 4 impacted third molar teeth **Included criteria:** adult patients, grade ASA I or II, scheduled for extraction of 3 or 4 impacted third molar teeth under general anaesthesia

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Baxendale 1993 *(Continued)*

	Excluded criteria: NA **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes
Interventions	**Intervention characteristics** Dexamethasone + hyoscine • *Dose*: dexamethasone 8 mg, hyoscine 0.3 mg • *Time point of administration*: dexamethasone: approximately 2 hours before surgery, hyoscine at premedication • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Placebo + hyoscine • *Dose* placebo, hyoscine 0.3 mg • *Time point of administration*: placebo approximately 2 hours before surgery, hyoscine at premedication • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Vomiting (immediate postoperative period)* • Outcome type: dichotomous outcome *Postoperative wound infection (after one week)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** inpatient, single-centre **Author's name:** B.R. Baxendale **Institution:** Queen's Medical Centre, Nottingham **Email:** NA **Address:** University Department of Anaesthesia, Queen's Medical Centre, Nottingham NG7 2UH **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None
Risk of bias	

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Baxendale 1993 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomisation and preparation of dexamethasone or placebo powders were undertaken by the Pharmacy Department" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Low risk	Judgement comment: central randomisation and allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patient randomisation and preparation of dexamethasone or placebo powders were undertaken by the Pharmacy Department" Judgement comment: blinding ensured (central randomisation, allocation, preparation of drugs)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: blinding ensured (central randomisation, allocation, preparation of drugs)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one patient in the dexamethasone group was omitted from the study as only two teeth were removed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there were no differences between the groups in respect of gender, age, weight, or duration of surgery (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Beattie 1993

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 8 groups, dose-finding study, monoprophylaxis
Participants	**Baseline characteristics** Placebo (menstrual group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 9 • *Received treatment (n)*: 9 • *Analysed (n)*: 9 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Beattie 1993 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic tubal ligation

Droperidol (10 µg/kg, menstrual group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 9
- *Received treatment (n)*: 9
- *Analysed (n)*: 9
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic tubal ligation

Droperidol (20 µg/kg, menstrual group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 8
- *Received treatment (n)*: 8
- *Analysed (n)*: 8
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 22.2 (menstrual group)
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic tubal ligation

Droperidol (30 µg/kg, menstrual group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 9
- *Received treatment (n)*: 9
- *Analysed (n)*: 9
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA

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Beattie 1993 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic tubal ligation

Placebo (non-menstrual group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 17
- *Received treatment (n)*: 17
- *Analysed (n)*: 17
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic tubal ligation

Droperidol (10 µg/kg, non-menstrual group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 17
- *Received treatment (n)*: 17
- *Analysed (n)*: 17
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic tubal ligation

Droperidol (20 µg/kg, non-menstrual group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 16
- *Received treatment (n)*: 16

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Beattie 1993 *(Continued)*

- *Analysed (n)*: 16
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic tubal ligation

Droperidol (30 µg/kg, non-menstrual group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: 15
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic tubal ligation

Included criteria: female, ASA I or II, scheduled for elective laparoscopic tubal ligation

Excluded criteria: patients who were taking contraceptive or antiemetic medication, patients not sure of the date of their last menstruation, patients who had given birth recently but had not yet had normal menstruation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Placebo (menstrual group)

- *Dose*: placebo
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (10 µg/kg, menstrual group)

- *Dose*: 10 µg/kg
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

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Beattie 1993 *(Continued)*

	Droperidol (20 µg/kg, menstrual group) • *Dose*: 20 µg/kg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (30 µg/kg, menstrual group) • *Dose*: 30 µg/kg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo (non-menstrual group) • *Dose*: placebo • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (10 µg/kg, non-menstrual group) • *Dose*: 10 µg/kg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (20 µg/kg, non-menstrual group) • *Dose*: 20 µg/kg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (30 µg/kg, non-menstrual group) • *Dose*: 30 µg/kg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Canada

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Beattie 1993 *(Continued)*

Setting: outpatient, single-centre

Author's name: W.S. Beattie

Institution: McMaster University, Hamilton, Ontario, Canada

Email: NA

Address: Department of Anaesthesia, Room HSC-2U, McMaster University, 1200 Main Street West, Hamilton, Ontario, Canada L8N 3Z5

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	Eight groups were pooled into 4 groups (menstrual and non-menstrual groups with same doses pooled for analysis)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized study drug" No information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "nausea or vomiting was recorded in a blinded manner"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Benevides 2013

Study characteristics

Methods	**Study design:** randomized controlled trial

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Benevides 2013 *(Continued)*

Study grouping: 3 groups, monoprophylaxis and combination prophylaxis

Participants

Baseline characteristics

Ondansetron (Group O)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: 31
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 34 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 118.7 ± 23.1
- *BMI (mean ± SD, median (IQR), median (range))*: 43.3 ± 7.4
- *ASA I/II/III/IV (n)*: 1/26/3/0
- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (propofol, remifentanil, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 154
- *Use of perioperative opioids (if yes, which?)*: remifentanil and fentanyl (3 mg/kg) intraoperative, morphine 8.8 mg
- *Type of surgery*: laparoscopic sleeve gastrectomy

Dexamethasone + ondansetron (Group DO)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: 32
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 116.5 ± 25.1
- *BMI (mean ± SD, median (IQR), median (range))*: 41.9 ± 5.6
- *ASA I/II/III/IV (n)*: 0/27/3/0
- *Gender (female in %)*: 63.3
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (propofol, remifentanil, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142
- *Use of perioperative opioids (if yes, which?)*: remifentanil and fentanyl (3 mg/kg) intraoperative, morphine 7.8 mg
- *Type of surgery*: laparoscopic sleeve gastrectomy

Haloperidol + dexamethasone + ondansetron (Group HDO)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: 31
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 111.9 ± 15.4
- *BMI (mean ± SD, median (IQR), median (range))*: 41.3 ± 3.8
- *ASA I/II/III/IV (n)*: 0/30/0/0

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Benevides 2013 *(Continued)*

- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (propofol, remifentanil, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 146
- *Use of perioperative opioids (if yes, which?)*: remifentanil and fentanyl (3 mg/kg) intraoperative, morphine 4.4 mg
- *Type of surgery*: laparoscopic sleeve gastrectomy

Included criteria: patients over 18 years of age, ASA status I to III, body mass index (BMI) ≥ 35 kg/m^2, scheduled to undergo laparoscopic sleeve gastrectomy

Excluded criteria: patients with hypersensitivity or contraindication to haloperidol, dexamethasone, or ondansetron; any serious complications in the perioperative period (such as shock, cardiac arrest, haemorrhage needing transfusion); psychiatric disorder; history of migraine; use of opoid, hormonal anti-inflammatory, and antiemetic medication 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker -> no difference in the distribution of Apfel risk factors between the groups): unclear; (perioperative opioids): yes

Interventions

Intervention characteristics

Ondansetron (Group O)

- *Dose*: 8 mg
- *Time point of administration*: 20 to 30 minutes before end of operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 20% (metoclopramide 10 mg IV)

Dexamethasone + ondansetron (Group DO)

- *Dose*: dexamethasone 8 mg, ondansetron 8 mg
- *Time point of administration*: dexamethasone immediately after induction of anaesthesia, ondansetron 20 to 30 minutes before end of operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 40% (metoclopramide 10 mg IV)

Haloperidol + dexamethasone + ondansetron (Group HDO)

- *Dose*: haloperidol 2 mg, dexamethasone 8 mg, ondansetron 8 mg
- *Time point of administration*: haloperidol and dexamethasone immediately after induction of anaesthesia, ondansetron 20 to 30 minutes before end of operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 50% (metoclopramide 10 mg IV)

Outcomes

Vomiting (0 to 2 hours, PACU)

- Outcome type: dichotomous outcome

Vomiting (2 to 12 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 36 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Brazil

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Benevides 2013 *(Continued)*

Setting: inpatient, single-centre

Author's name: M.L. Benevides

Institution: Department of Surgery, Medical School, Federal University of Mato Grosso, Cuiabá, Mato Grosso, Brazil

Email: mmmmb@terra.com.br

Address: Department of Surgery, Medical School, Federal University of Mato Grosso, Cuiabá, Mato Grosso, Brazil

Duration of study: January to October 2011

Language: English

Study's primary outcome: primary endpoints of the study were occurrence of PONV, time to first administration of rescue antiemetic drug, and number of rescues

Trial registry number: RBR-4bxdhb

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization lists were computer-generated. In the operating room, sealed envelopes containing the groups were opened"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: it is not clear who performed randomization and allocation Not stated sequentially numbered, opaque, sealed envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the patients, anesthesiologists, and surgeons were unaware of the randomization process and the types of drugs used"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "data collection was done by blinded personnel"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred three patients were recruited for the study. Ninety-six patients were randomized to the study. One patient was excluded due to conversion to laparotomy and another patient was excluded due to cancelation of the operation. Three patients were excluded due to loss of follow-up, and two patients were excluded due to postoperative complications (one case for upper digestive hemmorage and another for dehiscence of the suture line requiring reoperation). Another patient was excluded for having allergy to dipyrone (angioedema). One patient was excluded from analysis for having received droperidol (protocol violation). Of these 90 patients, three patients in group O and four in group HDO were discharged prior to completing the postoperative follow-up at 36 h"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: RBR-4bxdhb (retrospective registration)
Other bias	High risk	Quote: "there were no significant differences between groups regarding patient demographics, ASA physical status, Apfel score, duration of preoperative

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Benevides 2013 *(Continued)*

	fasting, anesthesia time, volume of fluids infused during surgery, and duration of PACU stay (Table 1)"
	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker -> no difference in the distribution of Apfel risk factors between the groups): unclear; (perioperative opioids): yes

Bergese 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Aprepitant + promethazine + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 48 • *Age (mean ± SD, median (IQR), median (range))*: 52.1 ± 14.5 • *Weight (mean ± SD, median (IQR), median (range))*: 86.2 ± 21.6 • *BMI (mean ± SD, median (IQR), median (range))*: 29.5 ± 6.5 • *ASA I/II/III/IV (n)*: 13/34/1/0 • *Gender (female in %)*: 54 • *Non-smoker (%)*: 73 • *History of PONV/motion sickness (%)*: 40 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, sevoflurane, desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 308.4 • *Use of perioperative opioids (if yes, which?)*: 54.0 mg morphine, fentanyl 0.75 to 1.5 µg/kg IV + boluses of 0.5 to 2.0 µg/kg IV • *Type of surgery*: elective craniotomy Ondansetron + promethazine + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 47 • *Age (mean ± SD, median (IQR), median (range))*: 51.4 ± 16.8 • *Weight (mean ± SD, median (IQR), median (range))*: 86.8 ± 18.6 • *BMI (mean ± SD, median (IQR), median (range))*: 30.5 ± 7.3 • *ASA I/II/III/IV (n)*: 13/28/6/0 • *Gender (female in %)*: 53 • *Non-smoker (%)*: 77 • *History of PONV/motion sickness (%)*: 36 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, sevoflurane, desflurane)

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Bergese 2016 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 345 mg morphine, fentanyl 0.75 to 1.5 µg/kg IV + boluses of 0.5 to 2.0 µg/kg IV
- *Use of perioperative opioids (if yes, which?)*: 75.0
- *Type of surgery*: elective craniotomy

Included criteria: neurosurgical patients whose ages ranged from 18 to 85 years, American Society of Anesthesiologist (ASA) physical status of I to III, scheduled to undergo elective craniotomy (opening of the cranium and dura mater) requiring at least 1 hour of general anaesthesia, moderate to severe risk for PONV as assessed by having 2 or more risk factors on the simplified Apfel score

Excluded criteria: prisoners or mentally ill people, past medical history of alcohol or drug abuse, history of allergy reaction or intolerance to any study medications, pregnant or breastfeeding women, history of nausea and/or vomiting within 24 hours of procedure, history of treatment with antiemetic medication for nausea or vomiting within 24 hours of procedure, history of chemotherapy treatment within 4 weeks before surgery. Only patients having craniotomy procedures and requiring admission were included. Patients who had received any medication with antiemetic properties before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Aprepitant + promethazine + dexamethasone • *Dose*: aprepitant 40 mg, promethazine 25 mg, dexamethasone 10 mg, placebo • *Time point of administration*: aprepitant 30 to 60 minutes before induction of anaesthesia; placebo, promethazine, and dexamethasone at induction of anaesthesia • *Route of administration*: aprepitant: oral, placebo, promethazine, and dexamethasone IV • *Rescue antiemetics (if yes, which?)*: 44% (choice left to investigator's discretion) Ondansetron + promethazine + dexamethasone • *Dose*: ondansetron 4 mg, promethazine 25 mg, dexamethasone 10 mg, placebo • *Time point of administration*: placebo pill 30 to 60 minutes before induction of anaesthesia; ondansetron, promethazine, and dexamethasone at induction of anaesthesia • *Route of administration*: placebo pill oral, ondansetron, promethazine, and dexamethasone IV • *Rescue antiemetics (if yes, which?)*: 53% (choice left to investigator's discretion)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 5-day follow-up)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this research pilot study was funded by The Ohio State University Medical Center, Department of Anesthesiology **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Alberto A. Uribe **Institution:** Department of Anesthesiology, The Ohio State University Wexner Medical Center, Columbus, OH, USA

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Bergese 2016 *(Continued)*

Email: alberto.uribe@osumc.edu

Address: Department of Anesthesiology, The Ohio State University Wexner Medical Center, Columbus, OH, USA

Duration of study: January 2009 to April 2012

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NCT01474915

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the method used for randomization was simple randomization using a random list generator"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the health-care providers and researchers were blinded throughout the study, the only unblinded personnel was the pharmacist who prepared the study drug based on the randomization list"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the health-care providers and researchers were blinded throughout the study, the only unblinded personnel was the pharmacist who prepared the study drug based on the randomization list"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "total of 121 subjects were screened and enrolled to participate in this study. However, 6 subjects were considered screen failures due to failure to meet inclusion criteria or meeting exclusion criteria, and 20 subjects were removed from the study due to protocol deviations that could affect our data analysis. Deviations from the protocol included anesthesia care staff not administrating the triple therapy as directed, prolonged intubation after surgery, and/or loss of follow-up. Ninety-five subjects completed the study: 48 in the aprepitant group and 47 in the ondansetron group"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01474915 (retrospective registration)
Other bias	Low risk	Quote: "there were no statistically significant differences among subjects' demographics, risk factors for PONV, duration of anaesthesia, and postoperative opioid consumption between the two groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Bestas 2007

Study characteristics

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Bestas 2007 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 39.1 ± 4.8 • *Weight (mean ± SD, median (IQR), median (range))*: 74.9 ± 10.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 80 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 89.5 • *Use of perioperative opioids (if yes, which?)*: 145.5 µg fentanyl intraoperative + 107.5 µg fentanyl post-operative • *Type of surgery*: laparoscopic cholecystectomy Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 41.6 ± 8.3 • *Weight (mean ± SD, median (IQR), median (range))*: 71.9 ± 8.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 73 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 92.1 • *Use of perioperative opioids (if yes, which?)*: 156.5 µg fentanyl intraoperative + 118.5 µg fentanyl post-operative • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 40.6 ± 9.9 • *Weight (mean ± SD, median (IQR), median (range))*: 73.6 ± 13.0

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Bestas 2007 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 77
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 85.5
- *Use of perioperative opioids (if yes, which?)*: 154.1 µg fentanyl intraoperative + 113.3 µg fentanyl post-operative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: consecutive adult patients of both sexes classified as American Society of Anesthesiologists physical status I or II, scheduled for elective laparoscopic cholecystectomy

Excluded criteria: patients with history of PONV and/or motion sickness; patients who were pregnant, lactating, or menstruating; those with clinically notable gastrointestinal, cardiovascular, neurological, renal, hepatic, or endocrinological disease (e.g. obesity, diabetes mellitus); those receiving drugs with known antiemetic effects

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 100 µg /kg • *Time point of administration*: approximately 20 to 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 30% (metoclopramide 10 mg) Granisetron • *Dose*: 40 µg /kg • *Time point of administration*: approximately 20 to 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (metoclopramide 10 mg) Placebo • *Dose*: saline • *Time point of administration*: approximately 20 to 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 60% (metoclopramide 10 mg)
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey

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Bestas 2007 *(Continued)*

Setting: inpatient, single-centre

Author's name: Azize Bestas

Institution: Firat University School of Medicine, Elazig, Turkey

Email: abestas@firat.edu.tr

Address: Flrat Üniversitesi Tip Fakfiltesi, Anesteziyoloji ve Reanimasyon AD, 23119 Elazlg, Turkey

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all study drugs (ondansetron 100 µg/kg, granisetron 40 µg/kg, and normal saline) were diluted by a nurse anesthetist to a fixed volume of 100 ml and marked with a coded label to ensure the double-blind nature of the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all patients were observed in the recovery room during the first postoperative hour and then in the ward by the same investigator (A.Y.) who was blinded to the treatment groups"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "ninety patients (69 women, 21 men) were included in the study. There were 30 patients in each group, and all of the patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the 3 groups in regard to demographic characteristics, mean duration of surgery, mean duration of anesthesia, or intraoperative total fentanyl consumption (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Bhalla 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 38.18 • *Weight (mean ± SD, median (IQR), median (range))*: 67.12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 30/20/0/0 • *Gender (female in %)*: 52 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 33.82 • *Use of perioperative opioids (if yes, which?)*: 98.5 µg fentanyl • *Type of surgery*: laparoscopic cholecystectomy Palonosetron (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 36.92 • *Weight (mean ± SD, median (IQR), median (range))*: 65.92 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 28/22/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 34.58 • *Use of perioperative opioids (if yes, which?)*: 97.8 µg fentanyl • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** 18 to 60 years of age, ASA grade I and II and Apfel score ≥ 2, undergoing elective laparoscopic cholecystectomy under general anaesthesia **Excluded criteria:** history of allergy to any drug being used in the study, history of vomiting/retching/nausea/antiemetics in 24 hours preceding administration of anaesthesia, taking chronic steroids/prokinetics/antiemetics/antacids, menstruating/lactating or pregnant females, alcohol or substance abuse, significant disease of major organs like liver, kidneys, heart, lungs, and bone marrow

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Bhalla 2015 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Ondansetron (group A) • *Dose*: 4 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 32% (dexamethasone 8 mg) Palonosetron (group B) • *Dose*: 0.075 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16% (dexamethasone 8 mg)
Outcomes	*Vomiting or retching (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** nil **Country:** India **Setting:** inpatient, single-centre **Author's name:** Dr. Neha Baduni **Institution:** tertiary care hospital of New Delhi **Email:** moc.liamg@ahen.inudaB **Address:** GH 12/183, Paschim Vihar, New Delhi - 110 087, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Bhalla 2015 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "these patients were divided (chit in the box)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "(palonosetron 0.075 mg fixed dose). The syringes containing the study drug (10 ml) were prepared by an anaesthesiologist who was blinded to randomization schedule and not involved in the study. A written informed consent form"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "accepted as statistically significant. The two groups were comparable with respect to age, gender, weight and ASA grading [Table 1]. The mean duration of anesthesia and the mean amount of intraoperative fentanyl used were comparable in the two groups [Table 2]. The incidence of nausea was..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Bhatia 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Bhatia 2008 *(Continued)*

- *Type of general anaesthesia*: combined anaesthesia (N_2O, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: diagnostic or therapeutic gynaecological laparoscopic surgery

Metoclopramide (group II)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (N_2O, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: diagnostic or therapeutic gynaecological laparoscopic surgery

Ondansetron (group III)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (N_2O, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: diagnostic or therapeutic gynaecological laparoscopic surgery

Granisetron (group IV)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0

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Bhatia 2008 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (N_2O, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: diagnostic or therapeutic gynaecological laparoscopic surgery

Included criteria: female patients, ASA grade I and II, 18 to 40 years of age, scheduled to undergo diagnostic or therapeutic gynaecological laparoscopic surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, BMI, ASA -> no data provided): no. Potential effect modifiers (gender, duration of anaesthesia -> no data provided): no; (non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo (group I) • *Dose*: 0.9% saline • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16.67% (ondansetron 4 mg, dexamethasone 8 mg) Metoclopramide (group II) • *Dose*: 10 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 13.33% (ondansetron 4 mg, dexamethasone 8 mg) Ondansetron (group III) • *Dose*: 4 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 6.67% (ondansetron 4 mg, dexamethasone 8 mg) Granisetron (group IV) • *Dose*: 3 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 3.33% (ondansetron 4 mg, dexamethasone 8 mg)
Outcomes	*Sedation/drowsiness (0 hours to discharge)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** outpatient, single-centre

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Bhatia 2008 *(Continued)*

Author's name: Nidhi Bhatia

Institution: Dept. of Anaesthesiology, Govt. Medical College Hospital

Email: bhatia.nidhi@yahoo.co.in

Address: 32B, Sector 32, Chandigarh, 160030, India

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly divided into four groups of 30 patients" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind design")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind design")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data (no statement, but data in tables (%) support the assumption of no missing data)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients in all the groups were statistically comparable as regards to age, body mass index (BMI) and duration of anaesthesia (DOA)" Judgement comment: baseline characteristics (age, BMI, ASA -> no data provided): no. Potential effect modifiers (gender, duration of anaesthesia -> no data provided): no; (non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Bhatnagar 2007

Study characteristics

Methods	**Study design:** randomized controlled trial

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Bhatnagar 2007 *(Continued)*

Study grouping: 3 groups, monoprophylaxis

Participants

Baseline characteristics

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 13.33/10
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction, 10 patients with postoperative tramadol 100 mg, 1 patient with morphine 3 mg within 2 hours
- *Type of surgery*: modified radical mastectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 48 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 16.67/13.33
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction, 10 patients with postoperative tramadol 100 mg, no patients with morphine 3 mg within 2 hours
- *Type of surgery*: modified radical mastectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0

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Bhatnagar 2007 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 16.67/13.33
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 141
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction, 9 patients with postoperative tramadol 100 mg, no patients with morphine 3 mg within 2 hours
- *Type of surgery*: modified radical mastectomy

Included criteria: ASA physical status I and II, hospitalised female patients, 18 to 65 years of age, scheduled for modified radical mastectomy

Excluded criteria: patients with gastrointestinal (GI) disease (e.g. hiatal hernia, gastro-oesophageal regurgitation disorder, non-ulcerative dyspepsia, peptic ulcer disease, and autonomic dysfunction disorder); those who were menstruating; those who had received any antiemetic medication within 24 hours of surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: placebo • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Granisetron • *Dose*: 2 mg • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Ondansetron • *Dose*: 4 mg • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 2, 2 to 6, 6 to 12, 12 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 2, 2 to 6, 6 to 12, 12 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 2, 2 to 6, 6 to 12, 12 to 24 hours)*

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Bhatnagar 2007 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Sushma Bhatnagar **Institution:** Department of Anesthesiology, Institute Rotary Cancer Hospital (IRCH), All India Institute of Medical Sciences (AIIMS) **Email:** shumob@yahoo.com **Address:** Department of Anesthesiology, Institute Rotary Cancer Hospital (IRCH), All India Institute of Medical Sciences (AIIMS), Ansari Nagar, New Delhi 110029, India **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "generated by a random number function in a computer spreadsheet"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients and data collectors were both blinded to treatment" Quote: "all three study drugs were provided as identical, blue, cylindrical capsules and administered according to a randomization list"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients and data collectors were both blinded to treatment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "no patient was withdrawn from the study" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "in our study, the groups were similar with respect to age, weight, preoperative chemotherapy, history of motion sickness or previous PONV, last menstrual period, duration of anesthesia and surgery, and postoperative analgesia"

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Bhatnagar 2007 *(Continued)*

Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Bhattacharjee 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron (group G) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 42.3 ± 4.32 • *Weight (mean ± SD, median (IQR), median (range))*: 52.24 ± 7.36 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 52.72 • *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction • *Type of surgery*: laparoscopic cholecystectomy Palonosetron (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 43.4 ± 6.46 • *Weight (mean ± SD, median (IQR), median (range))*: 54.42 ± 8.22 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: Inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 55.82 • *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** ASA I and II female patients, 18 to 65 years of age, undergoing elective laparoscopic cholecystectomy

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Bhattacharjee 2010 *(Continued)*

	Excluded criteria: gastrointestinal disease; history of smoking, motion sickness, and/or PONV; pregnant or menstruating; taking antiemetic medication within last 24 hours **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear
Interventions	**Intervention characteristics** Granisetron (group G) • *Dose*: 2.5 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide10 mg IV Palonosetron (group P) • *Dose*: 75 µg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide10 mg IV
Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 3, 3 to 24, 24 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 3, 3 to 24, 24 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Dhurjoti Prosad Bhattacharjee **Institution:** Department of Anaesthesiology, Calcutta National Medical College, Kolkata **Email:** dhurjotib@yahoo.com **Address:** 32 Gorachand Road, Beniapukur, Kolkata, West Bengal 700014, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA

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Bhattacharjee 2010 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated randomization schedule"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "identical syringes containing study medications (2.5 ml) were prepared by the [personnel] who were blinded to the computer generated randomization"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all patients were observed postoperatively by resident doctors who were unaware of the study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Bhattacharya 2003

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 32 (28 to 40) • *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 2.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Bhattacharya 2003 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 45
- *Use of perioperative opioids (if yes, which?)*: pethidine for anaesthesia
- *Type of surgery*: laparoscopic tubal ligation

Granisetron (group B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 33 (26 to 42)
- *Weight (mean ± SD, median (IQR), median (range))*: 51 ± 2.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 44
- *Use of perioperative opioids (if yes, which?)*: pethidine for anaesthesia
- *Type of surgery*: laparoscopic tubal ligation

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 30 (26 to 35)
- *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 0.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 42
- *Use of perioperative opioids (if yes, which?)*: pethidine for anaesthesia
- *Type of surgery*: laparoscopic tubal ligation

Included criteria: ASA grade I and II, in the postmenstrual phase (first half of menstrual cycle), undergoing laparoscopic tubal ligation under general anaesthesia, admitted for day case surgery following an overnight fast of 8 to 10 hours

Excluded criteria: lactating, body weight > 80 kg, taking any medications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics**
	Ondansetron (group A)

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Bhattacharya 2003 *(Continued)*

- *Dose*: 4 mg
- *Time point of administration*: two minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV

Granisetron (group B)

- *Dose*: 2 mg
- *Time point of administration*: two minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV

Placebo (group C)

- *Dose*: saline
- *Time point of administration*: two minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV

Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** outpatient, single-centre **Author's name:** Dipasri Bhattacharya **Institution:** Dept. of Anaesthesiology, R.G.Kar Medical College, Kolkata **Email:** dbhattacharya1@rediffmail.com **Address:** B/26/10, Abhyudoy Cooperative; E.C.T.P. Phase IV, P.O. ECT. Kolkata - 700107 **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "90 patients were allocated into three equal groups in a double blind randomized placebo controlled manner" Judgement comment: no further Information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Bhattacharya 2003 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "study medications (2 ml) were prepared by one of the investigators and were administered using double blind design. Group A (n=30) received 2" Judgement comment: insufficient information on blinding ("double-blind design")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "emetic episodes were assessed immediately after operation and at one hour interval for six hours" Judgement comment: insufficient information on blinding ("double-blind design")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Bhattarai 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 30.71 ± 9.29 (males), 28.58 ± 5.85 (females) • *Weight (mean ± SD, median (IQR), median (range))*: 59.57 ± 5.29 (males), 49.63 ± 7.03 (females) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 86 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 66.26 • *Use of perioperative opioids (if yes, which?)*: pethidine intraoperatively • *Type of surgery*: diagnostic laparoscopy, cholecystectomy, appendectomy Ondansetron + dexamethasone (group II) • *Assessed for eligibility (n)*: -

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Bhattarai 2011 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 33 ± 10.11 (males), 26.36 ± 6.29 (females)
- *Weight (mean ± SD, median (IQR), median (range))*: 59.14 ± 8 (males), 51 ± 7.40 (females)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 80
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 68.10
- *Use of perioperative opioids (if yes, which?)*: pethidine intraoperatively
- *Type of surgery*: diagnostic laparoscopy, cholecystectomy, appendectomy

Included criteria: ASA I and II, undergoing laparoscopic surgery, between 18 and 55 years of age, weighing between 30 and 75 kg

Excluded criteria: ASA III and IV; had received opioids, non-steroidal anti-inflammatory drugs, steroids, and antiemetic agents during the previous 24 hours; history of PONV/ motion sickness, previous PONV

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group I) • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV (22%) Ondansetron + dexamethasone (group II) • *Dose*: ondansetron 4 mg, dexamethasone 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV (8%)
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (study period)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** nil

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Bhattarai 2011 *(Continued)*

Country: Nepal

Setting: single-centre, NA

Author's name: Basant Bhattarai

Institution: Department of Anesthesiology, Dhulikhel Hospital

Email: moc.oohay@iarattahbtnasab

Address: Dhulikhel 45200, Nepal

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "2 patients undergoing laparoscopic surgery. They were then randomly divided into Group I and Group II with sealed envelope technique of 50 patients in each"
Allocation concealment (selection bias)	Unclear risk	Quote: "with sealed envelope technique of 50 patients in each group" Judgement comment: not stated; "sequentially numbered, opaque" envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "use of opioids, and pain. In our study, the majority of these factors (age, gender, weight, duration of the procedure, anesthetic technique, and medication) were not significant among both the study groups. The selection of drug dosages..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

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Bianchin 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline Characteristics** Dexamethasone (group DESA) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 55 (24 to 80) • *Weight (mean ± SD, median (IQR), median (range))*: 69 (51 to 104) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 69.44 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 78 • *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia up to 3 µg/kg • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 56 (31 to 80) • *Weight (mean ± SD, median (IQR), median (range))*: 71 (49 to 100) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 59.46 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 86 • *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia up to 3 µg/kg • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** scheduled for laparoscopic cholecystectomy **Excluded criteria:** ASA status III and IV, over 80 years or under 20 years of age, endoscopic retrograde cholangiopancreatography within 1 month before operation, chronic pain disorder; history of alcohol abuse, uncontrolled metabolic disease (diabetes mellitus, hypertension), previous PONV for general anaesthesia

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Bianchin 2007 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Dexamethasone (group DESA) • *Dose*: 8 mg • *Time point of administration*: 2 minutes before beginning of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo • *Dose*: normal saline • *Time point of administration*: 2 minutes before beginning of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (postoperatively)* • Outcome type: dichotomous outcome *Subjects with any AE (postoperatively)* • Outcome type: dichotomous outcome *Postoperative wound infection (postoperatively)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** A. Bianchin **Institution:** Anesthesia Department, ASL 8 Asolo, G. Carretta City Hospital, Montebelluna, Treviso, Italy **Email:** andbia@libero.it **Address:** Via Marco Polo 25/7, 31031 Caerano S. Marco (TV), Italy **Language:** English **Duration of study:** NA **Trial registry number:** NA

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Bianchin 2007 *(Continued)*

	Study's primary outcome: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "each patient was allocated randomly to one of the two groups using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patient, anaesthesiologist, surgeon and nurses were all blinded with respect to the study group"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "nurses were all blinded with respect to the study group" Judgement comment: no information on outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "eighty patients were enrolled. Seven were excluded: 4 laparotomic conversions, 2 for anaesthesiological reasons (droperidol, fentanyl over 3 µg/kg), 1 laparoscopic [cholecystectomy and hernioplasty]. Seventy-three patients have completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Biedler 1998

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 195 • *Received treatment (n)*: 195 • *Analysed (n)*: 195 • *Age (mean ± SD, median (IQR), median (range))*: 51.4 ± 13.5 • *Weight (mean ± SD, median (IQR), median (range))*: 68.8 ± 11.6 • *BMI (mean ± SD, median (IQR), median (range))*: 25.5 ± 4.1 • *ASA I/II/III/IV (n)*: NA/NA/NA/0

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Biedler 1998 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 39/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, volatile anaesthetic)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 154.7
- *Use of perioperative opioids (if yes, which?)*: fentanyl, piritramide
- *Type of surgery*: major gynaecological surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 195
- *Received treatment (n)*: 192
- *Analysed (n)*: 192
- *Age (mean ± SD, median (IQR), median (range))*: 49.9 ± 12.9
- *Weight (mean ± SD, median (IQR), median (range))*: 69.9 ± 11.1
- *BMI (mean ± SD, median (IQR), median (range))*: 25.8 ± 4.0
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 29/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, volatile anaesthetic)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 157.5
- *Use of perioperative opioids (if yes, which?)*: fentanyl, piritramide
- *Type of surgery*: major gynaecological surgery

Included criteria: women scheduled for major gynaecological surgery under general anaesthesia

Excluded criteria: younger than 18 years of age; weight > 100 kg; ASA IV or V, nausea; vomiting or antiemetic therapy during the last 24 hours before application of study drug; contraindications against ondansetron; history of drug or alcohol abuse; pregnancy or breastfeeding

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, peri-operative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 8 mg • *Time point of administration*: before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 28% (ondansetron 4 mg and additional other antiemetics) Placebo • *Dose*: saline • *Time point of administration*: before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 47% (ondansetron 4 mg and additional other antiemetics)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)*

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Biedler 1998 *(Continued)*

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** supported by Glaxo Wellcome, Bad Oldesloe **Country:** Germany **Setting:** inpatient, multi-centre (14) **Author's name:** A. Biedler **Institution:** Department of Anaesthesiology, Intensive Care and Pain Therapy, Saarland University Medical Center and Saarland University Faculty of Medicine **Email:** NA **Address:** Department of Anaesthesiology, Intensive Care and Pain Therapy, Saarland University Medical Center and Saarland University Faculty of Medicine, D-66421 Homburg/Saar. **Duration of study:** NA **Language:** German (reviewers were native speakers) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	All patients who have received ondansetron as prophylaxis or as rescue medication (from the placebo group) were combined for analysis of adverse events

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "menge physiologische Kochsalzlösung als Plazebo) erfolgte i.v. doppelblind und randomisiert unmittelbar vor Narkosebeginn. Prämedikation, Narkoseeinleitung und -führung" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "doppelblind" Judgement comment: insufficient information on blinding provided ("doppelblind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("doppelblind")

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Biedler 1998 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "insgesamt konnten die Studienprotokolle von 387 Patientinnen ausgewertet werden. Drei der 390 randomisierten Patientinnen erhielten keine Studienmedikation"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference at a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "die demographischen, anamnestischen und operativen Daten zeigt Tabelle 1. Zwischen beiden Gruppen bestand kein signifikanter Unterschied. Der Anteil von Patientinnen mit Übelkeit oder Erbrechen nach früheren Operationen war in der Ondansetrongruppe mit 39% tendenziell höher (p=0,06) als in der Plazebogruppe (29%)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Bilgin 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 39.55 ± 11.93 • *Weight (mean ± SD, median (IQR), median (range))*: 67.36 ± 11.37 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 93.64 • *Use of perioperative opioids (if yes, which?)*: 1 mg/kg tramadol at end of surgery, 18 participants needed rescue analgesic postoperatively • *Type of surgery*: total abdominal hysterectomy Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40

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Bilgin 2010 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 43.25 ± 10.24
- *Weight (mean ± SD, median (IQR), median (range))*: 71.92 ± 10.28
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100.83
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg tramadol at end of surgery, 22 participants needed rescue analgesic postoperatively
- *Type of surgery*: total abdominal hysterectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 46.38 ± 7.35
- *Weight (mean ± SD, median (IQR), median (range))*: 76.92 ± 12.37
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 107.69
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg tramadol at end of surgery, 25 participants needed rescue analgesic postoperatively
- *Type of surgery*: total abdominal hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 43.50 ± 7.18
- *Weight (mean ± SD, median (IQR), median (range))*: 71.43 ± 9.35
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100.36
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg tramadol at the end of surgery, 19 participants needed rescue analgesic postoperatively
- *Type of surgery*: total abdominal hysterectomy

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Bilgin 2010 *(Continued)*

	Included criteria: female, ASA class I and II, 20 to 60 years of age, scheduled for elective total abdominal hysterectomy with bilateral salpingo-oophorectomy under general anaesthesia **Excluded criteria:** history of motion sickness; previous postoperative vomiting, gastroesophageal reflux, or gastrointestinal disorders; taking medications with known antiemetic activity; pregnant or breastfeeding; previous adverse reaction to dexamethasone, ondansetron, metoclopramide, any other antiemetic; long-term opioid use; body weight > 100% over ideal; history of alcohol or drug abuse; receipt of an antiemetic agent within 24 hours; significant hepatic impairment; difficult endotracheal intubation **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0 to 2 hours 10% (metoclopramide 10 mg) Ondansetron • *Dose*: ondansetron 4 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0 to 2 hours 10% (metoclopramide 10 mg) Metoclopramide • *Dose*: metoclopramide 10 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0 to 2 hours 15% (metoclopramide 10 mg) Placebo • *Dose*: saline 0.9% • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0 to 2 hours 45% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 12 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome

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Bilgin 2010 *(Continued)*

	Adverse events (general notes in the publication, 24 hours' observation) • Outcome type: general notes on side effects
Identification	**Sponsorship source:** departmental sources **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Tugsan Egemen Bilgin **Institution:** Department of Anesthesiology and Reanimation, Mersin University School of Medicine, Mersin, Turkey **Email:** tugsanb@yahoo.com **Address:** Mersin University School of Medicine, Department of Anesthesiology and Reanimation, 33079 Mersin, Turkey **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** reduction in the incidence of PONV at 24 hours
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomly to receive 1 of 4 study drugs. Randomization was done by random number table generated by a computer program. The drugs were prepared by an anesthetist who..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "program. The drugs were prepared by an anesthetist, who was not one of the observers, in three 2 ml syringes, which contained either 8 mg dexamethasone, 4 mg ondansetron, 10 mg metoclopramide, or 0.9% saline per syringe. They were marked only with a coded label to maintain the double-blind nature of the study. Thus, before induction of an..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "12–24 hours on the ward. This anesthetist, blinded to the study group, performed continuous observation of the patients in the recovery room. Nausea was defined as..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "Kruskal-Wallis test, followed by Mann-Whitney sum rank test for intergroup differences. Values for P less than.05 were considered significant. Data are shown as mean ± SD or n (%). There was no difference between groups in demographic data, duration of surgery, and anesthesia (Table 1). There was no

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Bilgin 2010 *(Continued)*

	statistically significant difference between groups in hemodynamic variables or SPO2"
	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Bisgaard 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 44 • *Received treatment (n)*: 44 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 46 (20 to 41) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26 (20 to 41) • *ASA I/II/III/IV (n)*: 33/7/0/0 • *Gender (female in %)*: 67.5 • *Non-smoker (%)*: 57.5 • *History of PONV/motion sickness (%)*: 32.5/57.5 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 78 • *Use of perioperative opioids (if yes, which?)*: 110 mg opioids • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 44 • *Received treatment (n)*: 44 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 39 (22 to 69) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25 (28 to 39) • *ASA I/II/III/IV (n)*: 34/6/0/0 • *Gender (female in %)*: 82.5 • *Non-smoker (%)*: 60 • *History of PONV/motion sickness (%)*: 27.5/47.5 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 68 • *Use of perioperative opioids (if yes, which?)*: 255 mg opioids • *Type of surgery*: laparoscopic cholecystectomy

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Bisgaard 2003 *(Continued)*

Included criteria: NA

Excluded criteria: ASA III or IV; over 75 years of age; pregnancy; having papillotomy by endoscopic retrograde cholangiopancreatography (ERCP) within 1 month before and during first month after operation; chronic pain disease other than gallstone disease; any signs of endocrine, renal, hepatic, or immunological disease; or received opioids or tranquillizers (treatment of over 1 week before LC); foreign language or mental disorder; history of alcohol or drug abuse; operation converted from LC to open procedure or additional fifth trocar needed to complete the operation. Finally, because development of surgical complications might influence chosen outcome parameters, we decided before study start to exclude these patients from the study and we analysed results by protocol

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: 90 minutes before surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 53.33% (ondansetron 4 mg IV)

Placebo

- *Dose*: -
- *Time point of administration*: 90 minutes before surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 37.5% (ondansetron 4 mg IV)

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (0 to 6 hours)

- Outcome type: dichotomous outcome

Vomiting (6 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Postoperative wound infection (0 to 7 days)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 30 days' follow-up)

- Outcome type: general notes on side effects

Identification

Sponsorship source: grants from University of Copenhagen and The Danish Medical Research Council (journal no. 9902757) supported this study

Country: Denmark

Setting: inpatient and outpatient, single-centre

Author's name: Thue Bisgaard

Institution: Department of Surgical Gastroenterology, University of Copenhagen, Hvidovre Hospital

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Bisgaard 2003 *(Continued)*

Email: huebisgaard@tdcadsl.dk

Address: Department of Surgical Gastroenterology 435, University of Copenhagen, Hvidovre Hospital, DK-2650 Hvidovre, Denmark

Duration of study: February 1999 to November 2000

Language: English

Study's primary outcome: primary endpoints were fatigue and pain

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomized by the sealed envelope method (on the basis of a block-randomized computer-generated list)"
Allocation concealment (selection bias)	Unclear risk	Quote: "patients were randomized by the sealed envelope method (on the basis of a block-randomized computer-generated list), and the randomization code was kept separate and not known to any of the investigators until the study was finished" Judgement comment: not stated; "sequentially numbered, opaque, sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the drug/placebo solution was drawn into a syringe by a nurse not participating in the study and was delivered to the investigator (TB) who was outside the medicine room and unaware of the content. The saline and dexamethasone solutions appeared transparent and completely identical at the time syringes were given to the investigator. Thus, the patient, the anesthesiologist, the surgeon, and the study observer were all blinded with respect to the study group"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "thus, the patient, the anesthesiologist, the surgeon, and the study observer were all blinded with respect to the study group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the study drugs were observed. Four patients in each study group were excluded from the study. In the dexamethasone group, 2 patients had cholecystectomy performed using an additional trocar (5-port cholecystectomy), since a laparoscopic paddle retractor was used to lift the liver to avoid conversion to open procedure. In 1 patient, preoperative cholangiography revealed a retained stone in the common bile duct, and endoscopic retrograde cholangiography (ERCP) with stone extraction was performed the next day. One patient developed an infection in the umbilical incision (skin opened 5 days after operation). In the placebo group, the operation was converted to open procedure in 2 patients (due to dense abdominal adhesions), 1 patient withdrew from the study postoperatively, and 1 patient developed an infection in the umbilical incision (skin opened 6 days after)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "with a significantly lower total dose of morphine in the dexamethasone group"

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Bisgaard 2003 *(Continued)*

	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Bisgaard 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Prednisolone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: 99 • *Analysed (n)*: 94 • *Age (mean ± SD, median (IQR), median (range))*: 44 (18 to 70) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27 (18 to 39) • *ASA I/II/III/IV (n)*: 77/17/0/0 • *Gender (female in %)*: 78.72 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 60 • *Use of perioperative opioids (if yes, which?)*: 3066 mg remifentanil, 16 µg sufentanil, 559 mg morphine, ketobemidone 5 mg at discharge • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: 100 • *Analysed (n)*: 90 • *Age (mean ± SD, median (IQR), median (range))*: 45 (18 to 74) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27 (20 to 41) • *ASA I/II/III/IV (n)*: 65/25/0/0 • *Gender (female in %)*: 78.89 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 53 • *Use of perioperative opioids (if yes, which?)*: 2940 mg remifentanil, 15 µg sufentanil, 639 mg morphine, ketobemidone 5 mg at discharge • *Type of surgery*: laparoscopic cholecystectomy

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Bisgaard 2008 *(Continued)*

	Included criteria: undergoing elective laparoscopic cholecystectomy, incorrect timing of tablet intake not considered a protocol violation. Patients with postoperative complications were also included in the analysis **Excluded criteria:** ASA physical class IV, younger than 18 and over 75 years of age, pregnancy. Patients were not included if they had chronic pain disease other than gallstone disease; history of or any signs of endocrine, renal, hepatic, or immunological disease; received opioids or tranquilizers (treatment for 1 week before laparoscopic cholecystectomy); foreign language or mental disorder; history of alcohol or drug abuse. Patients were excluded from the study (and study data were not collected) if the operation was converted from a laparoscopic to an open procedure. Patients were also excluded in the case of protocol violation (ingestion of none or only 1 study drug tablet), whereby incorrect timing of tablet intake (see below) was not considered a protocol violation **Pretreatment:** baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Prednisolone • *Dose*: 50 mg • *Time point of administration*: 2 hours before laparoscopic cholecystectomy • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: 27.66% (ondansetron 1 mg, dehydrobenzperidol 0.612 mg) Placebo • *Dose*: placebo tablets • *Time point of administration*: 2 hours before laparoscopic cholecystectomy • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: 41.11% (ondansetron 1 mg, dehydrobenzperidol 0.612 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (1 week)* • Outcome type: dichotomous outcome *Headache (one week)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 1 week of observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** study authors would like to thank Nycomed Danmark A/S, Denmark, for providing randomized concealed containers of study drugs for the trial

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Bisgaard 2008 *(Continued)*

Country: Denmark

Setting: inpatient and outpatient, single-centre

Author's name: T. Bisgaard

Institution: Department of Surgical Gastroenterology, Glostrup University Hospital, Glostrup, Denmark

Email: thuebisgaard@tdcadsl.dk

Address: Department of Surgical Gastroenterology, Glostrup University Hospital, Glostrup, Denmark

Duration of study: September 2003 to March 2005

Language: English

Study's primary outcome: primary outcome was pain 24 hours after operation

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were consecutively enrolled in the trial by the medical staff in the ambulatory unit and block-randomized by the manufacturer (Nycomed Danmark A/S)" Judgement comment: previous study (Bisgaard-2008) described the same study design and used a computer-generated list. We assumed the same procedure here
Allocation concealment (selection bias)	Low risk	Quote: "the study drugs were delivered in sealed indistinguishable containers bearing random numbers" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "boxes contained either two tablets of prednisone (25 mg each, total of 50 mg) or two placebo tablets of identical appearances. Patients were instructed to ingest the two tablets 2 h before the scheduled operation time. The randomization code was kept separate from the investigators by the manufacturer"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the randomization code was kept separate from the investigators by the manufacturer. The sequence was concealed until data analysis was completed more than 1 month after ending the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "in total, 184 patients were available for analysis and 16 patients (6 and 10 in the prednisone and placebo groups, respectively) were excluded from the study analysis (Fig. 1). Patient data were not available in nine patients due to the loss of the patient diary, four patients were converted to open procedure, one patient refused to participate after ingestion of the study tablets, one patient violated the study protocol, and one patient had the operation cancelled after the ingestion of the study tablets"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Bisgaard 2008 *(Continued)*

Other bias	Unclear risk	Quote: "there were no significant differences between the study groups except for the time interval between intake of tablets and operation [170 min (prednisone) versus 163 min (placebo)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Biswas 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 41.3 • *Weight (mean ± SD, median (IQR), median (range))*: 54 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 76.67 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 90 • *Use of perioperative opioids (if yes, which?)*: 241.5 mg pethidine postoperative • *Type of surgery*: laparoscopic cholecystectomy Granisetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 42.4 • *Weight (mean ± SD, median (IQR), median (range))*: 56 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 83.33 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 87

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Biswas 2003 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 242.0 mg pethidine postoperative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA physical status I or II, 21 to 55 years of age, patients of both sexes scheduled for laparoscopic cholecystectomy

Excluded criteria: gastrointestinal disease, history of motion sickness and/or previous history of PONV, pregnant or menstruating, smokers, diabetes mellitus, neuromuscular disorders, had taken antiemetic drugs within 3 days

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Granisetron • *Dose*: 40 µg/kg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV; 3% Granisetron + dexamethasone • *Dose*: granisetron 40 µg/kg, dexamethasone 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV; 0%
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 4, 4 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 4, 4 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Biswanath Biswas

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Biswas 2003 *(Continued)*

Institution: Department of Anesthesiology, Calcutta National Medical College and Hospital, Calcutta, India

Email: mita-tota@yahoo.co.in

Address: HA 327, Flat no. 8, Salt Lake, Sector III, Calcutta 700097, India

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: complete response

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications were prepared by personnel not involved in this study in identical 5 ml syringes to ensure blinding of the anesthetists"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients and investigators who collected postoperative data were blinded to the study drug administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to study protocol or trial registry number reported
Other bias	Low risk	Quote: "the treatment groups were comparable with regard to patient demographics and types of operation" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Bjerregaard 2018

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis

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Bjerregaard 2018 *(Continued)*

Participants

Baseline characteristics

Methylprednisolone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 59
- *Received treatment (n)*: 59
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 68 (61 to 75)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 21.2 ± 4.0
- *ASA I/II/III/IV (n)*: 3/30/23/0
- *Gender (female in %)*: 64
- *Non-smoker (%)*: 77
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol/remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104
- *Use of perioperative opioids (if yes, which?)*: remifentanil for anaesthesia, 5 mg morphine postoperative day 0, 0 mg morphine postoperative day 1, 0 mg morphine postoperative day 2
- *Type of surgery*: elective VATS lobectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: 60
- *Analysed (n)*: 47
- *Age (mean ± SD, median (IQR), median (range))*: 66.5 (60 to 73)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 21.8 ± 3.9
- *ASA I/II/III/IV (n)*: 8/18/30/0
- *Gender (female in %)*: 47
- *Non-smoker (%)*: 74
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol/remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102
- *Use of perioperative opioids (if yes, which?)*: remifentanil for anaesthesia, 5 mg morphine postoperative day 0, 0 mg morphine postoperative day 1, 0 mg morphine postoperative day 2
- *Type of surgery*: elective VATS lobectomy

Included criteria: consenting patients over 18 years of age who underwent elective VATS lobectomy at the Department of Cardiothoracic Surgery, Rigshospitalet, Copenhagen University Hospital, Denmark

Excluded criteria: inability to cooperate; inability to speak or understand Danish; no planned follow-up at Rigshospitalet; allergies to any used medicines; symptomatic gastric ulceration; New York Heart Association functional classification of III or more; preoperative increased plasma creatinine; pharmacologically treated diabetes mellitus; abuse of medicine or alcohol (over 5 units/d); use of psychopharmacological agents, systemic steroids (except inhalations), and/or opioid agonists; neurological deficits affecting pain perception; previous ipsilateral pulmonary resection; pregnant and/or breastfeeding. Included patients were withdrawn if they were re-operated on within 72 hours, had massive intrathoracic adherences, deviated from the standard postoperative analgesia, converted to thoracotomy, and/or breached protocol rules

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Bjerregaard 2018 *(Continued)*

	Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear
Interventions	**Intervention characteristics** Methylprednisolone • *Dose*: 125 mg • *Time point of administration*: after induction of anaesthesia, but before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: 2 mL saline • *Time point of administration*: after induction of anaesthesia, but before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Arrhythmia (during study period)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (during study period)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, study period)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by the 'Doctor Fritz Karner and wife Edith Karner's Foundation' and the 'Doctor Edgar Schnohr and wife Gilberte Schnohr's Foundation' **Country:** Denmark **Setting:** inpatient, single-centre **Author's name:** Lars S. Bjerregaard **Institution:** Rigshospitalet, Copenhagen University, Copenhagen East, Denmark **Email:** lars.stryhn.bjerregaard@regionh.dk **Address:** Section for Surgical Pathophysiology, Rigshospitalet, Copenhagen University, Blegdamsvej 9, Section 7621, 2100 Copenhagen, Denmark **Language:** English **Duration of study:** 21 March 2013 to 23 September 2015 **Trial registry number:** EUCTR2012-004451-37 **Study's primary outcome:** pain in the first 48 hours postoperatively
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Bjerregaard 2018 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "computer-generated randomization sequence"
Allocation concealment (selection bias)	Low risk	Quote: "before the start of the study, 100 sealed opaque envelopes were prepared by persons with no relation to the study" Judgement comment: quote: "opened the next envelope"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, caregivers and investigators were blinded to group assignment" Quote: "...depending on the enclosed information. The syringe was blinded by a plaster bandage and brought to the investigator who administered the medicine to the patient after induction of anaesthesia..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients, caregivers and investigators were blinded to group assignment" Quote: "postoperative pain, nausea and sedation were scored by trained nurses every 3rd hour from arrival in the PACU until midnight on the day of surgery"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "one (1%) patient withdrew informed consent and 23 (19%) patients were withdrawn by the investigators, leaving 96 (80%) patients for the final analysis" Judgement comment: high rate of missing data. Participants withdrawn by investigators > 15%, but reasons described and unrelated to outcomes of interest
Selective reporting (reporting bias)	Low risk	Judgement comment: EUCTR2012-004451-37 (prospective registration). The prospectively registered primary outcome (pain) was reported in the pre-specified way in the final study report. The primary outcome was not PONV-related
Other bias	Unclear risk	Quote: "baseline characteristics and perioperative data are presented in Tables 2 and 3, and with the exception of gender, these showed an acceptable balance between the groups" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear

Blitz 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Palonosetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 59 • *Received treatment (n)*: NA

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Blitz 2012 *(Continued)*

- *Analysed (n)*: 59
- *Age (mean ± SD, median (IQR), median (range))*: 35.2 ± 8.8
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 37.8 ± 11.5
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 81.36
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl during anaesthesia
- *Type of surgery*: laparoscopic abdominal or gynaecological surgery

Palonosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 59
- *Received treatment (n)*: NA
- *Analysed (n)*: 59
- *Age (mean ± SD, median (IQR), median (range))*: 36.2 ± 8.1
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 36.6 ± 9.9
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 88.14
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl during anaesthesia
- *Type of surgery*: laparoscopic abdominal or gynaecological surgery

Included criteria: ASA I and II, 3 or more risk factors for PONV, scheduled to undergo elective outpatient laparoscopic abdominal or gynaecological surgery under general anaesthesia

Excluded criteria: pregnant or nursing mothers, received antiemetics within 24 hours of surgery, experienced retching or vomiting within 24 hours before surgery, on long-term steroid therapy, were immunocompromised, documented allergy to 5-HT3 receptor antagonists or dexamethasone

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Palonosetron + dexamethasone • *Dose*: palonosetron 0.075 mg, dexamethasone 8 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: at the discretion of the patient's anaesthesiologist (no 5-HT3 receptor antagonists) Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV

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Blitz 2012 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: at the discretion of the patient's anaesthesiologist (no 5-HT3 receptor antagonists)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** funding provided by Eisai Inc. **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Jeanna D. Blitz **Institution:** Department of Anesthesiology, New York University Langone Medical Centre, New York **Email:** jeanna.viola@nyumc.org **Address:** Department of Anesthesiology, New York University Langone Medical Centre, 550 1st Avenue RR 605, New York, NY 10016 **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response **Trial registry number:** NCT00952133
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00952133 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Booij 1988

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, dose-finding study, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 31.8 ± 5.3 • *Weight (mean ± SD, median (IQR), median (range))*: 65.2 ± 8.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 46.9 • *Use of perioperative opioids (if yes, which?)*: 162.0 • *Type of surgery*: gynaecological laparoscopic procedures Alizapride (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 31.0 ± 3.9 • *Weight (mean ± SD, median (IQR), median (range))*: 62.8 ± 10.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 41.5 • *Use of perioperative opioids (if yes, which?)*: 181.3 • *Type of surgery*: gynaecological laparoscopic procedures Alizapride (group 3) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20

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Booij 1988 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 31.5 ± 5.5
- *Weight (mean ± SD, median (IQR), median (range))*: 61.2 ± 6.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female (in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 37.0
- *Use of perioperative opioids (if yes, which?)*: 140
- *Type of surgery*: gynaecological laparoscopic procedures

Alizapride (group 4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 31.5 ± 3.9
- *Weight (mean ± SD, median (IQR), median (range))*: 63.4 ± 6.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 44.6
- *Use of perioperative opioids (if yes, which?)*: 148 µg fentanyl intraoperative
- *Type of surgery*: gynaecological laparoscopic procedures

Included criteria: female patients, ASA I and II, admitted for gynaecological laparoscopic procedures

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids > 20%): yes

Interventions	**Intervention characteristics** Placebo (group 1) • *Dose*: saline • *Time point of administration*: 10 minutes before expected end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% NA Alizapride (group 2) • *Dose*: 50 mg • *Time point of administration*: 10 minutes before expected end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% NA Alizapride (group 3)

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Booij 1988 *(Continued)*

- *Dose*: 100 mg
- *Time point of administration*: 10 minutes before expected end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 0% NA

Alizapride (group 4)

- *Dose*: 200 mg
- *Time point of administration*: 10 minutes before expected end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 0% NA

Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Netherlands **Setting:** outpatient, single-centre **Author's name:** L.H.D.J. Booij **Institution:** Department of Anaesthesiology, Free University Hospital, Amsterdam, The Netherlands **Email:** NA **Address:** Free University Hospital, P.O. Box 7057, 1007 MB Amsterdam **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "according to a randomly as signed treatment schedule" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "all observations were made by the same two observers" Insufficient information on blinding ("double-blind")

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Booij 1988 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids > 20%): yes

Bopp 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Meclizine + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 37.4 ± 8.95 • *Weight (mean ± SD, median (IQR), median (range))*: 81.1 ± 16.43 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 45.71 • *Non-smoker (%)*: 88.57 • *History of PONV/motion sickness (%)*: 74.29/80 • *Type of general anaesthesia*: inhalational anaesthesia (iso-/des-/ sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 124.23 • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: NA Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 36.14 ± 11.06 • *Weight (mean ± SD, median (IQR), median (range))*: 83.57 ± 18.61 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 48.57 • *Non-smoker (%)*: 91.43

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Bopp 2010 *(Continued)*

- *History of PONV/motion sickness (%)*: 68.57/74.28
- *Type of general anaesthesia*: inhalational anaesthesia (iso-/des-/ sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 147.34
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: NA

Included criteria: having at least 3 of 5 risk factors for PONV (general anaesthesia scheduled for longer than 1 hour, female, history of motion sickness, non-smoker, history of PONV), scheduled to undergo elective surgery with a likelihood of general anaesthesia, older than 18 years of age, ASA I to III

Excluded criteria: sensitivity to ondansetron or meclizine, had taken an antiemetic within 24 hours of surgery, body mass index (BMI) greater than 35 kg/m^2, pregnant women

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Meclizine + ondansetron • *Dose*: meclizine 2 × 50 mg, ondansetron 4 mg • *Time point of administration*: meclizine the night before surgery at bedtime but no later than midnight and approximately 30 to 45 minutes before transport to the operative suite, ondansetron 15 to 30 minutes before conclusion of surgery • *Route of administration*: meclizine PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: promethazine 25 mg IV every 30 minutes up to a total dose of 50 mg, ondansetron 4 mg IV every 30 minutes up to a total dose of 8 mg, metoclopramide 10 mg IV every 30 minutes up to a total dose of 30 mg, ondansetron 7%, promethazine 18% Ondansetron • *Dose*: 2 × placebo capsules, ondansetron 4 mg • *Time point of administration*: placebo the night before surgery at bedtime but no later than midnight and approximately 30 to 45 minutes before transport to the operative suite, ondansetron 15 to 30 minutes before conclusion of surgery • *Route of administration*: placebo PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: promethazine 25 mg IV every 30 minutes up to a total dose of 50 mg, ondansetron 4 mg IV every 30 minutes up to a total dose of 8 mg, metoclopramide 10 mg IV every 30 minutes up to a total dose of 30 mg; ondansetron 37%, promethazine 44%
Outcomes	*Vomiting and retching (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient and inpatient, single-centre **Author's name:** Eric J. Bopp **Institution:** Naval Medical Center San Diego in California

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Bopp 2010 *(Continued)*

Email: NA

Address: 34800 Bob Wilson Dr., San Diego, CA 92134, USA

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: postdischarge incidence of nausea

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed by the pharmacy using a computer-generated randomization process"
Allocation concealment (selection bias)	Low risk	Quote: "these bubble packs were specifically designed by the pharmacy to ensure that each capsule looked alike and to ensure that both investigators and subjects were blind to the actual contents until the conclusion of the study. The pharmacy maintained a master list as to the actual contents of the capsules" Quote: "the study medication was prepared before initiation of this study by the pharmacy, which created 88 “bubble packs,” each containing 2 capsules of either 50 mg of meclizine or placebo. These bubble packs were specifically designed by the pharmacy to ensure that each capsule looked alike" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "individual group assignment was not divulged to the subjects or investigators until conclusion of the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "individual group assignment was not divulged to the subjects or investigators until conclusion of the study"
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: high dropout rates (> 15%)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "no significant differences were demonstrated between the meclizine and control groups with regard to demographic variables (gender, age, height, and weight), risk factors for PONV, anesthesia and surgical times, and preoperative and postoperative sleepiness scale scores (Table) or in the number of laparoscopic procedures performed" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

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Broome 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide (fentanyl group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 28.2 ± 8.4 • *Weight (mean ± SD, median (IQR), median (range))*: 66.1 ± 10.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 85.71 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (enflurane, N_2O, propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 100 µg • *Type of surgery*: multiple third molar tooth extractions Metoclopramide (tramadol group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 28.1 ± 9.6 • *Weight (mean ± SD, median (IQR), median (range))*: 67.1 ± 10.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 72 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (enflurane, N_2O, propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: tramadol 100 mg • *Type of surgery*: multiple third molar tooth extractions Ondansetron (fentanyl group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30

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Broome 1999 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 26.0 ± 5.1
- *Weight (mean ± SD, median (IQR), median (range))*: 66.8 ± 7.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 73.33
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (enflurane, N_2O, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl 100 µg
- *Type of surgery*: multiple third molar tooth extractions

Ondansetron (tramadol group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 26
- *Age (mean ± SD, median (IQR), median (range))*: 27.1 ± 6.3
- *Weight (mean ± SD, median (IQR), median (range))*: 62.6 ± 17.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 73.08
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (enflurane, N_2O, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: tramadol 100 mg
- *Type of surgery*: multiple third molar tooth extractions

Included criteria: 18 to 60 years of age, ASA I or II, scheduled to undergo elective multiple third molar tooth extractions as day cases

Excluded criteria: inability or unwillingness to give written consent, contraindications to the use of NSAIDs, parkinsonism or history of extrapyramidal reaction to metoclopramide or other drugs, use of other analgesics in the 12 hours before surgery, contraindications to tramadol, hypersensitivity, monoamine oxidase inhibitor therapy, severe renal or hepatic disease, epilepsy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear

Interventions

Intervention characteristics

Metoclopramide (fentanyl group)

- *Dose*: 10 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM up to 8-hourly

Metoclopramide (tramadol group)

- *Dose*: 10 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV

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Broome 1999 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM up to 8-hourly

Ondansetron (fentanyl group)

- *Dose*: 4 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM up to 8-hourly

Ondansetron (tramadol group)

- *Dose*: 4 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM up to 8-hourly

Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** outpatient, single-centre **Author's name:** G.J. Wardall **Institution:** Department of Anaesthetics, Falkirk and District Royal Infirmary, Major's Loan, Falkirk FK1 5QE, UK **Email:** NA **Address:** Department of Anaesthetics, Falkirk and District Royal Infirmary, Major's Loan, Falkirk FK1 5QE, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** pain or nausea score **Trial registry number:** NA
Notes	Four groups were pooled into 2 groups (with same antiemetic medication) for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated into four treatment groups" Judgement comment: no further information on sequence generation provided

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Broome 1999 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "to ensure blinding, these were performed by an assessor who had not anaesthetised the patient and who was unaware which study drugs had been given intraoperatively"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "in all, 109 patients were recruited; 83 were female. Eleven patients were withdrawn from the study, six because of the need for more extensive surgery and five due to failure to return postdischarge questionnaires"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the four groups with regard to age, sex or weight (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear

Bugedo 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 62 • *Received treatment (n)*: 62 • *Analysed (n)*: 62 • *Age (mean ± SD, median (IQR), median (range))*: 39 (18 to 60) • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 77.42 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, 3.5 mg morphine postoperative • *Type of surgery*: gynaecological or biliary surgical procedures by laparotomy or laparoscopy

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Bugedo 1999 *(Continued)*

Droperidol (group 2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: 60
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 38 (18 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 81.67
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, 2.8 mg morphine postoperative
- *Type of surgery*: gynaecological or biliary surgical procedures by laparotomy or laparoscopy

Ondansetron (group 3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 57
- *Received treatment (n)*: 57
- *Analysed (n)*: 57
- *Age (mean ± SD, median (IQR), median (range))*: 38 (19 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 77.19
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, 3.2 mg morphine postoperative
- *Type of surgery*: gynaecological or biliary surgical procedures by laparotomy or laparoscopy

Droperidol + ondansetron (group 4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 63
- *Received treatment (n)*: 63
- *Analysed (n)*: 63
- *Age (mean ± SD, median (IQR), median (range))*: 40 (18 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 82.54
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA

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Bugedo 1999 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, 3.1 mg morphine postoperative
- *Type of surgery*: gynaecological or biliary surgical procedures by laparotomy or laparoscopy

Included criteria: ASA I or II, 18 to 60 years of age, undergoing elective gynaecological or biliary surgical procedures by laparotomy or laparoscopy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo (group 1) • *Dose*: saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (group 2) • *Dose*: 2.5 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (group 3) • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol + ondansetron (group 4) • *Dose*: droperidol 2.5 mg, ondansetron 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Chile

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Bugedo 1999 *(Continued)*

Setting: inpatient, NA

Author's name: G. Bugedo

Institution: Departamento de Anestesiología, Hospital Clínico Pontificia Universidad Católica de Chile

Email: NA

Address: Departamento de Anestesiología, Hospital Clínico Pontificia Universidad Católica de Chile, PO Box 114-D, Santiago, Chile

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "patients were allocated by random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the anaesthetist and investigator were blinded to..."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear

Cabrera 1997

Study characteristics

Methods	**Study design:** randomized controlled trial

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Cabrera 1997 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 24 • *Received treatment (n)*: NA • *Analysed (n)*: 23 • *Age (mean ± SD, median (IQR), median (range))*: 54.82 ± 12.92 • *Weight (mean ± SD, median (IQR), median (range))*: 69.21 ± 10.73 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 12/9/2/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 21.74/26.09 • *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 82.52 • *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperatively • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 17 • *Age (mean ± SD, median (IQR), median (range))*: 56.29 ± 15.95 • *Weight (mean ± SD, median (IQR), median (range))*: 64.25 ± 10.23 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 7/9/1/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 17.65/23.52 • *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 81.07 • *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperatively • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** women over 18 years of age who were scheduled for non-urgent laparoscopic cholecystectomy under general anaesthesia **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia

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Cabrera 1997 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo

- *Dose*: physiological serum
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Identification

Sponsorship source: NA

Country: Spain

Setting: inpatient, single-centre

Author's name: J.C. Cabrera

Institution: Servicio de Anestesiologia y Reanimación, Hospital de la Esperanza, Sant Josep de la Muntanya, Barcelona

Email: NA

Address: Servicio de Anestesiologia y Reanimación, Hospital de la Esperanza, Sant Josep de la Muntanya 12, 08024 Barcelona

Duration of study: NA

Language: Spanish (translated by Insa Backhaus)

Study's primary outcome: NA

Trial registry number: NA

Notes

None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "patients were divided according to a sequence of random computer-generated numbers" (translated)
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")

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Cabrera 1997 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: quote: "the number of cases initially included in the study was 44"; "One patient from the ondansetron group and two from the control group were excluded. Another patient from the control group was excluded due to reintervention due to hemoperitoneum" (translated) Reasons for exclusion not reported for all participants
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Campbell 1995

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 16 • *Received treatment (n)*: 16 • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 37.2 ± 3.4 (SE) • *Weight (mean ± SD, median (IQR), median (range))*: 76.6 ± 5.5 (SE) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 44 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 50.0/6.3 • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, alfentanil, or fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 65.1 • *Use of perioperative opioids (if yes, which?)*: 2.8 mg alfentanil, fentanyl, codeine, propoxyphene, oxycodone • *Type of surgery*: gynaecological, genitourinary, ear/nose/throat, oral, orthopaedic, eye, other surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 16 • *Received treatment (n)*: 16 • *Analysed (n)*: 16

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Campbell 1995 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 34.2 ± 4.0 (SE)
- *Weight (mean ± SD, median (IQR), median (range))*: 75.4 ± 5.0 (SE)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 50.0/25.0
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, alfentanil, or fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 71.1
- *Use of perioperative opioids (if yes, which?)*: 2.6 mg alfentanil, fentanyl, codeine, propoxyphene, oxycodone
- *Type of surgery*: gynaecological, genitourinary, ear/nose/throat, oral, orthopaedic, eye, other surgery

Included criteria: ASA I or II, male or nonpregnant female, elective outpatient surgery, 18 to 70 years of age

Excluded criteria: laboratory or clinical evidence of renal, haematological, or hepatic dysfunction; morbid obesity; history of substance abuse or recent use (within 24 hours) of an antiemetic, histamine H2-antagonist, corticosteroid, or psychotropic drug; emesis or retching within 24 hours before surgery; expected to require continuous intraoperative or postoperative gastric suctioning; undergoing liver biopsy or surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 19% (prochlorperazine 5 mg to 10 mg) Placebo • *Dose*: isotonic solution of citric acid monohydrate, sodium citrate, sodium chloride, and water • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 19% (prochlorperazine 5 mg to 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Glaxo Inc., Research Triangle Park, North Carolina **Country:** USA

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Campbell 1995 *(Continued)*

Setting: outpatient, single-centre

Author's name: Christina Campbell

Institution: Department of Anesthesia, Indiana University School of Medicine, Indianapolis, Indiana

Email: NA

Address: NA

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: complete response (no nausea, retching, or vomiting)

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly assigned" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "were dissolved in a similar sterile, isotonic solution of the same volume to maintain the study's blindness" Insufficient information on blinding provided (who was blinded)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "in addition, a single, independent, blinded observer assessed nausea and emesis for 2 hours"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Candiotti 2008

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study

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Candiotti 2008 *(Continued)*

Participants

Baseline characteristics

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 136
- *Analysed (n)*: 135
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 5
- *ASA I/II/III/IV (n)*: 56/72/7/0
- *Gender (female in %)*: 96
- *Non-smoker (%)*: 86
- *History of PONV/motion sickness (%)*: 64/NA
- *Type of general anaesthesia*: inhalational anaesthesia (volatile agent, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic abdominal or gynaecological surgery

Palonosetron (0.025 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 136
- *Analysed (n)*: 136
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 27 ± 6
- *ASA I/II/III/IV (n)*: 70/59/7/0
- *Gender (female in %)*: 96
- *Non-smoker (%)*: 85
- *History of PONV/motion sickness (%)*: 63/NA
- *Type of general anaesthesia*: inhalational anaesthesia (volatile agent, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic abdominal or gynaecological surgery

Palonosetron (0.050 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 137
- *Analysed (n)*: 137
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 5
- *ASA I/II/III/IV (n)*: 69/62/6/0
- *Gender (female in %)*: 96
- *Non-smoker (%)*: 85
- *History of PONV/motion sickness (%)*: 66/NA

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Candiotti 2008 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (volatile agent, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic abdominal or gynaecological surgery

Palonosetron (0.075 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 138
- *Analysed (n)*: 138
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 28 ± 5
- *ASA I/II/III/IV (n)*: 72/62/4/0
- *Gender (female in %)*: 96
- *Non-smoker (%)*: 85
- *History of PONV/motion sickness (%)*: 66/NA
- *Type of general anaesthesia*: inhalational anaesthesia (volatile agent, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic abdominal or gynaecological surgery

Included criteria: at least 18 years of age, ASA physical status I to III, scheduled to undergo elective laparoscopic abdominal or gynaecological surgery of at least 1 hour duration. All patients had at least 2 risk factors for PONV: female gender, history of PONV and/or motion sickness, non-smoking status (never smoked or quit over 12 months ago). All patients were expected to go home on the same day that they underwent surgery

Excluded criteria: received cancer chemotherapy within 4 weeks or emetogenic radiotherapy within 8 weeks before study entry

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, history of PONV, non-smoker): no; (duration of anaesthesia, history of motion sickness, perioperative opioid): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 52% (at the discretion of the investigator, except droperidol and palonosetron)

Palonosetron (0.025 mg group)

- *Dose*: 0.025 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: at the discretion of the investigator, except droperidol and palonosetron

Palonosetron (0.050 mg group)

- *Dose*: 0.050 mg

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Candiotti 2008 *(Continued)*

- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: at the discretion of the investigator, except droperidol and palonosetron

Palonosetron (0.075 mg group)

- *Dose*: 0.075 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 44% (at the discretion of the investigator, except droperidol and palonosetron)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 72 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 72 hours)* • Outcome type: dichotomous outcome *QT prolongation (0 to 72 hours)* • Outcome type: dichotomous outcome *Headache (0 to 72 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 72 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, in the study)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** sponsored by Helsinn Healthcare SA and MGIPHARMA INC. **Country:** USA, Romania **Setting:** outpatient, multi-centre (36 USA and 7 Romania) **Author's name:** Giuseppina Clerici **Institution:** Research and Development Department, Helsinn Healthcare SA, Lugano, Switzerland **Email:** gcl@helsinn.com

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Candiotti 2008 *(Continued)*

Address: P.O. Box 357–6915 Pambio-Noranco (Lugano), Switzerland

Duration of study: NA

Language: English

Study's primary outcome: complete response

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization to treatment was stratified by gender, history of PONV and/or motion sickness, and smoking status. A dynamic adaptive stratification type of randomization method was used to balance the four groups across the entire study and not within each individual site"
Allocation concealment (selection bias)	Low risk	Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "at each study site, palonosetron and placebo were prepared for administration to patients by an unblinded research pharmacist or designee who was otherwise not involved in the conduct of the study" Quote: "...(minutes) before induction of anesthesia. The assigned randomization number was associated with sealed cartons containing the study drug which were provided to the unblinded research pharmacist at each site"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "six hundred thirty-nine patients were screened for this study, of which 65 were screening failures. Of the 574 remaining patients, 489 were randomized at 36 centers in the United States, and 85 were randomized at seven centers in Romania. Five hundred forty-seven patients were treated: palonosetron 0.025 mg (n 136), 0.050 mg (n 137), 0.075 mg (n 138), and placebo (n 136); 27 patients were not treated. The 48 patients who were randomized but did not complete the study were distributed across the three treatment groups and placebo group as follows: placebo (n 7), palonosetron 0.025 mg (n 18), palonoestron 0.050 mg (n 9), and palonosetron 0.075 mg (n 14). There were no statistically significant..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no statistically significant differences in age, height, weight, body mass index, PONV risk factors, type of surgery or ASA status in patients across all treatment groups" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, history of PONV, non-smoker): no; (duration of anaesthesia, history of motion sickness, perioperative opioid): unclear

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Capouet 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 97 • *Age (mean ± SD, median (IQR), median (range))*: 41 (22 to 74) • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 22/14 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 74 • *Use of perioperative opioids (if yes, which?)*: 326 µg fentanyl, 16.8 µg sufentanil, 14.9 mg piritramide IM, 5.3 mg piritramide IV, 18.9 mg piritramide on ward • *Type of surgery*: laparoscopic surgery, abdominal hysterectomy, other gynaecological laparotomy, vaginal hysterectomy, other vaginal surgery, breast surgery Tropisetron (0.5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 97 • *Age (mean ± SD, median (IQR), median (range))*: 38 (19 to 69) • *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 18/20 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 76 • *Use of perioperative opioids (if yes, which?)*: 284 µg fentanyl, 15.5 µg sufentanil, 14.9 mg piritramide IM, 5.3 mg piritramide IV, 22.0 mg piritramide on ward • *Type of surgery*: laparoscopic surgery, abdominal hysterectomy, other gynaecological laparotomy, vaginal hysterectomy, other vaginal surgery, breast surgery Tropisetron (2 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Capouet 1996 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 95
- *Age (mean ± SD, median (IQR), median (range))*: 38 (24 to 67)
- *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 23/11
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80
- *Use of perioperative opioids (if yes, which?)*: 286 µg fentanyl, 17.9 µg sufentanil, 15.8 mg piritramide IM, 3.7 mg piritramide IV, 19.4 mg piritramide on ward
- *Type of surgery*: laparoscopic surgery, abdominal hysterectomy, other gynaecological laparotomy, vaginal hysterectomy, other vaginal surgery, breast surgery

Tropisetron (5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 96
- *Age (mean ± SD, median (IQR), median (range))*: 41 (18 to 74)
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 23/8
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 78
- *Use of perioperative opioids (if yes, which?)*: 293 µg fentanyl, 18.2 µg sufentanil, 15.7 mg piritramide IM, 5.8 mg piritramide IV, 22.3 mg piritramide on ward
- *Type of surgery*: laparoscopic surgery, abdominal hysterectomy, other gynaecological laparotomy, vaginal hysterectomy, other vaginal surgery, breast surgery

Included criteria: ASA grade I and II women; between 18 and 75 years of age; undergoing abdominal or vaginal gynaecological surgery, including laparoscopy, under general anaesthesia; expected to remain in hospital for at least 6 hours after surgery

Excluded criteria: had vomited during 24 hours before surgery or had received antiemetics during the same period; were expected to have a nasogastric tube after surgery; history of alcohol or drug abuse; known to have hypersensitivity reactions; pregnant or lactating with the exception of those undergoing termination of early pregnancy combined with laparoscopic tubal ligation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 1 minute before the start of induction of anaesthesia • *Route of administration*: IV

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Capouet 1996 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: 39% (the choice of rescue treatment was at the discretion of the investigator, most frequently alizapride 50 mg to 250 mg followed by metoclopramide 10 mg to 40 mg)

Tropisetron 0.5 mg

- *Dose*: 0.5 mg
- *Time point of administration*: 1 minute before the start of induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 29% (the choice of rescue treatment was at the discretion of the investigator, most frequently alizapride 50 mg to 250 mg followed by metoclopramide 10 mg to 40 mg)

Tropisetron 2 mg

- *Dose*: 2 mg
- *Time point of administration*: 1 minute before the start of induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 23% (the choice of rescue treatment was at the discretion of the investigator, most frequently alizapride 50 mg to 250 mg followed by metoclopramide 10 mg to 40 mg)

Tropisetron 5 mg

- *Dose*: 5 mg
- *Time point of administration*: 1 minute before the start of induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 35% (the choice of rescue treatment was at the discretion of the investigator, most frequently alizapride 50 mg to 250 mg followed by metoclopramide 10 mg to 40 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *QT prolongation (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** study was funded by Sandoz Pharma Ltd. **Country:** Belgium **Setting:** inpatient and outpatient, multi-centre (8) **Author's name:** V. Capouet **Institution:** Centre Hospitalier Universitaire Vésale, Montigny-le-Tilleul

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Capouet 1996 *(Continued)*

Email: NA

Address: Department of Anaesthesiology, CHU Vésale, Route de Gozée 706, B-6110 Montigny-le-Tilleul, Belgium

Duration of study: NA

Language: English

Study's primary outcome: primary efficacy variable was the proportion of patients defined by the presence or absence of any emetic episodes over the 24-hour period regardless of rescue treatment given

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "allocated randomly" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Low risk	Quote: "the study medication consisted of 5 ml ampoules containing 5 mg of tropisetron or perfectly matching placebo ampoules and was supplied to the centres in a sealed box containing a leaflet with instructions for preparation. The randomization number was printed on the box. A 5 ml syringe was prepared by the local pharmacist (in four centres) or a physician or nurse not participating in the study in any other way" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "a 5 ml syringe was prepared by the local pharmacist (in four centres) or a physician or nurse not participating in the study in any other way"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "informed consent was obtained and study medication was prepared for a total of 391 sequential patients. The number of patients enrolled per centre varied between 33 and 70. Three patients withdrew their consent before administration of the study drug. Three ineligible patients were withdrawn from the study before administration of study medication because of a history of angioneurotic oedema, an ovarian carcinoma with metastases and a positive pregnancy test. The study medication was administered to a total of 385 patients in the 1 hour period before the start of induction. In a single patient, induction followed 125 min after study drug administration because of unexpected delay in the surgery schedule. All 385 female patients were included in the analysis"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "in this study 381 of 385 patients (99%) were white. The groups were comparable in age, weight, height, days since last menstrual cycle and propor-

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Capouet 1996 *(Continued)*

	tion of patients with a history of general anaesthesia and PONV or motion sickness (table 1)"
	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Cekmen 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group K) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 45.80 ± 5.15 • *Weight (mean ± SD, median (IQR), median (range))*: 76.40 ± 10.93 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 12/3/0/0 • *Gender (female in %)*: 53.33 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 90.33 • *Use of perioperative opioids (if yes, which?)*: 2.60 g (not specified) • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide (group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 48.93 ± 10.24 • *Weight (mean ± SD, median (IQR), median (range))*: 81.93 ± 14.42 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 12/3/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 97.00 • *Use of perioperative opioids (if yes, which?)*: 2.60 g (not specified) • *Type of surgery*: laparoscopic cholecystectomy

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Cekmen 2003 *(Continued)*

Dexamethasone (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 44.00 ± 11.73
- *Weight (mean ± SD, median (IQR), median (range))*: 76.40 ± 14.32
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 12/3/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93.66
- *Use of perioperative opioids (if yes, which?)*: 2.33 g (not specified)
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, undergoing laparoscopic cholecystectomy

Excluded criteria: pregnancy; narrow-angle glaucoma; gastrointestinal system obstruction; POBK; peptic ulcer and carriage history; antiemetic, anticholinergic, or antihistaminic treatment

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

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Interventions

Intervention characteristics

Control (group K)

- *Dose*: no treatment
- *Time point of administration*: -
- *Route of administration*: -
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Metoclopramide (group M)

- *Dose*: 10 mg
- *Time point of administration*: 10 minutes before extubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Dexamethasone (group D)

- *Dose*: 5 mg
- *Time point of administration*: 10 minutes before extubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

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Cekmen 2003 *(Continued)*

- Outcome type: dichotomous outcome

Arrhythmia (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Nedim ÇEKMEN **Institution:** Gazi Üniversitesi Tip Fakültesi Ankara **Email:** NA **Address:** NA **Duration of study:** NA **Language:** Turkish (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Cekmen 2003 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Chakravarty 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 42.7 ± 6.92 • *Weight (mean ± SD, median (IQR), median (range))*: 49.03 ± 8.04 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 13/15/0/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 98.66 • *Use of perioperative opioids (if yes, which?)*: none • *Type of surgery*: tympanomastoid surgery Palonosetron (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 38.9 ± 9.76 • *Weight (mean ± SD, median (IQR), median (range))*: 48.7 ± 7.95 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 14/16/0/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 98.9 • *Use of perioperative opioids (if yes, which?)*: none • *Type of surgery*: tympanomastoid surgery

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Chakravarty 2013 *(Continued)*

	Included criteria: ASA I or II, 20 to 50 years of age, BMI 30 kg/m^2; scheduled for elective tympanomastoid surgery under general anaesthesia **Excluded criteria:** history of allergy or hypersensitivity to 5-HT3 antagonists; history of/or prolonged cardiac conduction/QTc interval on preoperative ECG; gastrointestinal liver or renal disease; menstruating; pregnant or lactating mothers; smokers; history of motion sickness and/ or PONV; had received antiemetic premedication in the past 24 hours **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Palonosetron (group P) • *Dose*: 0.075 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Nupur Chakravarty **Institution:** L.N. Medical College and J.K.Hospital, Bhopal **Email:** NA **Address:** 71, Sai Hills, Kolar Road Bhopal M.P. **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

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Chakravarty 2013 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were assigned by closed envelope randomization schedule to one of two groups"
Allocation concealment (selection bias)	Unclear risk	Quote: "closed envelope randomization" Judgement comment: not mentioned: "sequentially numbered, opaque, sealed envelopes (SNOSE)"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "before surgery, drugs were prepared in identical 2.5 ml syringes and coded by an anaesthesia assistant not involved in the surgery. Patients were fasted 6 hours preoperatively and after securing an intravenous line, were premedicated with intravenous ranitidine 50 mg and intravenous Midazolam 2 mg, and study drugs were administered by a blinded anaesthetist just prior to induction"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were evaluated in the recovery room by an assistant who was ignorant about the coding and identity of the antiemetic drug given. When awake (judged by spontaneous"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "value < 0.05 was considered significant. Both groups were comparable in terms of age, weight, ASA physical status and duration of surgery (table 1). The type and amount of drugs used in anaesthesia, and any intraoperative and postoperative haemodynamics which may have had an impact on PONV in these patients were also not significantly different. In the early recovery period" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Chan 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50

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Chan 1998 *(Continued)*

- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 47 (19 to 74)
- *Weight (mean ± SD, median (IQR), median (range))*: 55 (40 to 67)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 26/24/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 38/38
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 156
- *Use of perioperative opioids (if yes, which?)*: 19.5 mg postoperative PCA morphine IV, induction morphine 0.15 mg/kg
- *Type of surgery*: radical mastectomy, lumpectomy, axillary dissection

Tropisetron (2 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 52 (29 to 75)
- *Weight (mean ± SD, median (IQR), median (range))*: 55 (35 to 73)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 26/23/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31/24
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 162
- *Use of perioperative opioids (if yes, which?)*: 18.5 mg postoperative PCA morphine IV, induction morphine 0.15 mg/kg
- *Type of surgery*: radical mastectomy, lumpectomy, axillary dissection

Tropisetron (5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 45 (32 to 73)
- *Weight (mean ± SD, median (IQR), median (range))*: 53 (36 to 77)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 30/19/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 27/29
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 156
- *Use of perioperative opioids (if yes, which?)*: 17.1 mg postoperative PCA morphine IV, induction morphine 0.15 mg/kg
- *Type of surgery*: radical mastectomy, lumpectomy, axillary dissection

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Chan 1998 *(Continued)*

Included criteria: female patients with breast cancer undergoing modified radical mastectomy or lumpectomy with axillary dissection, ASA I or II, 18 to 75 years of age

Excluded criteria: patients who had preexisting nausea or vomiting or had received opioids or drugs with known antiemetic properties in the 24 hours before surgery; pregnant patients; history of oesophageal reflux or opioid or alcohol abuse

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: before induction of anaesthesia over 30 seconds • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 78% (prochlorperazine 12.5 mg) Tropisetron (2 mg group) • *Dose*: 2 mg • *Time point of administration*: before induction of anaesthesia over 30 seconds • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 55.10% (prochlorperazine 12.5 mg) Tropisetron (5 mg group) • *Dose*: 5 mg • *Time point of administration*: before induction of anaesthesia over 30 seconds • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 24.49% (prochlorperazine 12.5 mg)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (early postoperative period)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** tropisetron was kindly supplied by Novartis Pharmaceutical, Hong Kong **Country:** China **Setting:** inpatient, single-centre **Author's name:** Matthew Chan **Institution:** Department of Anaesthesia and Intensive Care, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong

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Chan 1998 *(Continued)*

Email: mtvchan@cuhk.edu.hk

Address: Department of Anaesthesia and Intensive Care, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random number"
Allocation concealment (selection bias)	Unclear risk	Quote: "concealed in an envelope" Judgement comment: not mentioned: "sequentially numbered, opaque, sealed envelopes (SNOSE)"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study drugs were prepared by an anaesthesiologist not otherwise involved in the study..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patient interviews were conducted in a standardized fashion by trained nurses who were blinded to the study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "forty-eight patients completed the study (placebo, n = 50; tropisetron 2 mg, y1 = 49; tropisetron 5 mg, n = 49). One patient who received tropisetron 5 mg was excluded because of missing data. Another patient who received tropisetron 2 mg was erroneously given metoclopramide just before the end of surgery and was excluded from the study. This patient continued to suffer"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "age, weight, height, and variables that may influence PONV did not differ among the groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Chan 2006

Study characteristics

Methods	**Study design:** randomized controlled trial

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Chan 2006 *(Continued)*

Study grouping: 4 groups, monocombination and combination prophylaxis

Participants

Baseline characteristics

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 100
- *Received treatment (n)*: 97
- *Analysed (n)*: 97
- *Age (mean ± SD, median (IQR), median (range))*: 37 (18 to 51)
- *Weight (mean ± SD, median (IQR), median (range))*: 50 (39 to 65)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 47/50/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 85
- *History of PONV/motion sickness (%)*: 32/18
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 56
- *Use of perioperative opioids (if yes, which?)*: 115 µg fentanyl, 4.1 mg morphine
- *Type of surgery*: laparoscopic gynaecological surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 100
- *Received treatment (n)*: 100
- *Analysed (n)*: 100
- *Age (mean ± SD, median (IQR), median (range))*: 32 (19 to 50)
- *Weight (mean ± SD, median (IQR), median (range))*: 52 (35 to 73)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 51/49/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 83
- *History of PONV/motion sickness (%)*: 12/12
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 42
- *Use of perioperative opioids (if yes, which?)*: 112 µg fentanyl, 4.4 mg morphine
- *Type of surgery*: laparoscopic gynaecological surgery

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 100
- *Received treatment (n)*: 98
- *Analysed (n)*: 98
- *Age (mean ± SD, median (IQR), median (range))*: 35 (18 to 77)
- *Weight (mean ± SD, median (IQR), median (range))*: 53 (36 to 77)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100

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Chan 2006 *(Continued)*

- *Non-smoker (%)*: 79
- *History of PONV/motion sickness (%)*: 23/15
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 55
- *Use of perioperative opioids (if yes, which?)*: 109 µg fentanyl, 3.7 mg morphine
- *Type of surgery*: laparoscopic gynaecological surgery

Ondansetron + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 100
- *Received treatment (n)*: 99
- *Analysed (n)*: 99
- *Age (mean ± SD, median (IQR), median (range))*: 49 (33 to 75)
- *Weight (mean ± SD, median (IQR), median (range))*: 49 (33 to 75)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 41/58/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 87
- *History of PONV/motion sickness (%)*: 17/17
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 48
- *Use of perioperative opioids (if yes, which?)*: 110 µg fentanyl, 3.9 mg morphine
- *Type of surgery*: laparoscopic gynaecological surgery

Included criteria: ASA I or II, between 18 and 45 years of age; scheduled for laparoscopic gynaecological surgery

Excluded criteria: preexisting nausea or vomiting; had received opioids or drugs with known antiemetic properties in the 24 hours before surgery; pregnant patients; history of oesophageal reflux, opioid or alcohol abuse

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: in the operating room, before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: in the operating room, before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: in the operating room, before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM

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Chan 2006 *(Continued)*

	Ondansetron + droperidol • *Dose*: ondansetron 4 mg, droperidol 1.25 mg • *Time point of administration*: in the operating room, before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Arrhythmia (PACU)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Matthew Chan **Institution:** Department of Anaesthesia and Intensive Care, Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong **Email:** mtvchan@cuhk.edu.hk **Address:** Department of Anaesthesia and Intensive Care, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong Special Administrative Region **Duration of study:** September 2002 and June 2004 **Language:** English **Study's primary outcome:** primary endpoint was complete response to treatment. This was defined as no nausea or episodes of emesis; receiving rescue antiemetic during the entire 48 hours' observation **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random number concealed in an opaque envelope"
Allocation concealment (selection bias)	Unclear risk	Quote: "concealed in an opaque envelope" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelope (SNOSE)"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study drugs, up to 10 ml with normal saline, were prepared by an anesthesiologist independent of the study and were injected IV over 30 s"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patient interviews were conducted in a standardized fashion by trained nurses who were blinded to the study drug"

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Chan 2006 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "among 518 eligible patients, 400 were enrolled into the study. Six patients were withdrawn after randomization because of cancellation of surgery (three in the control group; two in the droperidol group and one in the ondansetron and droperidol group). None of these patients received the assigned study drug. Therefore, the final dataset consisted of 394 patients (Fig. 1). One patient in the control group mistakenly received metoclopramide before the end of surgery. This patient was included in the allocated group for all analyses"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "at baseline, patient characteristics and operative details were similar among groups (Table 1). Overall, 285 patients (72%) reported three or more of the common risk factors for PONV, namely female gender, history of PONV or motion sickness, nonsmoker or use of postoperative opioids. The incidence of risk factors was evenly distributed among groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Chaparro 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: 80 • *Analysed (n)*: 80 • *Age (mean ± SD, median (IQR), median (range))*: 29.5 ± 7.3 • *Weight (mean ± SD, median (IQR), median (range))*: 56.0 ± 7.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 21.2/30 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 144.5 • *Use of perioperative opioids (if yes, which?)*: intraoperative morphine 0.05 mg/kg, 4.09 mg postoperative morphine consumption • *Type of surgery*: plastic or ENT surgery Dexamethasone + haloperidol • *Assessed for eligibility (n)*: -

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Chaparro 2010 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: 80
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: 30.1 ± 7.5
- *Weight (mean ± SD, median (IQR), median (range))*: 55.9 ± 7.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 21.5/40
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142.3
- *Use of perioperative opioids (if yes, which?)*: intraoperative morphine 0.05 mg/kg, 3.28 mg postoperative morphine consumption
- *Type of surgery*: plastic or ENT surgery

Included criteria: non-smoking women, between 18 and 50 years of age, ASA I or II, scheduled for ambulatory surgery (plastic and otorhinolaryngologic procedures), under general anaesthesia

Excluded criteria: allergies to metoclopramide, non-steroidal anti-inflammatory drugs (NSAIDs), morphine, or haloperidol; history of extrapyramidal syndrome or akathisia; had used antiemetics within 24 hours preceding surgery or steroids anytime during the previous 3 months

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 18.75% (metoclopramide 10 mg) Dexamethasone + haloperidol • *Dose*: dexamethasone 8 mg, haloperidol 1.5 mg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 15% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0.5 hours, 0.5 to 2 hours, 2 to 6 hours)*

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Chaparro 2010 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** supported by a grant from the Department of Anesthesia, University of Antioquia **Country:** Colombia **Setting:** outpatient, single-centre **Author's name:** Luis E. Chaparro **Institution:** Toronto Western Hospital, Canada **Email:** luisdr74@yahoo.com **Address:** Toronto Western Hospital, Comprehensive Pain Program, Rm 811-4 Fell Pavilion, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada **Duration of study:** April to December 2005 **Language:** English **Study's primary outcome:** postoperative nausea and vomiting **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "which randomized these two treatment groups according to a computer-generated list using"
Allocation concealment (selection bias)	Low risk	Quote: "at study onset, the hospital pharmacist prepared a concealed treatment allocation schedule" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "staff members involved in patient care were blinded to the patients' assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "[8]. All data were collected by an anaesthesiologist (L.E.C.) or resident (N.J.G., M.F.R., and T.G.) who [was] blinded to the patient group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 192 consecutive patients were screened (Fig. 1). Twenty-two did not meet inclusion criteria, seven did not accept to participate and three preferred a 5-HT3 antagonist as antiemetic. One hundred and sixty nonsmoker women were recruited and randomized" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Chaparro 2010 *(Continued)*

Other bias	Low risk	Quote: "there were no differences in the various demographic variables between the two groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Chen 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 40.1 ± 8.8 • *Weight (mean ± SD, median (IQR), median (range))*: 55.7 ± 8.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 21/30 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 106.0 • *Use of perioperative opioids (if yes, which?)*: 17.4 mg methadone, 11 pethidine • *Type of surgery*: abdominal hysterectomy or ovarian surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 39.7 ± 9.0 • *Weight (mean ± SD, median (IQR), median (range))*: 56.2 ± 7.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 12/20 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 112.7 • *Use of perioperative opioids (if yes, which?)*: 19 mg methadone, 17 pethidine

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Chen 1996 *(Continued)*

- *Type of surgery*: abdominal hysterectomy or ovarian surgery

Included criteria: ASA I or II, 18 to 60 years of age, scheduled for abdominal hysterectomy or ovarian surgery

Excluded criteria: preexisting nausea or vomiting, antiemetics or opioids given in the 24 hours before surgery, pregnancy, gastro-oesophageal reflux, alcohol or drug abuse

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Metoclopramide • *Dose*: 10 mg • *Time point of administration*: end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 42% (prochlorperazine 12.5 mg IM) Ondansetron • *Dose*: 4 mg • *Time point of administration*: end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 36% (prochlorperazine 12.5 mg IM)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** P.P. Chen **Institution:** Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, NT, Hong Kong **Email:** NA

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Chen 1996 *(Continued)*

	Address: NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "allocated randomly to receive either ondasetron 4 mg or metoclopramide 10 mg using a series of sealed envelopes" Insufficient information on the sequence generation process
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "allocated randomly to receive either ondasetron 4 mg or metoclopramide 10 mg using a series of sealed envelopes" Detailed information on envelopes is missing (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "double-blinded" Insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "sedation, nausea and vomiting were assessed by an investigator blinded to the study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "twenty-five patients were initially recruited into each Group. One Patient in the metoclopramide group was excluded after she developed post-operative respiratory depression" Reasons for missing data from 1 patient were described and are unlikely related to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Chen 2006

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics**

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Chen 2006 *(Continued)*

Placebo (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 350
- *Received treatment (n)*: 350
- *Analysed (n)*: 350
- *Age (mean ± SD, median (IQR), median (range))*: 51 ± 15
- *Weight (mean ± SD, median (IQR), median (range))*: 65.2 ± 7.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 65
- *Non-smoker (%)*: 75
- *History of PONV/motion sickness (%)*: 33
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 170
- *Use of perioperative opioids (if yes, which?)*: 167 µg fentanyl, meperidine consumption at 0 to 12 hours of 21.2 mg and at 12 to 24 hours of 12.4 mg
- *Type of surgery*: otolaryngological, orthopaedic, ophthalmological, laparoscopic, laparotomy, other

Dexamethasone (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 350
- *Received treatment (n)*: 350
- *Analysed (n)*: 350
- *Age (mean ± SD, median (IQR), median (range))*: 52 ± 15
- *Weight (mean ± SD, median (IQR), median (range))*: 61.7 ± 6.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: 74
- *History of PONV/motion sickness (%)*: 37
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 163
- *Use of perioperative opioids (if yes, which?)*: 177 µg fentanyl, meperidine consumption at 0 to 12 hours of 22.3 mg and at 12 to 24 hours of 11.7 mg
- *Type of surgery*: otolaryngological, orthopaedic, ophthalmological, laparoscopic, laparotomy, other

Included criteria: ASA I or II, surgical patients about to undergo surgery under general anaesthesia

Excluded criteria: significant medical disease; had received antiemetics within 24 hours before surgery; history of immunosuppression, significant oesophageal-gastric reflux, Cushing's syndrome, or liver/renal disease; presented difficult intubation during induction of anaesthesia

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Placebo (group P)

- *Dose*: saline
- *Time point of administration*: 1 minute before induction of anaesthesia
- *Route of administration*: IV

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Chen 2006 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Dexamethasone (group D) • *Dose*: 10 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (8 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (during hospital stay)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (during hospital stay)* • Outcome type: dichotomous outcome *Postoperative wound infection (during hospital stay)* • Outcome type: dichotomous outcome *Headache (during hospital stay)* • Outcome type: dichotomous outcome *Sedation/drowsiness (during hospital stay)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Chung-Hang Wong **Institution:** Department of Anaesthesiology, Chang Gung Memorial Hospital **Email:** wong@adm.cgmh.org.tw **Address:** Department of Anesthesiology, Chang Gung Memorial Hospital. 6, Section West, Chia-Pu Rd., Puzih City, Chiayi, Taiwan 613 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

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Chen 2006 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomization was achieved using the envelope method (700 envelopes, 350 stated as control group and 350 stated as study group were polled together. The researcher picked one of these envelopes after the patient agreed to enroll into the study)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not stated: "sequentially numbered, opaque, sealed envelopes (SNOSE)"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blinded" Judgement comment: insufficient information on blinding ("double-blinded")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "data obtained from the 700 patients (350 in each group) were analyzed" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "the incidence of background factors and factors related to operation and anesthesia, which may modify PONV, did not differ between the two groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Chen 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Saline (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 40.3 ± 1.70 • *Weight (mean ± SD, median (IQR), median (range))*: 57.9 ± 0.91

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Chen 2014 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 22.0 ± 0.38
- *ASA I/II/III/IV (n)*: 4/26/8/2
- *Gender (female in %)*: 80
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (sevoflurane, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66.2
- *Use of perioperative opioids (if yes, which?)*: 0.39 mg fentanyl
- *Type of surgery*: laparoscopic procedure (gynaecological laparoscopic surgery or laparoscopic cholecystectomy)

Ondansetron (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 42
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 42.6 ± 1.43
- *Weight (mean ± SD, median (IQR), median (range))*: 59.3 ± 1.25
- *BMI (mean ± SD, median (IQR), median (range))*: 22.5 ± 0.34
- *ASA I/II/III/IV (n)*: 7/22/8/3
- *Gender (female in %)*: 80
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (sevoflurane, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 67.1
- *Use of perioperative opioids (if yes, which?)*: 0.40 mg fentanyl
- *Type of surgery*: laparoscopic procedure (gynaecological laparoscopic surgery or laparoscopic cholecystectomy)

Included criteria: patients of either sex, over 18 years of age, scheduled to undergo a laparoscopic procedure (e.g. gynaecological laparoscopic surgery or laparoscopic cholecystectomy)

Excluded criteria: had vomited or retched within 24 hours before surgery; had taken an antiemetic, glucocorticosteroid, or psychoactive drug within 24 hours before surgery; implanted cardiac pacemaker or defibrillator; had surgical technique changed; any infectious disease within 2 weeks before surgery; local infection near acupuncture points; pregnant or with menstrual symptoms; allergic to vitamin B1

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear (data not shown, but no difference in risk scores between groups)

Interventions	**Intervention characteristics** Saline (group A) • *Dose*: saline • *Time point of administration*: on arrival in the PACU • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (droperidol 0.625 mg IV, dexamethasone 4 mg IV, ondansetron 1 mg) Ondansetron (group C) • *Dose*: NA

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Chen 2014 *(Continued)*

- *Time point of administration*: on arrival in the PACU
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 17.5% (droperidol 0.625 mg IV, dexamethasone 4 mg IV, ondansetron 1 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Qu L. Guo **Institution:** Department of Anesthesiology, Xiangya Hospital, Central South University, Changsha, Hunan 410008, PR China **Email:** qulianguo2@hotmail.com **Address:** Department of Anesthesiology, Xiangya Hospital, Central South University, Changsha, Hunan 410008, PR China **Duration of study:** November 2009 to January 2010 **Language:** English **Study's primary outcome:** the incidence of POV **Trial registry number:** NA
Notes	Two out of 4 groups relevant (vitamin B1 acupuncture point injection)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "simple randomisation, using computer-generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Quote: "concealed until the patient entered the postanaesthesia care unit" Judgement comment: no details on allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...injection[s] were also recorded carefully. Patients, anaesthetists, surgical, nursing staff and our follow-up investigators were all blinded to the group allocation. The investigator [was] responsible for collecting"

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Chen 2014 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "by an observer who was blinded to the research design" Quote: "the investigator responsible for collecting data was also unaware of the treatments assigned"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "(Figure 2)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "demographic characteristics, the risk score for POV and all the perioperative variables in the four groups were not significantly different (table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear (data not shown, but no difference in risk scores between groups)

Chia 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different timing of administration
Participants	**Baseline characteristics** Promethazine (pre group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 44.7 ± 7.4 • *Weight (mean ± SD, median (IQR), median (range))*: 53.6 ± 5.2 • *BMI (mean ± SD, median (IQR), median (range)*: NA • *ASA I/II/III/IV (n)*: 13/17/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (fentanyl, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 102 • *Use of perioperative opioids (if yes, which?)*: 161.6 ± 35.3 µg perioperative fentanyl, 24.1 ± 3.9 mg morphine consumption in 24 hours • *Type of surgery*: abdominal hysterectomy Promethazine (post group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Chia 2004 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 44.0 ± 10.2
- *Weight (mean ± SD, median (IQR), median (range))*: 59.3 ± 9.6
- *BMI (mean ± SD, median (IQR), median (range)*: NA
- *ASA I/II/III/IV (n)*: 11/19/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (fentanyl, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 118
- *Use of perioperative opioids (if yes, which?)*: 155.3 ± 29.2 µg perioperative fentanyl, 30.0 ± 4.6 mg morphine consumption in 24 hours
- *Type of surgery*: abdominal hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 31
- *Age (mean ± SD, median (IQR), median (range))*: 47.0 ± 5.2
- *Weight (mean ± SD, median (IQR), median (range))*: 55.3 ± 5.6
- *BMI (mean ± SD, median (IQR), median (range)*: NA
- *ASA I/II/III/IV (n)*: 13/17/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (fentanyl, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 117
- *Use of perioperative opioids (if yes, which?)*: 160.9 ± 35.4 µg perioperative fentanyl, 32.1 ± 4.8 mg morphine consumption in 24 hours
- *Type of surgery*: abdominal hysterectomy

Included criteria: ASA I or II, female patients, undergoing abdominal total hysterectomy

Excluded criteria: history of severe heart, pulmonary, hepatic, renal, or psychological disease; allergy to narcotics

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Promethazine (pre group) • *Dose*: 0.1 mg/kg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV, 0 to 24 hours 3%, 24 to 48 hours 0% Promethazine (post group) • *Dose*: 0.1 mg/kg • *Time point of administration*: at end of surgery

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Chia 2004 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV, 0 to 24 hours 7%, 24 to 48 hours 0% Placebo • *Dose*: saline • *Time point of administration*: 30 minutes before induction of anaesthesia and at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV, 0 to 24 hours 22%, 24 to 48 hours 3%
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (after 48 hours with sedation score > 2)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** the study was supported in part by grants from Tsou's Medical Research Foundation and Kaohsiung Veterans General Hospital (VGHKS92-04) **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Yuan-Yi Chia **Institution:** Department of Anaesthesiology Kaohsiung Veterans General Hospital Kaohsiung Taiwan **Email:** yychia@isca.vghks.gov.tw **Address:** 386 Ta-Chung 1st Road Kaohsiung 813,Kaohsiung Veterans General Hospital Kaohsiung, Taiwan **Duration of study:** NA **Language:** English **Study's primary outcome:** primary endpoint was pain intensity and morphine consumption **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly and equally divided into three groups, using a computer-generated table of random numbers"

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Chia 2004 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "the pharmacy personnel who were not involved in patient care or evaluation was allowed to undertake group-assignment and randomization, which was achieved using a sequence of random numbers from a computer-generated sequence. The group-assignment code indicating group assign was retained by the pharmacy until the conclusion of the study. To ensure patient safety, however, a sealed opaque envelope containing the randomized treatment assignment was kept with the patient in the operating room and intensive care unit (ICU) to permit immediate unmasking if necessary"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blinding was achieved by having our hospital pharmacy personnel prepare the infusion bags with promethazine or not for each group of patients and label them with the subject's identification number only" Quote: "an anaesthesiologist, blinded to group membership and not involved in postoperative evaluation or patient contact, conducted the anaesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an anaesthesiologist blinded to group allocation evaluated the patients when they were sufficiently awake and alert post surgery, and recorded the data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 102 patients were evaluated. Of these, six were excluded due to surgical complications such as massive perioperative bleeding and wound infection. In addition, six patients did not complete the experiment due to transfer for chemotherapy or addition of non-steroidal anti-inflammatory drugs to their treatment regimen for pain management. This left a sample population of 90 patients in the three groups"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Choi 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 7.7 • *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 6.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Choi 1999 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: nalbuphine PCA 60 mg postoperative
- *Type of surgery*: total abdominal hysterectomy or myomectomy or ovarian ectomy

Ondansetron (group 2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 7.9
- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 8.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: nalbuphine PCA 60 mg postoperative
- *Type of surgery*: total abdominal hysterectomy or myomectomy or ovarian ectomy

Ondansetron (group 3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 9.3
- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 7.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: nalbuphine PCA 60 mg postoperative
- *Type of surgery*: total abdominal hysterectomy or myomectomy or ovarian ectomy

Granisetron (group 4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 8.4
- *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 6.3

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Choi 1999 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: nalbuphine PCA 60 mg postoperative
- *Type of surgery*: total abdominal hysterectomy or myomectomy or ovarian ectomy

Granisetron (group 5)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 9.0
- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 7.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: nalbuphine PCA 60 mg postoperative
- *Type of surgery*: total abdominal hysterectomy or myomectomy or ovarian ectomy

Included criteria: total abdominal hysterectomy or myomectomy or ovarian ectomy, ASA I or II

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Placebo (group 1)

- *Dose*: NaCl 3 mL
- *Time point of administration*: before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ondansetron (group 2)

- *Dose*: 4 mg
- *Time point of administration*: before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ondansetron (group 3)

- *Dose*: 8 mg
- *Time point of administration*: before anaesthesia

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Choi 1999 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Granisetron (group 4) • *Dose*: 1.5 mg • *Time point of administration*: before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Granisetron (group 5) • *Dose*: 3 mg • *Time point of administration*: before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Sounth Korea **Setting:** inpatient, single-centre **Author's name:** Sang Hwan Do **Institution:** Department of Anaesthesiology, College of Medicine, Seoul National University, Seoul, Korea **Email:** shdo@snu.ac.kr **Address:** 101 Daehak-ro, Ihwa-dong, Jongno-gu, Seoul, Sounth Korea **Duration of study:** NA **Language:** Korean (translated by Woocheol Sim) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement

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Choi 1999 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: insufficient information on randomization provided ("randomized")
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: study authors stated that a blinded investigator assessed PONV, retching, and pain after 24 hours
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Choi 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 4.6 • *Weight (mean ± SD, median (IQR), median (range))*: 55.5 ± 9.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 32 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 137.4 • *Use of perioperative opioids (if yes, which?)*: fentanyl via PCA • *Type of surgery*: gynaecological surgery

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Choi 2008 *(Continued)*

Ramosetron (group R15)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 43.2 ± 9.1
- *Weight (mean ± SD, median (IQR), median (range))*: 58.0 ± 8.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 34
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.6
- *Use of perioperative opioids (if yes, which?)*: fentanyl via PCA
- *Type of surgery*: gynaecological surgery

Ramosetron (group R30)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 45.8 ± 11.7
- *Weight (mean ± SD, median (IQR), median (range))*: 58.5 ± 8.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 26
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138.6
- *Use of perioperative opioids (if yes, which?)*: fentanyl via PCA
- *Type of surgery*: gynaecological surgery

Ramosetron (group R45)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 40.1 ± 10.6
- *Weight (mean ± SD, median (IQR), median (range))*: 55.3 ± 4.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 36
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 127.2

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Choi 2008 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: fentanyl via PCA
- *Type of surgery*: gynaecological surgery

Included criteria: 25 to 60 years of age, ASA corresponding to body class I or II, undergoing general anaesthesia, non-smoking status, had undergone surgery longer than 1 hour and less than 4 hours

Excluded criteria: gastrointestinal disorders such as gastritis and gastric ulcers, pregnant women, lactating women, had taken antiviral agent within 24 hours before the operation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, non-smoker): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo (group P) • *Dose*: saline • *Time point of administration*: at completion of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.25 mg/kg Ramosetron (group R15) • *Dose*: 0.15 mg • *Time point of administration*: at completion of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.25 mg/kg Ramosetron (group R30) • *Dose*: 0.3 mg • *Time point of administration*: at completion of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.25 mg/kg Ramosetron (group R45) • *Dose*: 0.45 mg • *Time point of administration*: at completion of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.25 mg/kg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** South Korea

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Choi 2008 *(Continued)*

Setting: inpatient, single-centre

Author's name: Young-Kyoo Choi

Institution: Department of Anesthesiology and Pain Medicine, College of Medicine, Kyung Hee University, Seoul, Korea

Email: cykyko@unitel.co.kr

Address: NA

Duration of study: NA

Language: Korean (Google Translator)

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "was randomized" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the drug was prepared according to the arm by an anesthesiologist who does not know what type of medication is being administered" (translated)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "a designated anesthesiologist who does not know the grouping of patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, non-smoker): no; (perioperative opioids): unclear

Choi 2010

Study characteristics

Methods	**Study design:** randomized controlled trial

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Choi 2010 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: 80 • *Analysed (n)*: 70 • *Age (mean ± SD, median (IQR), median (range))*: 57 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 39 • *Non-smoker (%)*: 51 • *History of PONV/motion sickness (%)*: 27 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 328 • *Use of perioperative opioids (if yes, which?)*: 345 µg fentanyl consumption after 1 hour, 869 µg fentanyl consumption after 24 hours, 1573 µg fentanyl consumption after 48 hours • *Type of surgery*: cardiac surgery Ramosetron (group R1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: 80 • *Analysed (n)*: 70 • *Age (mean ± SD, median (IQR), median (range))*: 59 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 40 • *Non-smoker (%)*: 47 • *History of PONV/motion sickness (%)*: 26 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 321 • *Use of perioperative opioids (if yes, which?)*: 375 µg fentanyl consumption after 1 hour, 905 µg fentanyl consumption after 24 hours, 1647 µg fentanyl consumption after 48 hours • *Type of surgery*: cardiac surgery **Included criteria:** adult patients scheduled for elective cardiac surgery **Excluded criteria:** abnormal hepatic or renal function, gastrointestinal disease, older than 80 years, undergoing emergency surgery, underwent reoperation for postoperative bleeding, were intubated over 48 hours after surgery **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no
Interventions	**Intervention characteristics** Placebo (group P)

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Choi 2010 *(Continued)*

	• *Dose*: saline • *Time point of administration*: 2 mL saline was injected at the end of surgery and 6 mL saline was added to the PCA regimen • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV (50%) Ramosetron (group R1) • *Dose*: 0.3 mg • *Time point of administration*: 0.3 mg ramosetron in 2 mL was injected at the end of surgery and normal saline 6 mL was added to the PCA regimen • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV (33%)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Arrhythmia (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this article was supported solely by institutional and/or departmental sources (Asan Medical Center) **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** In-Cheol Choi **Institution:** Department of Anesthesiology and Pain Medicine **Email:** icchoi@amc.seoul.kr **Address:** Asan Medical Center College of Medicine University of Ulsan 388-1 Pungnap 2-dong Song-pa-gu, Seoul 138-736, Korea **Duration of study:** September 2008 to February 2009 **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	Two out of 4 groups relevant (continuous infusion of antiemetics in 2 groups). Originally a dose-finding study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Choi 2010 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly assigned to one of four groups using a computer-generated randomization table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all the study drugs were prepared in identical syringes by personnel who were not involved in the study. The PCA pump (AutoMed 3200 s, Ace Medical Co., Seoul, Korea) held the same volume of solution and was blinded to data collection personnel"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "in addition, we monitored the severity of nausea and the use of rescue antiemetic medications. Rescue antiemetic medication (10 mg i.v. metoclopramide) was given in response to severe nausea, two or more episodes of vomiting, or patient's requests at the discretion of the attending physicians, who were blinded to the study groups"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 320 patients were enrolled. Of these, 41 patients were excluded from the study due to reoperation for post-operative bleeding (n 5 27) and prolonged intubation (448 h) in the ICU (n 5 14). The final analysis involved 279 patients: 70 in group P, 71 in group O, 70 in group R1, and 68 in group R2"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

Choi 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Aprepitant + palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 44 • *Received treatment (n)*: 44 • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 48.9 ± 10.6 • *Weight (mean ± SD, median (IQR), median (range))*: 58.9 ± 8.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 30 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 55.7

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Choi 2016 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 103.41 µg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Aprepitant + ramosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 44
- *Received treatment (n)*: 44
- *Analysed (n)*: 44
- *Age (mean ± SD, median (IQR), median (range))*: 48.8 ± 10.2
- *Weight (mean ± SD, median (IQR), median (range))*: 60.9 ± 8.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 25
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 63.5
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 102.27 µg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA physical status of I or II, non-smoking, female, 18 to 65 years of age, scheduled for laparoscopic cholecystectomy

Excluded criteria: gastrointestinal disorder; allergy to any study medication; had received any sedative, opioid, steroid, or antiemetic within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Aprepitant + palonosetron • *Dose*: aprepitant 80 mg, palonosetron 0.075 mg • *Time point of administration*: aprepitant 2 hours before surgery, palonosetron 10 minutes after induction of anaesthesia • *Route of administration*: aprepitant PO, palonosetron IV • *Rescue antiemetics (if yes, which?)*: 11.4% (metoclopramide 10 mg) Aprepitant + ramosetron • *Dose*: aprepitant 80 mg, ramosetron 0.3 mg • *Time point of administration*: aprepitant 2 hours before surgery, ramosetron 10 minutes after induction of anaesthesia • *Route of administration*: aprepitant PO, ramosetron IV • *Rescue antiemetics (if yes, which?)*: 40.9% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)*

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Choi 2016 *(Continued)*

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (overall, exact time point unknown)

- Outcome type: dichotomous outcome

Sedation/drowsiness (overall, exact time point unknown)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, overall, exact time point unknown)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Younghoon Jeon **Institution:** Department of Anesthesiology and Pain Medicine, School of Dentistry, Kyungpook National University, Daegu, Republic of Korea **Email:** jeon68@knu.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, School of Dentistry, Kyungpook National University, 188-1 Samdeok-Dong 2 Ga, Jung-gu, Daegue 700-421 Republic of Korea **Language:** English **Duration of study:** NA **Trial registry number:** NCT02597907 **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated to one of 2 groups (n = 44 in each) using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all data were assessed by another anesthesiologist blinded to the group assignments during the first 24 hours after surgery in 2 time periods (0 to 2 and 2 to 24 h after anesthesia),,,"

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Choi 2016 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 88 patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT02597907 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Cholwill 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline Characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 31 (22 to 42) • *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: 23 ± 2 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 22/20 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: orally: intraoperative morphine 0.18 mg/kg IV, postoperative codeine 60 mg PO (20 patients) or morphine IV (4 patients) • *Type of surgery*: gynaecological laparoscopy Cyclizine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 57 • *Age (mean ± SD, median (IQR), median (range))*: 32 (21 to 50) • *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: 23 ± 3 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Cholwill 1999 *(Continued)*

- *History of PONV/motion sickness (%)*: 25/26
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative morphine 0.18 mg/kg IV, postoperative codeine 60 mg PO (19 patients) or morphine IV (3 patients)
- *Type of surgery*: gynaecological laparoscopy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 58
- *Age (mean ± SD, median (IQR), median (range))*: 33 (22 to 46)
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: 23 ± 3
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 19/24
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative morphine 0.18 mg/kg IV, postoperative codeine 60 mg PO (21 patients) or morphine IV (7 patients)
- *Type of surgery*: gynaecological laparoscopy

Included criteria: ASA I or II, women undergoing day-case gynaecological laparoscopy

Excluded criteria: antiemetic drugs, pregnant or breastfeeding, body mass index (BMI) > 30 kg/m^2

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, (history of PONV/motion sickness, perioperative opioids): no; duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 28% (prochlorperazine 12.5 mg IM) Cyclizine • *Dose*: 50 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16% (prochlorperazine 12.5 mg IM) Placebo • *Dose*: 0.9% saline • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 47% (prochlorperazine 12.5 mg IM)

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Cholwill 1999 *(Continued)*

Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** outpatient, single-centre **Author's name:** J.M. Cholwill **Institution:** Department of Anaesthesia, Nottingham City Hospital, Nottingham, UK **Email:** NA **Address:** Department of Anaesthesia, Nottingham City Hospital, Hucknall Road, Nottingham NG5 1PB, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** primary outcome measures were incidence of moderate or severe nausea or vomiting and number of patients receiving escape antiemetic **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were allocated randomly, with stratification for past history of PONV" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the drugs were blinded to patients, investigators and recovery room staff"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the drugs were blinded to patients, investigators and recovery room staff"
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: 5 patients were withdrawn (1 required a mini-laparotomy, and data collection was incomplete in 4). All outcomes of the remaining

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Cholwill 1999 *(Continued)*

All outcomes		175 participants were analysed before discharge. Thirteen patients were admitted after surgery: 7 with PONV (2 from the ondansetron group and 4 from the saline group) and 6 for surgical reasons. Data from these patients and from the 53 patients who received rescue antiemetics were excluded from further analysis (after discharge)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patient data were comparable in all groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, (history of PONV/motion sickness, perioperative opioids): no; duration of anaesthesia, non-smoker): unclear

Chu 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: NA • *Analysed (n)*: 75 • *Age (mean ± SD, median (IQR), median (range))*: 43.8 ± 4.0 • *Weight (mean ± SD, median (IQR), median (range))*: 57.0 ± 9.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 25/50/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 7/16 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 112.7 • *Use of perioperative opioids (if yes, which?)*: 14 patients received 25 mg meperidine • *Type of surgery*: laparoscopic assisted vaginal hysterectomy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: NA • *Analysed (n)*: 77 • *Age (mean ± SD, median (IQR), median (range))*: 43.3 ± 3.8 • *Weight (mean ± SD, median (IQR), median (range))*: 55.8 ± 7.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 28/49/0/0

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Chu 2008 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 10/18
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 113.2
- *Use of perioperative opioids (if yes, which?)*: 20 patients received 25 mg meperidine
- *Type of surgery*: laparoscopic assisted vaginal hysterectomy

Haloperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 72
- *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 4.9
- *Weight (mean ± SD, median (IQR), median (range))*: 57.3 ± 9.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 25/47/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 6/17
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 117.6
- *Use of perioperative opioids (if yes, which?)*: 17 patients received 25 mg meperidine
- *Type of surgery*: laparoscopic assisted vaginal hysterectomy

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 74
- *Age (mean ± SD, median (IQR), median (range))*: 43.2 ± 5.4
- *Weight (mean ± SD, median (IQR), median (range))*: 58.0 ± 10.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/50/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 11/20
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 114.3
- *Use of perioperative opioids (if yes, which?)*: 15 patients received 25 mg meperidine
- *Type of surgery*: laparoscopic assisted vaginal hysterectomy

Haloperidol + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 74
- *Age (mean ± SD, median (IQR), median (range))*: 42.7 ± 5.2

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Chu 2008 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 58.1 ± 9.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 26/48/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 8/16
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115.2
- *Use of perioperative opioids (if yes, which?)*: 11 patients received 25 mg meperidine
- *Type of surgery*: laparoscopic assisted vaginal hysterectomy

Included criteria: ASA class I or II, women scheduled for laparoscopic assisted vaginal hysterectomy

Excluded criteria: clinical evidence of a difficult airway, obesity (body mass index 35 kg/m^2), pregnancy, psychiatric illness, clinically significant major organ disease, consumption of a drug with antiemetic properties within 24 hours before the study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 15 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 47% ondansetron 4 mg Droperidol • *Dose*: 1.25 mg • *Time point of administration*: 15 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 26% ondansetron 4 mg Haloperidol • *Dose*: 2 mg • *Time point of administration*: 15 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 25% ondansetron 4 mg Dexamethasone • *Dose*: 5 mg • *Time point of administration*: 15 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 24% ondansetron 4 mg Haloperidol + dexamethasone • *Dose*: haloperidol: 2 mg, dexamethasone: 5 mg • *Time point of administration*: 15 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 14% ondansetron 4 mg
Outcomes	*Vomiting (0 to 24 hours)*

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Chu 2008 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (0 to 2 hours)

- Outcome type: dichotomous outcome

Vomiting (2 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

QT prolongation (0 to 24 hours)

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Jhi-Joung Wang **Institution:** Department of Anesthesiology, Chi-Mei Medical Center, Tainan, Taiwan **Email:** 40002@mail.chimei.org.tw **Address:** Department of Anesthesiology, Chi-Mei Medical Center, Tainan, Taiwan **Duration of study:** NA **Language:** English **Study's primary outcome:** a complete response was defined as no PONV during the 0 to 24 hour post-operative period **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "assigned by use of a computer generated random number table into one of five groups"
Allocation concealment (selection bias)	Low risk	Judgement comment: no statement

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Chu 2008 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "study medications were prepared by a nurse anesthetist in identical syringes with a total volume of 2 ml (dilution with saline), and given IV 15 min after the induction of anesthesia. Patients and the investigators who collected the postoperative data were blinded to the randomization" Judgement comment: no information on blinding of anaesthesiologist
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients and the investigators who collected the postoperative data were blinded to the randomization"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "twenty-eight of the 400 patients enrolled in the study were excluded from the analysis; 16 patients required an abdominal hysterectomy, and, in 12 patients, we were unable to collect complete data. The data obtained from the remaining 372 patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patient characteristics such as age, weight, height, histories of PONV and motion sickness, and durations of surgery and anesthesia were not different among the five groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Chun 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 102 • *Received treatment (n)*: 102 • *Analysed (n)*: 95 • *Age (mean ± SD, median (IQR), median (range))*: 43 (20 to 70) • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 45.26 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: Inhalational anaesthesia (sevoflurane or desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 103 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 2 µg/kg

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Chun 2014 *(Continued)*

- *Type of surgery*: laparoscopic cholecystectomy 11, laparoscopic herniorrhaphy 13, minor orthopaedic surgery 23, plastic surgery 26, mastoidectomy with/or tympanoplasty 10, thyroidectomy 7, tonsillectomy 5

Palonosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 102
- *Received treatment (n)*: 102
- *Analysed (n)*: 94
- *Age (mean ± SD, median (IQR), median (range))*: 43 (20 to 70)
- *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 44.68
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane or desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 110
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 2 µg/kg
- *Type of surgery*: laparoscopic cholecystectomy 9, laparoscopic herniorrhaphy 14, minor orthopaedic surgery 22, plastic surgery 28, mastoidectomy with/or tympanoplasty 9, thyroidectomy 8, tonsillectomy 6

Included criteria: healthy inpatients; ASA I or II; 20 to 70 years of age; were undergoing elective surgery; underwent laparoscopic cholecystectomy or herniorrhaphy, minor orthopaedic surgery, plastic surgery, mastoidectomy and/or tympanoplasty, thyroidectomy, or tonsillectomy

Excluded criteria: pregnancy, body weight > 30% above ideal body weight, vomiting or retching within 24 hours before the operation, administration of antiemetics or steroids or psychoactive medications within 24 hours before the operation, had electively requested IV patient-controlled analgesia (IV PCA) using fentanyl for postoperative pain control or received IV PCA using fentanyl after operation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear. However, Apfel risk scores of participants were equally distributed among the groups

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Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg (11%)

Palonosetron

- *Dose*: 0.075 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg (11%)

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

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Chun 2014 *(Continued)*

- Outcome type: dichotomous outcome

Headache (0 to 72 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** S.I. Kim **Institution:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Hospital Seoul **Email:** soonnim@schmc.ac.kr **Address:** Soonchunhyang University Hospital Seoul, 657, Hannam-dong, Yongsan-gu, Seoul,Republic of Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV 0 to 24 hours after operation **Trial registry number:** KCT0000537
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed before surgery using a computer-generated randomized number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "the envelopes were opened before induction of anaesthesia by a trained nurse not involved in the study" Judgement comment: not mentioned: "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the nurse then prepared the appropriate study medication as an injectable solution (1.5 ml) placed in identical syringes, for i.v. administration after the induction of anaesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all patients and investigators collecting the postoperative data were blinded to the randomization"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "among the 204 patients enrolled in this study, 15 patients were withdrawn from the study due to receiving i.v. PCA using fentanyl for pain control after being transferred to the ward. Therefore, only data obtained from the re-

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Chun 2014 *(Continued)*

		maining 189 patients were analysed: 94 patients in the palonosetron group and 95 in the placebo group"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: KCT0000537 (retrospective registration)
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear. However, Apfel risk scores of participants were equally distributed among the groups

Contreras Dominguez 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 27.8 ± 3.7 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27.6 ± 3.1 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 52 • *Non-smoker (%)*: 68 • *History of PONV/motion sickness (%)*: 4/NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 47.2 • *Use of perioperative opioids (if yes, which?)*: fentanyl, 5 mg/48 h morphine • *Type of surgery*: appendectomy Droperidol (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 26.5 ± 3.1 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.8 ± 2.3 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 48 • *Non-smoker (%)*: 72 • *History of PONV/motion sickness (%)*: 4/NA

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Contreras Dominguez 2008 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 43.7
- *Use of perioperative opioids (if yes, which?)*: fentanyl, 3 mg/48 h morphine
- *Type of surgery*: appendectomy

Metoclopramide (group 3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 28.5 ± 2.8
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26.8 ± 6.5
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 44
- *Non-smoker (%)*: 64
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 56.8
- *Use of perioperative opioids (if yes, which?)*: fentanyl, 4 mg/48 h morphine
- *Type of surgery*: appendectomy

Tropisetron (group 4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 25.6 ± 3.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24.4 ± 3.7
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 52
- *Non-smoker (%)*: 64
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 59.2
- *Use of perioperative opioids (if yes, which?)*: fentanyl, 5 mg/48 h morphine
- *Type of surgery*: appendectomy

Granisetron (group 5)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 31.1 ± 3.6
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 27.6 ± 2.9
- *ASA I/II/III/IV (n)*: NA/NA/0/0

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Contreras Dominguez 2008 *(Continued)*

- *Gender (female in %)*: 44
- *Non-smoker (%)*: 68
- *History of PONV/motion sickness (%)*: 4/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 48.7
- *Use of perioperative opioids (if yes, which?)*: fentanyl, 6 mg/48 h morphine
- *Type of surgery*: appendectomy

Dexamethasone (group 6)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 34.2 ± 4.3
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 28.2 ± 3.1
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 56
- *Non-smoker (%)*: 60
- *History of PONV/motion sickness (%)*: 8/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 55.3
- *Use of perioperative opioids (if yes, which?)*: fentanyl, 3 mg/48 h morphine
- *Type of surgery*: appendectomy

Included criteria: adult patients, ASA I or II, stable, between 18 and 65 years of age, body mass index (BMI) < 30, undergoing appendectomy at the Emergency Service of the Hospital Clínico Regional de Concepción, Chile

Excluded criteria: NA

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

Interventions	**Intervention characteristics** Placebo (group 1) • *Dose*: normal saline • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Droperidol (group 2) • *Dose*: 0.625 mg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Metoclopramide (group 3) • *Dose*: 20 mg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV

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Contreras Dominguez 2008 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Tropisetron (group 4)

- *Dose*: 5 mg
- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Granisetron (group 5)

- *Dose*: 1 mg
- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Dexamethasone (group 6)

- *Dose*: 4 mg
- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Outcomes	*Arrhythmia (0 to 48 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Chile **Setting:** inpatient, single-centre **Author's name:** Víctor Contreras-Domínguez **Institution:** Hospital Clínico Regional de Concepción **Email:** viccontredom@yahoo.com **Address:** Hospital Clínico Regional de Concepción, Calle San Martín, 1436, Concepción, Chile **Duration of study:** December 2003 to February 2006 **Language:** English **Study's primary outcome:** incidence in PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement

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Contreras Dominguez 2008 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned to one of six groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperative follow-up was done by another anesthesiologist, who did not know which drug was given to the patient. The presence or absence (incidence)..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no statistically significant differences regarding gender, BMI, duration of anesthesia and postoperative morphine consumption among the study groups (Table I)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

Corcoran 2017

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 16 • *Received treatment (n)*: NA • *Analysed (n)*: 15 (24 hours) • *Age (mean ± SD, median (IQR), median (range))*: 44 (40 to 46) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27 (21 to 31) • *ASA I/II/III/IV (n)*: 11/4/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 93 • *History of PONV/motion sickness (%)*: 27/47

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Corcoran 2017 *(Continued)*

- *Type of general anaesthesia*: propofol infusions, intraoperative opioids were administered at the attending anaesthetist's discretion
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 135
- *Use of perioperative opioids (if yes, which?)*: total intraoperative fentanyl 225 µg, use of other intraoperative opioids (morphine 20%, methadone 0%, nil other 80%), postoperative fentanyl IV and oxycodone 5 mg to 15 mg orally
- *Type of surgery*: major laparoscopic surgery

Dexamethasone + granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 16
- *Received treatment (n)*: NA
- *Analysed (n)*: 16 (24 h)
- *Age (mean ± SD, median (IQR), median (range))*: 45 (41 to 48)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26 (23 to 35)
- *ASA I/II/III/IV (n)*: 7/9/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 56
- *History of PONV/motion sickness (%)*: 25/25
- *Type of general anaesthesia*: propofol infusions, intraoperative opioids were administered at the attending anaesthetist's discretion
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 123
- *Use of perioperative opioids (if yes, which?)*: total intraoperative fentanyl 250 µg, use of other intraoperative opioids (morphine 6%, methadone 6%, nil other 88%), postoperative fentanyl IV and oxycodone 5 mg to 15 mg orally
- *Type of surgery*: major laparoscopic surgery

Included criteria: adult females, ASA I or II, 18 to 60 years of age, undergoing elective major laparoscopic gynaecological surgery expected to require at least 90 minutes of operative time, requiring a hospital stay to include at least the first postoperative night

Excluded criteria: currently or recently taking immunosuppressive agents; had known or suspected malignancy, hypertension, or diabetes mellitus; history of peptic ulceration, chronic pain syndrome requiring regular opioid consumption, a predicted requirement for IV patient-controlled analgesia, or known hypersensitivity to dexamethasone or granisetron

Pretreatment: history of PONV/motion sickness

Interventions	**Intervention characteristics** Granisetron • *Dose*: 1 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 13%; NA Dexamethasone + granisetron • *Dose*: dexamethasone 4 mg + granisetron 1 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0%; NA
Outcomes	*Vomiting (PACU)*

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Corcoran 2017 *(Continued)*

- Outcome type: dichotomous outcome

Postoperative wound infection (day two)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** Royal Perth Hospital (departmental funds); Health Department of Western Australia (Raine Foundation Clinical Practitioner Fellowship to T.C.); University of Western Australia (T.C.). **Country:** Australia **Setting:** inpatient, single-centre **Author's name:** Tomas Corcoran **Institution:** Department of Anaesthesia and Pain Medicine, Royal Perth Hospital **Email:** tomas.corcoran@health.wa.gov.au **Address:** Royal Perth Hospital, Box X2213 GPO Perth 6847, Western Australia, Australia **Duration of study:** February 2010 to March 2013 **Language:** English **Study's primary outcome:** NA **Trial registry number:** ACTRN12608000340336
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomized before surgery, in a 1:1 ratio, using a computer-generated random number sequence"
Allocation concealment (selection bias)	Unclear risk	Quote: "and allocated to one of two groups using sealed opaque envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study drug was prepared by an observer who was not connected to the study and diluted to a total volume of 4 ml with 0.9% sodium chloride in an unmarked syringe"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patient, the patient's anaesthetist, and all investigators were blinded to the study drug identity"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of failure to comply with the study protocol, leaving data on 31 patients to be analysed. Two patients in each group did not complete cell count testing at 48 h, and five patients in the Control group and four in the Dexamethasone group did not complete cell count testing at 6 weeks after surgery"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: ACTRN12608000340336 (prospective registration). The prospectively registered primary outcome (T- and B-cell population) was re-

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Corcoran 2017 *(Continued)*

		ported in the protocol without any timing of assessment. The study paper included time measurements for the primary outcome at 24 hours, 7 days, and 6 weeks from baseline values. The focus of the study was not PONV, and primary and secondary outcomes were not defined in the study report
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): yes

Cortes Flores 2018

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 51.1 ± 14.5 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.4 ± 3.6 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 77 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 82.3 • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg (premedication) + 3 µg/kg (induction), 2.5 mg morphine for postoperative pain • *Type of surgery*: partial mastectomy Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 50.5 ± 12.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26.4 ± 4.4 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 80 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA

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Cortes Flores 2018 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 82.8
- *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg (premedication) + 3 µg/kg (induction), 2.5 mg morphine for postoperative pain
- *Type of surgery*: partial mastectomy

Included criteria: women scheduled to receive an elective partial mastectomy with or without axillary gland removal, confirmed diagnosis of breast carcinoma

Excluded criteria: ASA III or IV disease; over 70 years of age; pregnancy; previous steroid therapy; uncontrolled diabetes mellitus (serum glycated haemoglobin level > 8%); use of opioids, sedatives, or analgesics within a week before surgery; any history of alcohol or drug abuse, inner ear disease, and/or uncontrollable severe PONV after any surgical procedure

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Dexamethasone + ondansetron • *Dose*: dexamethasone 8 mg, ondansetron 4 mg • *Time point of administration*: dexamethasone 1 hour before surgery, ondansetron during surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Ondansetron • *Dose*: 4 mg • *Time point of administration*: placebo 1 hour before surgery, ondansetron during surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Mortality (during study, 24 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (during study, 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Mexico **Setting:** inpatient, single-centre **Author's name:** Alejandro González-Ojeda **Institution:** Biomedical Research Unit 02, Specialities Hospital of the Western National Medical Center,Mexican Institute of Social Security, Guadalajara, Mexico **Email:** avygail5@yahoo.com.mx ; avygail5@gmail.com

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Cortes Flores 2018 *(Continued)*

Address: Biomedical Research Unit 02, Specialties Hospital of the Western Medical Center, Mexican Institute of Social Security, Guadalajara, Mexico

Duration of study: June 2013 to October 2014

Language: English

Study's primary outcome: NA

Trial registry number: NCT02305173

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated by sealed envelope assignment"
Allocation concealment (selection bias)	Unclear risk	Quote: "sealed envelope assignment" Judgement comment: not stated; "sequentially numbered, opaque, sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT02305173 (retrospective registration)
Other bias	High risk	Quote: "the selection of patients is described in Figure 1. Age and anthropometric measures did not differ significantly between groups (Table 1). The most frequent comorbid conditions observed were type 2 diabetes and hypertension. Tobacco was used by 23% of patients in the treatment group and 20% in the control group. The anaesthesia and mask removal times and details about intraoperative blood loss for both groups are shown in Table 1. These variables did not differ significantly between the two groups. Analysis of the post operative..." Quote: "the frequency of use of morphine was significantly different between groups at 1 (p = .01), 6 (p = .02), and 12 (p = .04) hr" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness): unclear; (perioperative opioids): yes

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Cubukcu 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (tramadol group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 45.0 ± 19.4 • *Weight (mean ± SD, median (IQR), median (range))*: 74.0 ± 14.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 12/18/0/0 • *Gender (female in %)*: 68 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 142.4 • *Use of perioperative opioids (if yes, which?)*: tramadol 467.2 mg via PCA • *Type of surgery*: lower extremity surgery Ondansetron (tramadol group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 45.2 ± 19.2 • *Weight (mean ± SD, median (IQR), median (range))*: 68.7 ± 13.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 12/18/0/0 • *Gender (female in %)*: 64 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 165.4 • *Use of perioperative opioids (if yes, which?)*: tramadol 646.6 mg via PCA • *Type of surgery*: lower extremity surgery Placebo (morphine group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 43.9 ± 14.9 • *Weight (mean ± SD, median (IQR), median (range))*: 71.0 ± 11.3

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Cubukcu 2007 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 10/20/0/0
- *Gender (female in %)*: 72
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 160.0
- *Use of perioperative opioids (if yes, which?)*: morphine 34.9 mg via PCA
- *Type of surgery*: lower extremity surgery

Ondansetron (morphine group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 44.9 ± 18.6
- *Weight (mean ± SD, median (IQR), median (range))*: 68.5 ± 14.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 13/17/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 160.4
- *Use of perioperative opioids (if yes, which?)*: morphine 35.4 mg via PCA
- *Type of surgery*: lower extremity surgery

Included criteria: ASA I or II, elective lower extremity surgery

Excluded criteria: severe CHD; renal or liver disease; motion sickness; history of PONV; over 18 years of age; lack of understanding in using PCA pump; allergy to morphine, ondansetron, or tramadol

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, duration of anaesthesia): no; (non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Placebo (tramadol group) • *Dose*: saline • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (tramadol group) • *Dose*: 0.1 mg/kg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo (morphine group) • *Dose*: saline

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Cubukcu 2007 *(Continued)*

- *Time point of administration*: at induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron (morphine group)

- *Dose*: 4 mg
- *Time point of administration*: at induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Yasemin Günes **Institution:** Cukurova University Faculty Of Medicine Department Of Anesthesiology, Adana, Turkey **Email:** ygunes8cu.edu.tr **Address:** Cukurova University Faculty of Medicine, Department of Anesthesiology, 01330, Adana, Turkey **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Four groups (2 × tramadol, 2 × morphine). Same interventions (placebo, ondansetron) pooled for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote (translated): "outcome assessor was a blinded nurse"

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Cubukcu 2007 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, duration of anaesthesia): no; (non-smoker): unclear; (perioperative opioids): yes

Daabiss 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Saline (group S) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 30 ± 5.3 • *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 30/0/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 105 • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg for induction • *Type of surgery*: laparoscopic cholecystectomy Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 29 ± 7.4 • *Weight (mean ± SD, median (IQR), median (range))*: 76 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 30/0/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: 100

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Daabiss 2008 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115
- *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg for induction
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: non-smoker, adult patients, ASA I, undergoing elective laparoscopic cholecystectomy with general anaesthesia

Excluded criteria: history of gastro-oesophageal reflux or taking medications with known antiemetic activity

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia, non-smoker, perioperative opioids): no; (gender, history of PONV/motion sickness): unclear

Interventions	**Intervention characteristics** Saline (group S) • *Dose*: saline • *Time point of administration*: 10 minutes before end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 47% (ondansetron 4 mg IV) Dexamethasone (group D) • *Dose*: 5 mg • *Time point of administration*: 10 minutes before end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 23% (ondansetron 4 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Postoperative wound infection (after 1 week)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Saudi-Arabia **Setting:** outpatient, single-centre **Author's name:** Mohamed A. Daabiss **Institution:** Riyadh Armed Forces Hospital **Email:** NA

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Daabiss 2008 *(Continued)*

	Address: Riad 12233, Saudi-Arabia **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (ephedrine group not relevant)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized into three groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "these drugs were prepared and given ten minutes before the end of the procedure by a single anesthetist who took no part in data collection"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "for severe nausea or vomiting by trained nurse without knowledge of which drugs the patients had received. Emesis score < 2..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patient characteristics such as age, weight, duration of anesthesia and surgery, recovery time, and intraoperative fluid requirement were comparable in the 3 groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia, non-smoker, perioperative opioids): no; (gender, history of PONV/motion sickness): unclear

Dabbous 1998

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, combination prophylaxis
Participants	**Baseline characteristics**

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Dabbous 1998 *(Continued)*

Promethazine + ondansetron (females)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 26
- *Age (mean ± SD, median (IQR), median (range))*: 48.3 ± 16.6
- *Weight (mean ± SD, median (IQR), median (range))*: 68.3 ± 10.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 3.85/7.69
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102.6
- *Use of perioperative opioids (if yes, which?)*: 75 mg meperidine as premedication, 2 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic cholecystectomy

Promethazine + metoclopramide (females)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 27
- *Age (mean ± SD, median (IQR), median (range))*: 41.3 ± 13.4
- *Weight (mean ± SD, median (IQR), median (range))*: 69.1 ± 11.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 11.11/7.41
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90.9
- *Use of perioperative opioids (if yes, which?)*: 75 mg meperidine as premedication, 2 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic cholecystectomy

Promethazine + ondansetron (males)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 18
- *Age (mean ± SD, median (IQR), median (range))*: 47.1 ± 12.7
- *Weight (mean ± SD, median (IQR), median (range))*: 87.5 ± 18.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 0
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 5.56/0

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Dabbous 1998 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 103.3
- *Use of perioperative opioids (if yes, which?)*: 75 mg meperidine as premedication, 2 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic cholecystectomy

Promethazine + metoclopramide (males)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 14
- *Age (mean ± SD, median (IQR), median (range))*: 43.5 ± 9.8
- *Weight (mean ± SD, median (IQR), median (range))*: 84.3 ± 18.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 0
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 7.14/7.14
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115.8
- *Use of perioperative opioids (if yes, which?)*: 75 mg meperidine as premedication, 2 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, scheduled for laparoscopic cholecystectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Promethazine + ondansetron (females) • *Dose*: promethazine 25 mg, ondansetron 4 mg • *Time point of administration*: promethazine 45 minutes before induction of anaesthesia, ondansetron after induction • *Route of administration*: promethazine IM, ondansetron IV • *Rescue antiemetics (if yes, which?)*: NA Promethazine + metoclopramide (females) • *Dose*: promethazine 25 mg, metoclopramide 10 mg • *Time point of administration*: promethazine 45 minutes before induction of anaesthesia, metoclopramide after induction • *Route of administration*: promethazine IM, metoclopramide IV • *Rescue antiemetics (if yes, which?)*: NA Promethazine + ondansetron (males) • *Dose*: promethazine 25 mg, ondansetron 4 mg • *Time point of administration*: promethazine 45 minutes before induction of anaesthesia, ondansetron after induction • *Route of administration*: promethazine IM, ondansetron IV • *Rescue antiemetics (if yes, which?)*: NA

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Dabbous 1998 *(Continued)*

	Promethazine + metoclopramide (males) • *Dose*: promethazine 25 mg, metoclopramide 10 mg • *Time point of administration*: promethazine 45 minutes before induction of anaesthesia, metoclopramide after induction • *Route of administration*: promethazine IM, metoclopramide IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Lebanon **Setting:** inpatient, single-centre **Author's name:** Gattas Khoury **Institution:** Department of Surgery, American University of Beirut Medical Center, Beirut, Lebanon **Email:** NA **Address:** Department of Surgery, American University of Beirut Medical Center, Box B-37, P.O. Box 113-6044, Beirut, Lebanon **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Four groups pooled into 2 groups with same interventions for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a random number was used to assign prospectively each patient to receive after induction of anesthesia either ondansetron 4 mg (A), or metoclopramide 10 mg (B)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the staff caring for these patients were blinded to the study drug received"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an independent blinded observer recorded emetic episodes" Quote: "after two hours, patients were discharged to the floor, where they were followed up to 24 hours by another independent observer; the number of patients who vomited was recorded in each group" Quote: "the staff caring for these patients were blinded to the study drug received"

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Dabbous 1998 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no differences between study groups with respect to age, anaesthetic technique, duration of operation, diabetes, days since the last menstrual period in females, or history of previous postoperative nausea and vomiting as well as the need for postoperative analgesics (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Dabbous 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Granisetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 42 • *Age (mean ± SD, median (IQR), median (range))*: 46.5 ± 11.7 • *Weight (mean ± SD, median (IQR), median (range))*: 75.8 ± 16.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 47.62 • *Non-smoker (%)*: 52.38 • *History of PONV/motion sickness (%)*: 11.90/2.38 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 61 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl • *Type of surgery*: laparoscopic cholecystectomy or herniorrhaphy Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 42 • *Age (mean ± SD, median (IQR), median (range))*: 47.4 ± 14.2 • *Weight (mean ± SD, median (IQR), median (range))*: 77.5 ± 14.1

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Dabbous 2010 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 52.38
- *Non-smoker (%)*: 57.14
- *History of PONV/motion sickness (%)*: 9.52/4.76
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 62
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: laparoscopic cholecystectomy or herniorrhaphy

Included criteria: ASA I or II, scheduled for laparoscopic cholecystectomy or herniorrhaphy

Excluded criteria: known allergies or hypersensitivity to study drugs, history of chronic nausea and vomiting or experienced nausea and vomiting in the past 24 hours before anaesthesia, had received any antiemetics or any drug with antiemetic properties during the 24 hours before anaesthesia, BMI ≥ 35 kg/m^2, over 70 years of age, pregnant or breastfeeding, had a condition requiring long-term opioid use

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Granisetron + dexamethasone • *Dose*: granisetron 1 mg, dexamethasone 8 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Headache (PACU)* • Outcome type: dichotomous outcome *Sedation/drowsiness (PACU)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Lebanon **Setting:** inpatient, single-centre **Author's name:** Alia Dabbous

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Dabbous 2010 *(Continued)*

Institution: Department of Anesthesiology, American University of Beirut Medical Center, Beirut, Lebanon

Email: ad00@aub.edu.lb

Address: Department of Anesthesiology, American University of Beirut. P.O. Box 11-0236, Beirut 1107-2020, Lebanon

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer generated randomization method"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "were presented to blinded investigators as identical 2 ml filled syringes" Quote: "the study medications were prepared by a resident, who was not involved in any other part of the study, and were presented to blinded investigators..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "adverse events were evaluated and recorded by a resident who was blinded to the study drugs used"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "of the 100 patients initially signing the informed consent, 84 patients (42 in group I, 42 in group II) completed the study" Judgement comment: missing data > 15%. No reasons mentioned for loss of participants
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no statistically significant difference between the two groups in regards to gender, history of PONV and history of motion sickness, age, weight, type of surgery (laparoscopic cholecystectomy or laparoscopic herniorraphy), duration of surgery, history of prolonged gastric emptying, and smoking history (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

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Dagtekin 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Haloperidol (group H) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 51 ± 20 • *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 100 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane + remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: remifentanil, 3 mg piritramide, 10 mg oxycodone if necessary • *Type of surgery*: strabismus or retinal operation Haloperidol + ondansetron (group H/O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 53 ± 16 • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 100 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane + remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: remifentanil, 3 mg piritramide, 10 mg oxycodone if necessary • *Type of surgery*: strabismus or retinal operation **Included criteria:** female patients older than 18 years; non-smoking and with history of PONV or motion sickness; scheduled for strabismus or retinal operation with the use of postoperative opioids; ability to speak and write German required **Excluded criteria:** severe psychiatric or neurological diseases or drug abuse

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Dagtekin 2009 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (duration of anaesthesia, perioperative opioids): unclear
Interventions	**Intervention characteristics** Haloperidol (group H) • *Dose*: 10 µg/kg • *Time point of administration*: 20 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: intravenous dimenhydrinate 62 mg; 30% Haloperidol + ondansetron (group H/O) • *Dose*: haloperidol 10 µg/kg; ondansetron 0.1 mg/kg • *Time point of administration*: 20 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: intravenous dimenhydrinate 62 mg; 10%
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study is supported by internal sources of the Department of Anaesthesiology, University of Cologne, Cologne, Germany. Financial relationships between any of the study authors and any commercial interest with a vested interest in the outcome of the study are disclosed **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Oguzhan Dagtekin **Institution:** Department of Anaesthesiology, University of Cologne, Cologne, Germany **Email:** oguzhan.dagtekin@uk-koeln.de **Address:** Klinik für Anästhesiologie und Operative Intensivmedizin Klinikum der Universität zu Köln, Kerpener Strasse 62 DE–50937 Cologne (Germany) **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA

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Dagtekin 2009 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "excluded. Randomization was based on a computer-generated code"
Allocation concealment (selection bias)	Low risk	Quote: "prepared at a remote site and sealed in sequentially numbered, opaque envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the investigators involved [in] the operation and the postoperative care (P.W., M.M.H., and J.H.-L) were blinded regarding the content of the study medication"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "60 female patients were enrolled in our study, 30 for each group. The data of all patients were eligible for statistical analyses. The H-Group and the H/O-Group were comparable regarding demographic data (table 1). All patients completed the study protocol"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (duration of anaesthesia, perioperative opioids): unclear

DAngelo 2005

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Granisetron (0.1 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 31 • *Age (mean ± SD, median (IQR), median (range))*: 41.7 ± 4.7 • *Weight (mean ± SD, median (IQR), median (range))*: 73.8 ± 14.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100

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DAngelo 2005 *(Continued)*

- *Non-smoker (%)*: 65
- *History of PONV/motion sickness (%)*: 10/16
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 128.2
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg to 10 µg/kg, morphine 1 mg to 4 mg as rescue analgesic
- *Type of surgery*: open abdominal hysterectomy

Granisetron (0.2 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 27
- *Age (mean ± SD, median (IQR), median (range))*: 42.7 ± 7.1
- *Weight (mean ± SD, median (IQR), median (range))*: 72.9 ± 11.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 81
- *History of PONV/motion sickness (%)*: 33/30
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.3
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg to 10 µg/kg, morphine 1 mg to 4 mg as rescue analgesic
- *Type of surgery*: open abdominal hysterectomy

Granisetron (0.3 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 33
- *Age (mean ± SD, median (IQR), median (range))*: 45.2 ± 8.3
- *Weight (mean ± SD, median (IQR), median (range))*: 77.3 ± 13.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 67
- *History of PONV/motion sickness (%)*: 24/12
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115.1
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg to 10 µg/kg, morphine 1 mg to 4 mg as rescue analgesic
- *Type of surgery*: open abdominal hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA

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DAngelo 2005 *(Continued)*

- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 43.7 ± 10.4
- *Weight (mean ± SD, median (IQR), median (range))*: 73.3 ± 12.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 47
- *History of PONV/motion sickness (%)*: 33/10
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 113.1
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg to 10 µg/kg, morphine 1 mg to 4 mg as rescue analgesic
- *Type of surgery*: open abdominal hysterectomy

Included criteria: female patients 18 to 64 years of age were eligible for enrolment if they were scheduled to undergo elective open abdominal hysterectomy requiring general anaesthesia and had ASA status of I to III. Concomitant procedures were limited to salpingectomy, oophorectomy, and lysis of adhesions

Excluded criteria: scheduled to receive propofol for induction and/or maintenance of anaesthesia; had known hypersensitivity to granisetron, or any agent that was part of the anaesthesia regimen, or other medications to be administered relative to surgery; were pregnant or breastfeeding; had experienced retching/vomiting or moderate or severe nausea in the 24 hours before anaesthesia; had chronic nausea and/or vomiting; had received an antiemetic drug or a drug with antiemetic properties within the 24 hours before anaesthesia or were scheduled to receive such medications during surgery or within the 24 hours following surgery; had body mass index ≥ 34; had a condition that required long-term opioid use

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (perioperative opioids): unclear; (non-smoker, history of PONV/motion sickness): yes

Interventions	**Intervention characteristics** Granisetron (0.1 mg group) • *Dose*: 0.1 mg • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 55% (discretion of the investigator) Granisetron (0.3 mg group) • *Dose*: 0.2 mg • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 68% (discretion of the investigator) Granisetron (0.3 mg group) • *Dose*: 0.3 mg • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 43% (discretion of the investigator) Placebo • *Dose*: saline 0.9% • *Time point of administration*: 15 minutes before end of surgery

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DAngelo 2005 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 70% (discretion of the investigator)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (24 hours)* • Outcome type: dichotomous outcome *Headache (24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this research was supported by Roche Laboratories Inc., Nutley, New Jersey **Country:** USA **Setting:** inpatient, multi-centre (11) **Author's name:** Robert D'Angelo **Institution:** Wake Forest University School of Medicine, Winston-Salem, NC, USA **Email:** rdangelo@wfubmc.edu **Address:** Wake Forest University School of Medicine, Forsyth Medical Center, 333 Silas Street Parkway, Winston-Salem, NC 27013, USA **Language:** English **Duration of study:** 12 March to 16 August 2002 **Trial registry number:** NA **Study's primary outcome:** no vomiting in 0 to 6 hours
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "treatment assignment was based on computer-generated randomization lists prepared by the study sponsor prior to the study. Separate randomization lists were generated for each study site using a prespecified block size"
Allocation concealment (selection bias)	Low risk	Quote: "patient randomization numbers were assigned sequentially at each site in the order in which patients were enrolled. The randomization list at each site was provided only to the unblinded pharmacist who prepared the injection. The pharmacist was not involved in any other part of the study. To

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DAngelo 2005 *(Continued)*

		maintain blinding, study medications were presented by the pharmacist to the investigator as identical 5 ml solutions for injection in 10 ml syringes" Judgement comment: allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "in which patients were enrolled. The randomization list at each site was provided only to the unblinded pharmacist who prepared the injection. The pharmacist was not involved in any other part of the study. To maintain blinding, study medications were presented by the pharmacist to the investigator as identical 5 ml solutions for injection in 10 ml syringes. On the day of the scheduled surgery, a baseline physical examination..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: it is clear from the description of the the domains "sequence generation", "allocation concealment", and "blinding of participants and personnel" whether the only person who knew the group allocation was the unblinded pharmacist, who was not involved in any other part of the study. Therefore, all other study staff had to be blind to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "in all, 140 patients scheduled for abdominal hysterectomy were enrolled in the study between 12 March and 16 August 2002 at 11 study centres in the USA. Of these, 121 patients were randomized, treated with study medication and included in efficacy and safety analyses. One patient in the granisetron 0.1 mg treatment group was withdrawn from the study prematurely due to additional surgery requiring repeat anaesthesia approximately 2 hours after the original surgery was completed" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "patient characteristics and other baseline characteristics are summarized in Table 1. For some variables such as history of motion sickness or smoking, randomization did not result in equal distributions across treatment groups" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (perioperative opioids): unclear; (non-smoker, history of PONV/motion sickness): yes

Daria 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Metoclopramide (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 26.1 ± 5.33

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Daria 2012 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 52.63 ± 6.33
- *BMI (mean ± SD, median (IQR), median (range))*: 21.59 ± 2.88
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 11.06
- *Use of perioperative opioids (if yes, which?)*: intraoperative tramadol 2 mg/kg
- *Type of surgery*: laparoscopic gynaecological surgery

Ondansetron (group B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 26.4 ± 6.18
- *Weight (mean ± SD, median (IQR), median (range))*: 51.33 ± 7.58
- *BMI (mean ± SD, median (IQR), median (range))*: 21.44 ± 2.83
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 11.26
- *Use of perioperative opioids (if yes, which?)*: intraoperative tramadol 2 mg/kg
- *Type of surgery*: laparoscopic gynaecological surgery

Granisetron (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 27.4 ± 6.21
- *Weight (mean ± SD, median (IQR), median (range))*: 50.1 ± 9.05
- *BMI (mean ± SD, median (IQR), median (range))*: 21.40 ± 3.55
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 11.56
- *Use of perioperative opioids (if yes, which?)*: intraoperative tramadol 2 mg/kg
- *Type of surgery*: laparoscopic gynaecological surgery

Metoclopramide + dexamethasone (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30

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Daria 2012 *(Continued)*

- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 26.27 ± 5.13
- *Weight (mean ± SD, median (IQR), median (range))*: 48.9 ± 7.48
- *BMI (mean ± SD, median (IQR), median (range))*: 20.83 ± 2.77
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 11.1
- *Use of perioperative opioids (if yes, which?)*: intraoperative tramadol 2 mg/kg
- *Type of surgery*: laparoscopic gynaecological surgery

Ondansetron + dexamethasone (group E)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 27.47 ± 4.88
- *Weight (mean ± SD, median (IQR), median (range))*: 52.3 ± 8.90
- *BMI (mean ± SD, median (IQR), median (range))*: 21.69 ± 3.65
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 10.5
- *Use of perioperative opioids (if yes, which?)*: intraoperative tramadol 2 mg/kg
- *Type of surgery*: laparoscopic gynaecological surgery

Granisetron + dexamethasone (group F)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 26.33 ± 5.66
- *Weight (mean ± SD, median (IQR), median (range))*: 48.13 ± 7.39
- *BMI (mean ± SD, median (IQR), median (range))*: 20.8 ± 2.56
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 11.17
- *Use of perioperative opioids (if yes, which?)*: intraoperative tramadol 2 mg/kg
- *Type of surgery*: laparoscopic gynaecological surgery

Included criteria: adult female patients, ASA I or II, BMI 30 kg/m^2, 18 to 55 years of age, undergoing laparoscopic gynaecological surgery under general anaesthesia

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Daria 2012 *(Continued)*

Excluded criteria: gastrointestinal disease (i.e. patients with hiatus hernia, acid peptic disease, reflux oesophagitis, or cirrhosis liver), history of motion sickness, past history of PONV, menstruating, taking hormonal therapy, had taken antiemetic within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide (group A) • *Dose*: 10 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (group B) • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Granisetron (group C) • *Dose*: 3 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide + dexamethasone (group D) • *Dose*: metoclopramide 10 mg, dexamethasone 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron + dexamethasone (group E) • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Granisetron + dexamethasone (group F) • *Dose*: granisetron 3 mg, dexamethasone 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Headache (0 to 6 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 0 to 6 hours)*

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Daria 2012 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** India **Setting:** outpatient, single-centre **Author's name:** Usha Daria **Institution:** Department of Anaesthesia, Jhalawar Medical College, Jhalawar (Rajasthan), 326001 **Email:** drvinodusha@gmail.com **Address:** Department of Anaesthesia, Jhalawar Medical College, Jhalawar (Rajasthan), 326001 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly selected" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

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Delas Ramirez 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 44.56 ± 13.86 • *Weight (mean ± SD, median (IQR), median (range))*: 62.57 ± 9.52 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 17/18/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 106.14 • *Use of perioperative opioids (if yes, which?)*: 363 µg intraoperative fentanyl, 2 mg postoperative morphine • *Type of surgery*: major gynaecological surgery Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 42.38 ± 10.17 • *Weight (mean ± SD, median (IQR), median (range))*: 68.03 ± 7.96 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 19/16/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 117.5 • *Use of perioperative opioids (if yes, which?)*: 430 µg intraoperative fentanyl, 4 mg postoperative morphine • *Type of surgery*: major gynaecological surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 34 • *Received treatment (n)*: NA • *Analysed (n)*: 34

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Delas Ramirez 2001 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 41.17 ± 9.65
- *Weight (mean ± SD, median (IQR), median (range))*: 65.58 ± 9.91
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 23/11/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 118.34
- *Use of perioperative opioids (if yes, which?)*: 403 µg intraoperative fentanyl, 3.2 mg postoperative morphine
- *Type of surgery*: major gynaecological surgery

Included criteria: women ASA I to II, 18 to 65 years of age, weight 50 kg to 90 kg, scheduled to undergo major gynaecological surgery under general anaesthesia

Excluded criteria: BMI > 40 kg/m^2; history of cardiovascular, pulmonary, renal, hepatic or neurological disease; history of PONV; motion sickness; predisposing intestinal pathologies; symptoms of nausea, vomiting, and retching; use of antiemetics in the 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Droperidol • *Dose*: 1.25 mg • *Time point of administration*: immediately after surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% (ondansetron 8 mg) Metoclopramide • *Dose*: 10 mg • *Time point of administration*: immediately after surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% (ondansetron 8 mg) Placebo • *Dose*: saline • *Time point of administration*: immediately after surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% (ondansetron 8 mg)
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Spain **Setting:** inpatient, single-centre

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Delas Ramirez 2001 *(Continued)*

Author's name: F.J. Delás Ramírez

Institution: Servicio de Anestesiología, Reanimación y Terapéutica del Dolor, Hospital Universitarío de Girona Doctor Josep Trueta

Email: anestesia@htrueta.ses.es

Address: Hospital Universitario de Girona Doctor Josep Trueta, Avda. de Francia, s/n 17007 Girona

Duration of study: NA

Language: Spanish (2 reviewers with Spanish language skills)

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly to one of the following three groups" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Demiraran 2005

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different routes of administration
Participants	**Baseline characteristics**

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Demiraran 2005 *(Continued)*

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 31
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 16
- *Weight (mean ± SD, median (IQR), median (range))*: 68.4 ± 15.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 149
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative tramadol
- *Type of surgery*: gynaecological operations

Ondansetron (group O)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 49 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 73.7 ± 15.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 154
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative tramadol
- *Type of surgery*: gynaecological operations

Ondansetron (group DT)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 31
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 17
- *Weight (mean ± SD, median (IQR), median (range))*: 71.6 ± 15.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 145

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Demiraran 2005 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative tramadol
- *Type of surgery*: gynaecological operations

Included criteria: female inpatients, ASA I to III, scheduled to undergo gynaecological operations under general anaesthesia

Excluded criteria: had experienced nausea or vomiting 24 hours before the study, were taking antiemetic medication

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 15 minutes preoperative • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron (group O) • *Dose*: 8 mg • *Time point of administration*: 15 minutes preoperative • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron (group DT) • *Dose*: 8 mg • *Time point of administration*: 15 minutes preoperative • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Headache (0 to 6 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Ismail Özdemir **Institution:** Department Obstetrics and Gynecology, Abant Izzet Baysal University Düzce School of Medicine, Düzce, Turkey

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Demiraran 2005 *(Continued)*

Email: drismailozdemir@yahoo.com

Address: AIBÜ Düzce Tip Fakültesi, Kadin Hastaliklari ve Dogum AD, 81620 Konuralp, Düzce, Türkiye

Duration of study: January 2003 to December 2004

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were prospectively randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no blinding of participants or personnel (different routes of administration, no sham treatment)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the staff evaluating the patients during postoperative period was blinded for postoperative nausea and vomiting" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "two patients in group O (because of missing data), one patient in group DT and one patient in the placebo group discontinued and all were excluded. Data from the remaining 90 patients included in the study were analyzed (30 patients in each group)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no statistically significant differences between the group members in weight, height, age, bleeding and duration of general anesthesia (Table 2)" Judgement comment: baseline characteristics (age, weight): no; (ASA I to III): unclear. Potential effect modifiers (gender, anaesthesia): no; (non-smoker, history of PONV/motion sickness, use of perioperative opioids): unclear

Demirhan 2013

Study characteristics

Methods	**Study design:** randomized controlled trial

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Demirhan 2013 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 27.7 ± 8.3 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 23.6 ± 3.1 • *ASA I/II/III/IV (n)*: 13/7/0/0 • *Gender (female in %)*: 40 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 86.1 • *Use of perioperative opioids (if yes, which?)*: 580 µg remifentanil, 50 mg tramadol, 20% of patients needed pethidine • *Type of surgery*: elective rhinoplasty Dexamethasone (group PD) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 26.5 ± 8.9 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24.1 ± 3.0 • *ASA I/II/III/IV (n)*: 14/6/0/0 • *Gender (female in %)*: 25 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 81.3 • *Use of perioperative opioids (if yes, which?)*: 660 µg remifentanil, 20 mg tramadol, 5% of patients needed pethidine • *Type of surgery*: elective rhinoplasty **Included criteria:** ASA I and II, 18 to 75 years of age, waiting for elective rhinoplasty **Excluded criteria:** insufficient cooperation (e.g. psychiatric disorder, dementia); regular use of drugs (benzodiazepines, corticosteroids, tricyclic antidepressants, NSAIDs, or other analgesic drugs); preoperative current use of pregabalin or gabapentin; history of allergy to any of the study medications; pregnancy; obesity (body mass index > 35 kg/m^2); significant cardiac, pulmonary, hepatic, or renal disease **Pretreatment:** baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

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Demirhan 2013 *(Continued)*

Interventions	**Intervention characteristics** Placebo (group P) • *Dose*: saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (ondansetron 4 mg IV) Dexamethasone (group PD) • *Dose*: 8 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 30% (ondansetron 4 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Abdullah Demirhan **Institution:** Department of Anesthesiology and Reanimation, Abant Izzet Baysal University Medical School, Golkoy, Bolu, Turkey **Email:** dr_demirhan1@hotmail.com **Address:** Department of Anesthesiology and Reanimation, Abant Izzet Baysal University Medical School, Golkoy, 14280 Bolu, Turkey **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA

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Demirhan 2013 *(Continued)*

Notes	Two out of 3 groups relevant (co-administration of pregabalin in both groups)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated list of random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "by the same researcher who was not involved in the intraoperative or postoperative treatment and data collection" Quote: "...P and PD, and a similar-looking placebo capsule was given to the controls (Group C) by the same researcher who was not involved in the intraoperative or postoperative treatment and data collection. The exact same packaging was used for the placebo capsules as the active capsules. In the operating room, intravenous..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the NRS values were recorded at 30 min and 1 h in the PACU and at 2, 4, 8, 12, and 24 h in the inpatient unit by the same researcher who was totally unaware of the patient groups"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "Group P and Group PD exhibited statistically significant lower tramadol consumption compared to Group C within the 0–24-h postoperative period (p \ 0.01 for all). There was a statistically significant difference between Group P and Group PD with respect to tramadol consumption (p = 0.016) only in the first 1-h period. Table 2 and Fig. 1 give the mean tramadol consumption (mg) of the groups within the first 24-h period" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

DeOliveira 2011

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, combination prophylaxis, dose-finding study
Participants	**Baseline characteristics** Ondansetron + metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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DeOliveira 2011 *(Continued)*

- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 36 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25.3 ± 6.3
- *ASA I/II/III/IV (n)*: 22/14/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (remifentanil, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 81
- *Use of perioperative opioids (if yes, which?)*: 500 µg remifentanil, 20 mg opioid (oral morphine equivalent)
- *Type of surgery*: ambulatory gynaecological surgery

Dexamethasone (0.05 mg/kg) + ondansetron + metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 36 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24.9 ± 6.3
- *ASA I/II/III/IV (n)*: 17/17/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (remifentanil, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 618 µg remifentanil, 10 mg opioid (oral morphine equivalent)
- *Type of surgery*: ambulatory gynaecological surgery

Dexamethasone (0.1 mg/kg) + ondansetron + metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25.3 ± 4.4
- *ASA I/II/III/IV (n)*: 18/18/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (remifentanil, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 78
- *Use of perioperative opioids (if yes, which?)*: 575 µg remifentanil, 10 mg opioid (oral morphine equivalent)

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DeOliveira 2011 *(Continued)*

	• *Type of surgery*: ambulatory gynaecological surgery **Included criteria:** ASA I and II females undergoing outpatient gynaecological laparoscopy **Excluded criteria:** history of recent respiratory tract infection (1 month), current use of an opioid analgesic or corticosteroid, pregnancy, anticipated difficult airway. Reasons for exclusion from the study after study drug administration included difficult airway defined by more than 2 laryngoscopic attempts by the attending anaesthesiologist and conversion from a laparoscopic to an open laparotomy **Pretreatment:** baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes
Interventions	**Intervention characteristics** Ondansetron + metoclopramide • *Dose*: ondansetron 4 mg, metoclopramide 10 mg • *Time point of administration*: saline when patient was in the preoperative holding area, ondansetron + metoclopramide before end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone (0.05 mg/kg) + ondansetron + metoclopramide • *Dose*: dexamethasone 0.05 mg/kg, ondansetron 4 mg, metoclopramide 10 mg • *Time point of administration*: dexamethasone when patient was in the preoperative holding area, ondansetron + metoclopramide before end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone (0.1 mg/kg) + ondansetron + metoclopramide • *Dose*: dexamethasone 0.1 mg/kg, ondansetron 4 mg, metoclopramide 10 mg • *Time point of administration*: dexamethasone when patient was in the preoperative holding area, ondansetron + metoclopramide before end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** support was provided solely by institutional and/or departmental sources **Country:** USA

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DeOliveira 2011 *(Continued)*

Setting: outpatient, single-centre

Author's name: R.J. McCarthy

Institution: Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, USA

Email: r-mccarthy@northwestern.edu

Address: Department of Anesthesiology, Northwestern University Feinberg School of Medicine, 251 E. Huron St., Feinberg 5-704, Chicago, IL 60611, USA

Duration of study: January 2010 to September 2010

Language: English

Study's primary outcome: primary outcome was global QoR-40 at 24 hours

Trial registry number: NCT01052038

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated table into three groups"
Allocation concealment (selection bias)	Low risk	Quote: "group assignments were sealed in sequentially numbered opaque envelopes that were opened by a research nurse not involved with the subjects' care"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the anaesthesia care team was blinded to group allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "subjects were contacted 24 h after the procedure by an investigator unaware of group allocation and were asked about analgesic consumption and the QoR-40 questionnaire was administered" Quote: "the anaesthesia care team was blinded to group allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred and twenty subjects were randomized and 106 completed the study" Judgement comment: reasons for missing outcome data described and unrelated to outcomes of interest
Selective reporting (reporting bias)	High risk	Judgement comment: NCT01052038 (prospective registration). Primary outcome as defined in the protocol was changed in the study report from "sore throat pain" to "QoR-40 aggregate score" (which was one of the secondary outcomes in the protocol). Primary outcome was not PONV-related
Other bias	High risk	Quote: "patient's baseline characteristics and surgical factors were not different among groups (Table 2)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

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DeOliveira 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis, dose-finding study
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 35 (30 to 43) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26.1 ± 3.8 • *ASA I/II/III/IV (n)*: 15/12/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 95 • *Use of perioperative opioids (if yes, which?)*: 438 µg intraoperative remifentanil, postoperative hydromorphone orally • *Type of surgery*: gynaecological laparoscopy Diphenhydramine (25 mg group) + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 36.5 (29.5 to 44.5) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.7 ± 6.3 • *ASA I/II/III/IV (n)*: 13/11/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 90.5 • *Use of perioperative opioids (if yes, which?)*: 544.5 µg intraoperative remifentanil, postoperative hydromorphone orally • *Type of surgery*: gynaecological laparoscopy Diphenhydramine (50 mg group) + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30

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DeOliveira 2016 *(Continued)*

- *Received treatment (n)*: 30
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: 37 (33.5 to 43)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26.3 ± 4.8
- *ASA I/II/III/IV (n)*: 10/14/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105
- *Use of perioperative opioids (if yes, which?)*: 528 µg intraoperative remifentanil, postoperative hydromorphone orally
- *Type of surgery*: gynaecological laparoscopy

Included criteria: healthy women undergoing outpatient gynaecological laparoscopy

Excluded criteria: history of allergy to diphenhydramine, long-term use of an opioid analgesic or corticosteroid, pregnant subjects, conversion from a laparoscopic to an open incision

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: saline after anaesthesia induction, ondansetron at end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, prochlorperazine 5 mg IV Diphenhydramine (25 mg group) + ondansetron • *Dose*: diphenhydramine 25 mg, ondansetron 4 mg • *Time point of administration*: diphenhydramine after anaesthesia induction, ondansetron at end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, prochlorperazine 5 mg IV Diphenhydramine (50 mg group) + ondansetron • *Dose*: diphenhydramine 50 mg, ondansetron 4 mg • *Time point of administration*: diphenhydramine after anaesthesia induction, ondansetron at end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, prochlorperazine 5 mg IV
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** Department of Anesthesiology, Northwestern University **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Gildasio S. De Oliveira

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DeOliveira 2016 *(Continued)*

Institution: Department of Anesthesiology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

Email: g-jr@northwestern.edu

Address: Department of Anesthesiology, Feinberg School of Medicine, Northwestern University, 241 E Huron St F5-704, Chicago, IL 60611, USA

Duration of study: September 2011 to September 2012

Language: English

Study's primary outcome: Global Quality of Recovery–40 score at 24 hours

Trial registry number: NCT01451762

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated table of random numbers"
Allocation concealment (selection bias)	Low risk	Quote: "group assignments were sealed in sequentially numbered, opaque envelopes that were opened by a research nurse not involved with patient care or data collection after the subject provided written informed consent"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "subject provided written informed consent. The same nurse prepared syringes labeled with study drug to blind the anesthesia personnel and the investigators collecting..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "subject provided written informed consent. The same nurse prepared syringes labeled with study drug to blind the anesthesia personnel and the investigators collecting the data. All subjects were premedicated..."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the details of the conduct of the study are shown in Fig. 1. Ninety subjects were randomized, and 75 completed the study. Patients were enrolled consecutively from September 2011 through September 2012" Judgement comment: number of dropouts > 15%. Reasons described
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01451762 (retrospective registration)
Other bias	Unclear risk	Quote: "patient's baseline characteristics and surgical factors were not different between groups (Table 1)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Derbent 2005

Study characteristics

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Derbent 2005 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide (group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 43.5 ± 7.94 • *Weight (mean ± SD, median (IQR), median (range))*: 77.7 ± 9.94 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 53 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: Inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 89.00 • *Use of perioperative opioids (if yes, which?)*: intraoperative 2 µg/kg fentanyl • *Type of surgery*: elective laminectomy Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 16 • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 40.4 ± 8.51 • *Weight (mean ± SD, median (IQR), median (range))*: 78.4 ± 15.17 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 44 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: Inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 95.10 • *Use of perioperative opioids (if yes, which?)*: intraoperative 2 µg/kg fentanyl • *Type of surgery*: elective laminectomy Placebo (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 42.2 ± 9.31 • *Weight (mean ± SD, median (IQR), median (range))*: 74.2 ± 8.44 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0

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Derbent 2005 *(Continued)*

- *Gender (female in %)*: 47
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: Inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 92.30
- *Use of perioperative opioids (if yes, which?)*: intraoperative 2 µg/kg fentanyl
- *Type of surgery*: elective laminectomy

Included criteria: 18 to 60 years of age; required a laminectomy at 1 or 2 levels of the lumbar spine; met criteria of the American Society of Anesthesiologists for class I or class II anaesthesia

Excluded criteria: history of hypersensitivity to antiemetic drug; cardiac, hepatic, haematological, or renal disorder; extrapyramidal symptoms

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Metoclopramide (group M) • *Dose*: 0.5 mg/kg • *Time point of administration*: 30 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (group O) • *Dose*: 0.1 mg/kg • *Time point of administration*: 30 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo (group C) • *Dose*: saline • *Time point of administration*: 30 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Dr. Abdurrahim Derbent **Institution:** Department of Anesthesiology and Reanimation and of Algology*University Hospital, Izmir, Turkey **Email:** NA **Address:** 1833/1 SOK No:2 D:9 35510 Karsiyaka, Izmir, Turkey **Duration of study:** NA

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Derbent 2005 *(Continued)*

	Language: English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment:no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Desai 2013

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60

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Desai 2013 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 27.3 ± 8.1
- *Weight (mean ± SD, median (IQR), median (range))*: 56.0 ± 9.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 47
- *Non-smoker (%)*: 86
- *History of PONV/motion sickness (%)*: 3.3
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 201
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 3 µg/kg fentanyl for induction, 5.5 mg morphine, pethidine as rescue analgesic
- *Type of surgery*: middle ear surgery

Ramosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: 60
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 30.0 ± 9.0
- *Weight (mean ± SD, median (IQR), median (range))*: 59.1 ± 10.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 38
- *Non-smoker (%)*: 91
- *History of PONV/motion sickness (%)*: 3.3
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 186
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 3 µg/kg fentanyl for induction, 5.6 mg morphine, pethidine as rescue analgesic
- *Type of surgery*: middle ear surgery

Included criteria: 16 to 65 years of age, ASA I or II, undergoing middle ear surgery

Excluded criteria: received other antiemetic medication or perioperative steroids as anti-oedema therapy for facial nerve damage

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions

Intervention characteristics

Dexamethasone + ondansetron

- *Dose*: dexamethasone 8 mg + ondansetron 4 mg
- *Time point of administration*: dexamethasone at beginning of surgery, ondansetron near end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 25 mg

Ramosetron

- *Dose*: 0.3 mg
- *Time point of administration*: near end of surgery
- *Route of administration*: IV

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Desai 2013 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: prochlorperazine 25 mg
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, overall observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Dr. Sameer Desai **Institution:** Department of Anaesthesiology, SDM College of Medical Sciences and Hospital, Dharwar, Karnataka, India **Email:** sameeranaes@gmail.com **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "by a computer-generated randomization table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind study" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "pain intensity, and medication-associated complications. These variables were assessed by an investigator who was blinded to the treatment group. Evaluations were performed..."

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Desai 2013 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all the 120 patients completed the study protocol (no dropouts) and were analyzed for primary efficacy"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Desilva 1995

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 58 • *Age (mean ± SD, median (IQR), median (range))*: 49 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 6.90/5.17 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 174 • *Use of perioperative opioids (if yes, which?)*: 4.6 µg/kg fentanyl, 7.4 mg morphine bolus, 0.65 mg hydromorphone bolus, 31 mg meperidine bolus, 8.7 mg morphine PCA, 2.4 mg hydromorphone PCA • *Type of surgery*: total abdominal hysterectomy Droperidol (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 55 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Desilva 1995 *(Continued)*

- *History of PONV/motion sickness (%)*: 12.72/3.64
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 165
- *Use of perioperative opioids (if yes, which?)*: 4.2 µg/kg fentanyl, 7.3 mg morphine bolus, 1.7 mg hydromorphone bolus, 60 mg meperidine bolus, 25 mg morphine PCA, 1.9 mg hydromorphone PCA
- *Type of surgery*: total abdominal hysterectomy

Perphenazine (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 57
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 10.53/12.28
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 170
- *Use of perioperative opioids (if yes, which?)*: 4.4 µg/kg fentanyl, 6.8 mg morphine bolus, 0.4 mg hydromorphone bolus, 62 mg meperidine bolus, 5.9 mg morphine PCA, 1.3 mg hydromorphone PCA
- *Type of surgery*: total abdominal hysterectomy

Metoclopramide (group M)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 58
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 16
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 12.07/8.62
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 159
- *Use of perioperative opioids (if yes, which?)*: 4.3 µg/kg fentanyl, 8.7 mg morphine bolus, 0.75 mg hydromorphone bolus, 70 mg meperidine bolus, 8.4 mg morphine PCA, 2.7 mg hydromorphone PCA
- *Type of surgery*: total abdominal hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 58
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 7

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Desilva 1995 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 10.34/15.52
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 172
- *Use of perioperative opioids (if yes, which?)*: 4.3 µg/kg fentanyl, 7.5 mg morphine bolus, 0.68 mg hydromorphone bolus, 41 mg meperidine bolus, 9.3 mg morphine PCA, 2.0 mg hydromorphone PCA
- *Type of surgery*: total abdominal hysterectomy

Included criteria: ASA I to III, scheduled for total abdominal hysterectomy (TAH)

Excluded criteria: morbidly obese patients; history of liver disease or allergy to any of the study drugs: (1) opioid and/or antiemetic premedication; (2) deviation from the anaesthetic protocol; (3) performance of a lesser surgical procedure; (4) aggressive mask ventilation due to difficult airway management; (5) placement of a nasal or oral gastric tube; and (6) presence of an endotracheal tube or oral airway on arrival to the postanaesthesia care unit (PACU)

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions

Intervention characteristics

Ondansetron (group O)

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, droperidol 1.25 mg IV

Droperidol (group D)

- *Dose*: 1.25 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, droperidol 1.25 mg IV

Perphenazine (group P)

- *Dose*: 5 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, droperidol 1.25 mg IV

Metoclopramide (group M)

- *Dose*: 10 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, droperidol 1.25 mg IV

Placebo

- *Dose*: placebo
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV

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Desilva 1995 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, droperidol 1.25 mg IV
Outcomes	*Extrapyramidal symptoms (PACU, 4 hours of observation)* • Outcome type: dichotomous outcome *Sedation/drowsiness (PACU, 4 hours of observation)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by the Beth Israel Anesthesia Foundation **Country:** USA **Setting:** inpatient, single-centre **Author's name:** P.H.D.P. Desilva **Institution:** Department of Anaesthesia, Beth Israel Hospital, Harvard Medical School, Boston, MA, USA **Email:** NA **Address:** Department of. Anesthesia, Suite ST308, Beth Israel Hospital, Harvard Medical School, 330 Brookline Ave., Boston, MA, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "subjects were randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "pulse oximetry and electrocardiography, the study drug was administered IV in 50 ml normal saline over 3-5 min by an investigator blinded to the identity of the infusion. Subjects were observed for sedation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a PACU nurse, blinded to the study drugs, observed the subjects for signs of retching and/or vomiting"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "was considered statistically significant. Of the 360 patients entered in the study, 74 were excluded from the analysis. The reasons for the exclusion rate of 20% were: deviation from the anesthetic protocol, 27; performance of

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Desilva 1995 *(Continued)*

		a lesser surgical procedure, 28; opioid/antiemetic premeditation, 8; the placement of a gastric tube, 8; and difficult airway management, 3. Demographic data, duration of..." Judgement comment: high exclusion rate (20%). Reasons described and assumed not related to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Dewinter 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 200 • *Received treatment (n)*: 200 • *Analysed (n)*: 196 • *Age (mean ± SD, median (IQR), median (range))*: 38 (32 to 49) • *Weight (mean ± SD, median (IQR), median (range))*: 66 (59 to 74) • *BMI (mean ± SD, median (IQR), median (range))*: 24 (21 to 26) • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 76.4 • *History of PONV/motion sickness (%)*: 22/NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 108 • *Use of perioperative opioids (if yes, which?)*: 0.3 µg/kg sufentanil • *Type of surgery*: laparoscopic gynaecological surgery Alizapride • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 200 • *Received treatment (n)*: 200 • *Analysed (n)*: 196 • *Age (mean ± SD, median (IQR), median (range))*: 39 (31 to 50) • *Weight (mean ± SD, median (IQR), median (range))*: 65 (60 to 74) • *BMI (mean ± SD, median (IQR), median (range))*: 24 (22 to 27) • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Dewinter 2016 *(Continued)*

- *Non-smoker (%)*: 75.9
- *History of PONV/motion sickness (%)*: 18.1/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95
- *Use of perioperative opioids (if yes, which?)*: 0.3 µg/kg sufentanil
- *Type of surgery*: laparoscopic gynaecological surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 123
- *Received treatment (n)*: 123
- *Analysed (n)*: 123
- *Age (mean ± SD, median (IQR), median (range))*: 39 (31 to 51)
- *Weight (mean ± SD, median (IQR), median (range))*: 65 (57 to 73)
- *BMI (mean ± SD, median (IQR), median (range))*: 23 (21 to 26)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 71
- *History of PONV/motion sickness (%)*: 19/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 110
- *Use of perioperative opioids (if yes, which?)*: 0.3 µg/kg sufentanil
- *Type of surgery*: laparoscopic gynaecological surgery

Included criteria: ASA I or II, women older than 18 years of age, scheduled for laparoscopic gynaecological surgery

Excluded criteria: hypersensitivity to any of the study medications, ASA III to V, pregnancy, parkinsonism, mental disorders, psychiatric illness, consumption of antiemetic drugs within 24 hours before initiation of the study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

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Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: approximately 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: first-line droperidol 1.25 mg and dexamethasone 5 mg IV; second-line ondansetron 4 mg and alizapride 100 mg IV

Alizapride

- *Dose*: 100 mg
- *Time point of administration*: approximately 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: first-line droperidol 1.25 mg and dexamethasone 5 mg IV; second-line ondansetron 4 mg and alizapride 100 mg IV

Placebo

- *Dose*: saline

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Dewinter 2016 *(Continued)*

- *Time point of administration*: approximately 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: first-line droperidol 1.25 mg and dexamethasone 5 mg IV; second-line ondansetron 4 mg and alizapride 100 mg IV

Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** none **Country:** Belgium **Setting:** inpatient and outpatient, single-centre **Author's name:** Geertrui Dewinter **Institution:** Department of Anesthesiology, University Hospitals of the KU Leuven, Leuven, Belgium (SF) **Email:** geertrui.dewinter@uzleuven.be **Address:** Herestraat 49, Leuven 3000, Belgium **Duration of study:** November 2008 to July 2011 **Language:** English **Study's primary outcome:** incidences of PON (VAS score ≥ 1) and POV in PACU **Trial registry number:** EUCTR2008-004789-20
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomisation was performed using a computer-generated randomisation code (Microsoft Excel)"
Allocation concealment (selection bias)	Low risk	Quote: "allocation concealment was ensured by enclosing assignments in sealed, opaque, sequentially numbered envelopes that were opened only after arrival of the patient in the operation room"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, anaesthetists and the study nurse who collected the trial data were blinded to group allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients, anaesthetists and the study nurse who collected the trial data were blinded to group allocation"

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Dewinter 2016 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: reasons for exclusions were described and were unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: EUCTR2008-004789-20 (prospective registration). Timing of assessment of the primary outcome (PONV) was not defined in the protocol
Other bias	Unclear risk	Quote: "patients did not differ in respect of demographic/biometric data, risk factors for PONV, or durations of anaesthesia and surgery (Table 1). All patients received opioids perioperatively with no difference in opioid doses among the three groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

DeWitte 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 56 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 85 ± 18 • *BMI (mean ± SD, median (IQR), median (range))*: 29 ± 6 • *ASA I/II/III/IV (n)*: 10/10/0/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 82 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, postoperative tramadol via PCA, additional piritramide (from 1 to 4 hours postoperatively, tramadol consumption was 26% to 35% higher in the ondansetron group) • *Type of surgery*: lumbar laminectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20

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DeWitte 2001 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 54 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 76 ± 15
- *BMI (mean ± SD, median (IQR), median (range))*: 27 ± 5
- *ASA I/II/III/IV (n)*: 9/11/0/0
- *Gender (female in %)*: 55
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, postoperative tramadol via PCA, additional piritramide
- *Type of surgery*: lumbar laminectomy

Included criteria: adult patients undergoing lumbar laminectomy

Excluded criteria: history of alcohol or drug abuse or seizures, older than 70 years of age, intake of monoamine oxidase inhibitors

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: alizapride 50 mg to 100 mg IV Placebo • *Dose*: saline • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: alizapride 50 mg to 100 mg IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** tramadol (Contramal) was kindly provided by Searle Continental Pharma (Brussels, Belgium). The study authors also thank Glaxo Wellcome (Brussels, Belgium) for providing ondansetron (Zofran) **Country:** Belgium **Setting:** inpatient, single-centre **Author's name:** Jan De Witte **Institution:** Department of Anesthesia and Intensive Care, OLV-Hospital, Aalst, Belgium **Email:** jan.de.witte@olvz-aalst.be **Address:** Department of Anesthesia and Intensive Care, OLV-Hospital, Aalst, Belgium

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DeWitte 2001 *(Continued)*

	Duration of study: NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned to receive..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "patients and investigators were blinded to the study drug" Judgement comment: no information on blinding of anaesthesiologists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients and investigators were blinded to the study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "...was considered statistically significant. The patient groups were comparable with respect to age, weight, height, ASA physical status, and duration of surgery (Table 1). Cumulative tramadol consumption was larger in the Ondansetron group than in the Control group during the first 24 h (Fig. 1). From 1 to 4 h..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Diamond 1980

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics**

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Diamond 1980 *(Continued)*

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 53
- *Received treatment (n)*: NA
- *Analysed (n)*: 53
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 69.81
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane/enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: hydromorphone postoperatively
- *Type of surgery*: orthopaedic procedures on the knee or abdominal hysterectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 49
- *Received treatment (n)*: NA
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 69.39
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane/enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: hydromorphone postoperatively
- *Type of surgery*: orthopaedic procedures on the knee or abdominal hysterectomy

Included criteria: undergoing orthopaedic procedures on the knee or abdominal hysterectomy, avoidance of narcotics for premedication and anaesthetic

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: placebo • *Time point of administration*: 2 hours preoperatively • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: NA

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Diamond 1980 *(Continued)*

	Metoclopramide • *Dose*: 20 mg • *Time point of administration*: 2 hours preoperatively • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 6 hours, only hysterectomy patients)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** financial support and supply of metoclopramide (Maxeran) and placebo from Nordic Pharmaceuticals **Country:** Canada **Setting:** inpatient, single-centre **Author's name:** M.J. Diamond **Institution:** University of Western Ontario, Department of Anaesthesia at Victoria Hospital **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two studies. Only a subgroup of study II (hysterectomies) was eligible for this review (outcome reporting)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized within the two subgroups" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Diamond 1980 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Didehvar 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 39 • *Received treatment (n)*: 39 • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 35.2 ± 9.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 44.1 ± 6.8 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 79.48 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic bariatric surgery Palonosetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 37 • *Received treatment (n)*: 37 • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 35.6 ± 8.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 41.9 ± 6.3 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 81.08 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA

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Didehvar 2013 *(Continued)*

	• *Type of surgery*: laparoscopic bariatric surgery **Included criteria:** ASA I or II, patients with 3 or more risk factors for PONV scheduled to undergo elective laparoscopic gastric banding surgery under general anaesthesia (risk factors included female gender, history of motion sickness (MS) or PONV, non-smoking history, and use of postoperative opioids) **Excluded criteria:** pregnant, had received antiemetics within 24 hours of surgery, experienced retching or vomiting before surgery, were on long-term steroid therapy, were immunocompromised, had a documented allergy to either 5-HT3 receptor antagonists or dexamethasone **Pretreatment:** baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender): no; (duration of anaesthesia, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear. All participants must have at least three PONV risk factors (Apfel)
Interventions	**Intervention characteristics** Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: immediately after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide Palonosetron + dexamethasone • *Dose*: palonosetron 0.075 mg, dexamethasone 8 mg • *Time point of administration*: immediately after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** Eisai Inc. **Country:** USA **Setting:** outpatient, single-centre **Author's name:** S. Didehvar **Institution:** Department of Anesthesiology, NYU Langone Medical Center, New York, NY, USA **Email:** Sorosch.Didehvar@nyumc.org **Address:** Department of Anesthesiology, NYU Langone Medical Center, 550 1st Ave. RR 605, New York, NY 10016 **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response **Trial registry number:** NA
Notes	None

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Didehvar 2013 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomized to receive..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender): no; (duration of anaesthesia, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear. All participants must have at least 3 PONV risk factors (Apfel)

Diemunsch 1997

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 54 • *Received treatment (n)*: NA • *Analysed (n)*: 54 • *Age (mean ± SD, median (IQR), median (range))*: 34.7 ± 8.4 • *Weight (mean ± SD, median (IQR), median (range))*: 59.2 ± 9.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 53/1/0/0 • *Gender (female in %)*: 100

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Diemunsch 1997 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 35.8/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 300.5 µg fentanyl, 7.73 mg postoperative morphine
- *Type of surgery*: laparoscopy or other gynaecological surgery (laparotomy or vaginal hysterectomy)

Dolasetron (12.5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 54
- *Received treatment (n)*: NA
- *Analysed (n)*: 54
- *Age (mean ± SD, median (IQR), median (range))*: 37.1 ± 9.2
- *Weight (mean ± SD, median (IQR), median (range))*: 62.1 ± 11.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 50/4/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 33.3/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 387.5 µg fentanyl, 9.16 mg postoperative morphine
- *Type of surgery*: laparoscopy or other gynaecological surgery (laparotomy or vaginal hysterectomy)

Dolasetron (25 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: NA
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 38.2 ± 9.1
- *Weight (mean ± SD, median (IQR), median (range))*: 61.8 ± 10.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 57/3/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 20.0/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 347.9 µg fentanyl, 9.67 mg postoperative morphine
- *Type of surgery*: laparoscopy or other gynaecological surgery (laparotomy or vaginal hysterectomy)

Dolasetron (50 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 54
- *Received treatment (n)*: NA
- *Analysed (n)*: 54
- *Age (mean ± SD, median (IQR), median (range))*: 38.5 ± 8.1
- *Weight (mean ± SD, median (IQR), median (range))*: 63.9 ± 11.7

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Diemunsch 1997 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 46/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 14.8/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105.7
- *Use of perioperative opioids (if yes, which?)*: 345.9 µg fentanyl, 11.24 mg postoperative morphine
- *Type of surgery*: laparoscopy or other gynaecological surgery (laparotomy or vaginal hysterectomy)

Dolasetron (100 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 59
- *Received treatment (n)*: NA
- *Analysed (n)*: 59
- *Age (mean ± SD, median (IQR), median (range))*: 38.3 ± 8.5
- *Weight (mean ± SD, median (IQR), median (range))*: 61.4 ± 12.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 53/6/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 30.5/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 311.9 µg fentanyl, 6.51 mg postoperative morphine
- *Type of surgery*: laparoscopy or other gynaecological surgery (laparotomy or vaginal hysterectomy)

Included criteria: females between 18 and 55 years of age, ASA I or II, scheduled to undergo laparoscopy or other gynaecological surgery (laparotomy or vaginal hysterectomy) with general anaesthesia as inpatients

Excluded criteria: pregnant or lactating; surgical procedure scheduled during menstruation; significant history of hepatic, renal, cardiovascular, or metabolic disease; significant abnormalities in pre-study laboratory tests; treatment with antiarrhythmic drugs; vomiting from organic etiologies (i.e. bowel obstruction); vomiting or administration of a potential antiemetic drug within 24 hours before study drug administration; scheduled to receive an intragastric tube postoperatively; had taken an investigational drug within 21 days of study initiation; addicted to alcohol or other abusive substance

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of motion sickness, duration of anaesthesia, non-smoker): unclear; (history of PONV, perioperative opioids): yes.

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: at end of N_2O administration • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: e.g. metoclopramide, cyclizine Dolasetron (12.5 mg group) • *Dose*: 12.5 mg • *Time point of administration*: at end of N_2O administration

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- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: e.g. metoclopramide, cyclizine

Dolasetron (25 mg group)

- *Dose*: 25 mg
- *Time point of administration*: at end of N_2O administration
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: e.g. metoclopramide, cyclizine

Dolasetron (50 mg group)

- *Dose*: 50 mg
- *Time point of administration*: at end of N_2O administration
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: e.g. metoclopramide, cyclizine

Dolasetron (100 mg group)

- *Dose*: 100 mg
- *Time point of administration*: at end of N_2O administration
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: e.g. metoclopramide, cyclizine

Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by a grant from Hoechst Marion Roussel, Inc., Strasbourg, France **Country:** France **Setting:** inpatient, multi-centre (10) **Author's name:** Pierre Diemunsch **Institution:** Department of Anesthesiology, Les Hopitaux Universitaires de Strasbourg, Strasbourg, France **Email:** NA **Address:** Hopitaux Universitaires, 1, place de l'Hopital, 67000 Strasbourg, France **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response over 24 hours

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	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "followed cessation of N,O. Patients were stratified and randomly assigned via sealed envelope assignment from..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "...via sealed envelope assignment" Judgement comment: not stated; "sequentially numbered, opaque, sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "...or 100 mg dolasetron mesilate. Ampules containing 10 ml of placebo (sterile saline) or dolasetron mesilate in concentrations of 2.5 mg/ml, 5 mg/ml, 10 mg/ml, or 20 mg/ml were provided by Hoechst Marion Roussel, Inc. To achieve the required dose for each patient, 5 ml of solution was withdrawn from the appropriate ampule, diluted to 50 ml with sterile saline for injection, and administered IV..." Judgement comment: no detailed information on blinding of anaesthesiologists; syringes not stated identical; not clear who is preparing the study drugs
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "study at 10 investigative sites. There were no statistically significant differences among the five treatment groups with respect to age, weight, height, ASA physical status, and posttreatment administration of morphine (Table I). The difference in the proportion of patients with and without a history of PONV approached statistical significance ($I = 0.053); the 50 mg dolasetron mesilate treatment group had the lowest percentage of patients with a history of PONV (15%), and the placebo group had the highest percentage (36%). As shown in Table 2" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of motion sickness, duration of anaesthesia, non-smoker): unclear; (history of PONV, perioperative opioids): yes

Diemunsch 1998

Study characteristics

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Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 156 • *Received treatment (n)*: NA • *Analysed (n)*: 156 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 122/33/1/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 33/18 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 96 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or sufentanil • *Type of surgery*: major gynaecological surgery (including abdominal hysterectomy, gynaecological laparotomy, or vaginal hysterectomy) Dolasetron (25 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 159 • *Received treatment (n)*: NA • *Analysed (n)*: 159 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 117/41/1/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 30/22 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 96 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or sufentanil • *Type of surgery*: major gynaecological surgery (including abdominal hysterectomy, gynaecological laparotomy, or vaginal hysterectomy) Dolasetron (50 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 166 • *Received treatment (n)*: NA • *Analysed (n)*: 166 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 11

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- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 130/35/1/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31/15
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 96
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or sufentanil
- *Type of surgery*: major gynaecological surgery (including abdominal hysterectomy, gynaecological laparotomy, or vaginal hysterectomy)

Dolasetron (100 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 154
- *Received treatment (n)*: NA
- *Analysed (n)*: 154
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 113/41/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 30/16
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or sufentanil
- *Type of surgery*: major gynaecological surgery (including abdominal hysterectomy, gynaecological laparotomy, or vaginal hysterectomy)

Dolasetron (200 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 158
- *Received treatment (n)*: NA
- *Analysed (n)*: 158
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 114/43/1/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 39/22
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or sufentanil
- *Type of surgery*: major gynaecological surgery (including abdominal hysterectomy, gynaecological laparotomy, or vaginal hysterectomy)

Included criteria: ASA I, II, and III; females between 18 and 60 years of age; weighing between 45 and 100 kg; scheduled for major gynaecological surgery (including abdominal hysterectomy, gynaecological laparotomy, or vaginal hysterectomy) with general anaesthesia

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Diemunsch 1998 *(Continued)*

Excluded criteria: pregnancy; evidence of significant hepatic, renal, or endocrine dysfunction; cardiac dysfunction, such as greater than first-degree atrioventricular block or an arrhythmia requiring medication, if vomiting experienced due to any organic aetiology; received any investigational drug within 30 days before surgery; had previously received dolasetron mesylate; received a drug with antiemetic activity within 24 hours of surgery; received an intragastric tube or nasogastric suctioning intraoperatively or postoperatively

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: according to institutional practice (alizapride, cyclizine, droperidol, metoclopramide, ondansetron, and prochlorperazine) Dolasetron (25 mg group) • *Dose*: 25 mg • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: according to institutional practice (alizapride, cyclizine, droperidol, metoclopramide, ondansetron, and prochlorperazine) Dolasetron (50 mg group) • *Dose*: 50 mg • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: according to institutional practice (alizapride, cyclizine, droperidol, metoclopramide, ondansetron, and prochlorperazine) Dolasetron (100 mg group) • *Dose*: 100 mg • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: according to institutional practice (alizapride, cyclizine, droperidol, metoclopramide, ondansetron, and prochlorperazine) Dolasetron (200 mg group) • *Dose*: 200 mg • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: according to institutional practice (alizapride, cyclizine, droperidol, metoclopramide, ondansetron, and prochlorperazine)
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)*

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- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** supported by a research grant from Hoechst Marion Roussel, Strasbourg, France **Country:** France **Setting:** multi-centre (32) **Author's name:** Pierre Diemunsch **Institution:** Department of Anesthesiology, Les Hoˆpitaux Universitaires de Strasbourg, Strasbourg, France **Email:** NA **Address:** Experimental Anesthesiology Unit,Hoˆpitaux Universitaires, 1 Place de l'Hoˆpital, 67091 Strasbourg Cedex, France **Duration of study:** NA **Language:** English **Study's primary outcome:** number of emetic episodes during 24-hour study period **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "because dolasetron tablets vary in size according to dose, each patient received a total of four tablets: one containing either 25, 50, 100, or 200 mg dolasetron, plus three placebo tablets identical to the other sizes, or four placebo tablets" Judgement comment: insufficient information on blinding of anaesthesiologists
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 793 patients enrolled in the study, four did not undergo surgery (for reasons unrelated to study drug) and were excluded from the intent-to-treat efficacy data set"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Other bias	Unclear risk	Quote: "baseline characteristics were well balanced among treatment groups (Table 1). The study population was predominately Caucasian (96%) and of ASA physical status I (75%). Patients' mean age was 43 years, mean weight was 68 kg, and mean height was 163 cm. History of PONV was reported in 32% and history of motion sickness in 18% of patients. There were no statistically significant imbalances among treatment groups in duration of anesthesia. Additionally, there were no statistically significant imbalances among treatment groups in use of concomitant medications, use of postoperative opioids or NSAIDs, or in type or dose of medications used for premedication, induction, maintenance, and reversal of anesthesia" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Diemunsch 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Aprepitant (40 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 307 • *Received treatment (n)*: 303 • *Analysed (n)*: 303 (safety), 293 (efficacy) • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 56/41/2/0 • *Gender (female in %)*: 90 • *Non-smoker (%)*: 70 • *History of PONV/motion sickness (%)*: 17/14 • *Type of general anaesthesia*: volatile agent-based general anaesthesia including nitrous oxide • *Duration of anaesthesia or surgery (in min; as mean or median)*: 120 • *Use of perioperative opioids (if yes, which?)*: 95% of patients, postoperative opioids (0 to 24 hours) • *Type of surgery*: open abdominal surgery Aprepitant (125 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 313 • *Received treatment (n)*: 304 • *Analysed (n)*: 304 (safety), 293 (efficacy) • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA

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- *ASA I/II/III/IV (n)*: 54/43/3/0
- *Gender (female in %)*: 90
- *Non-smoker (%)*: 68
- *History of PONV/motion sickness (%)*: 13/15
- *Type of general anaesthesia*: volatile agent-based general anaesthesia including nitrous oxide
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 114
- *Use of perioperative opioids (if yes, which?)*: 95% of patients, postoperative opioids (0 to 24 hours)
- *Type of surgery*: open abdominal surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 302
- *Received treatment (n)*: 285
- *Analysed (n)*: 285 (safety), 280 (efficacy)
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 53/43/4/0
- *Gender (female in %)*: 93
- *Non-smoker (%)*: 69
- *History of PONV/motion sickness (%)*: 18/14
- *Type of general anaesthesia*: volatile agent-based general anaesthesia including nitrous oxide
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 108
- *Use of perioperative opioids (if yes, which?)*: 97% of patients, postoperative opioids (0 to 24 hours)
- *Type of surgery*: open abdominal surgery

Included criteria: over 18 years old, ASA I to III, undergoing open abdominal surgery requiring at least 1 overnight hospital stay, receiving volatile agent-based general anaesthesia including nitrous oxide

Excluded criteria: pregnancy/breastfeeding; need for nasogastric or oral-gastric tube; use of neuro axial- or propofol-maintained anaesthesia; vomiting within 24 hours before surgery or of any organic aetiology; allergy to any medications to be used before operation or intraoperatively; pre-established need for intensive care or step-down unit care after operation; evidence of disease or history of illness that according to the investigator rendered the patient inappropriate for the study; abnormal preoperative laboratory values (aspartate aminotransferase 2.5 > upper limit of normal, alanine aminotransferase 2.5 > upper limit of normal, bilirubin 1.5 > upper limit of normal, or creatinine 1.5 > upper limit of normal); need for opioid antagonists or benzodiazepine antagonists. Medications known to induce CYP3A4, such as phenytoin, carbamazepine, barbiturates, rifampicin, or rifabutin, were prohibited within 30 days of study start; those known to be CYP3A4 substrates (terfenadine, pimozide, cisapride, or astemizole) or CYP3A4 inhibitors (clarithromycin, ketoconazole, or itraconazole) were prohibited within 7 days of study start

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Aprepitant (40 mg group) • *Dose*: 40 mg • *Time point of administration*: within 3 hours of anticipated induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: type of rescue therapy was chosen by the investigator Aprepitant (125 mg group)

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- *Dose*: 125 mg
- *Time point of administration*: within 3 hours of anticipated induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: type of rescue therapy was chosen by the investigator

Ondansetron 4 mg

- *Dose*: 4 mg
- *Time point of administration*: 2 to 5 minutes immediately before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: type of rescue therapy was chosen by the investigator

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 48 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 48 hours)* • Outcome type: dichotomous outcome *QT prolongation* < 30 ms + 30 ms to 60 ms + > 60 ms *(0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was funded by Merck and Co., Inc. (Sponsor), West Point, PA 19486, USA. Drs. Diemunsch, Gan, Philip, Girao, Eberhart, Irwin, Pueyo, and Chelly received funding from Merck to perform the study. Drs. Carides, Reiss, Evans, and Lawson are employees of Merck and hold stock options or stock in Merck **Country:** USA/non-US sites in North America, South America, Europe, Australia, and Asia **Setting:** inpatient, multi-centre (42: 8 US and 34 non-US centres) **Author's name:** Pierre Diemunsch **Institution:** Services d'Anesthesiologie-Reanimation Chirurgicale, CHU, Hoˆpitale de Hautepierre **Email:** pierre.diemunsch@chru-strasbourg.fr **Address:** 1 Avenue de Moliere, Strasbourg 67000, France

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Diemunsch 2007 *(Continued)*

Duration of study: 28 May 2004 to 20 April 2005

Language: English

Study's primary outcome: primary endpoints for the efficacy analysis were (1) complete response (no vomiting and no use of rescue therapy) over 0 to 24 hours after surgery, to be analysed first for non-inferiority of aprepitant, followed by superiority of aprepitant if non-inferiority was demonstrated, and (2) no vomiting over 0 to 24 hours after surgery, to be tested for superiority of aprepitant

Trial registry number: NCT00090246

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the gender-stratified randomization schedule was computer-generated by the sponsor"
Allocation concealment (selection bias)	Low risk	Quote: "the sponsor provided supplies of aprepitant, placebo matching aprepitant, and blinded allocation schedules" Quote: "each site designated an unblinded pharmacist otherwise not involved with the study to receive, store, and prepare the ondansetron and saline placebo" Quote: "in order to ensure in-house blinding, the schedule was created by an assistant statistician who was otherwise not involved with the study"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patient and investigator blinding was maintained with matching placebos"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...investigator. In addition, to detect possible drug interactions, serious AEs of excessive sedation and respiratory depression were adjudicated in blinded fashion by two physicians not involved with the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "among 1004 patients screened, a total of 922 patients were randomized. Of these, 30 patients were excluded from the tolerability and efficacy analyses because they either did not receive any study drug (n 25) or received partial study drug that was found after unblinding to have been the inactive (placebo) portion of the regimen (n 5). In addition to these 30 patients, 26 other patients were excluded from the efficacy analyses for various reasons, as shown in the figure. Reasons for discontinuation were similar among treatment groups"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00090246 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

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Dimov 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 143 • *Received treatment (n)*: NA • *Analysed (n)*: 143 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 45/NA • *Type of general anaesthesia*: inhalational anesthesia (O_2/halothane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative tramadol • *Type of surgery*: total abdominal hysterectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 146 • *Received treatment (n)*: NA • *Analysed (n)*: 146 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 43/NA • *Type of general anaesthesia*: inhalational anaesthesia (O_2/halothane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative tramadol • *Type of surgery*: total abdominal hysterectomy **Included criteria:** patients undergoing total abdominal hysterectomy **Excluded criteria:** ASA over III, any discrepancy from standard anaesthetic technique, severe endocrinological disease, preoperative corticosteroid therapy **Pretreatment:** baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics**

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Dimov 2004 *(Continued)*

	Dexamethasone • *Dose*: 8 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: 0.9% NaCl • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Postoperative wound infection (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Bulgaria **Setting:** inpatient, single-centre **Author's name:** E. Dimov **Institution:** Department of Anaesthesiology, Reanimation and Intensive Care **Email:** NA **Address:** NA **Duration of study:** January to December 2003 **Language:** Bulgarian (translated by Kiril Penov) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement

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Dimov 2004 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Dobkin 1968

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 94 • *Received treatment (n)*: NA • *Analysed (n)*: 94 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 50 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (methoxyflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: major upper abdominal operations Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 96 • *Received treatment (n)*: NA • *Analysed (n)*: 96 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 62.5 • *Non-smoker (%)*: NA

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Dobkin 1968 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (methoxyflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major upper abdominal operations

Trimethobenzamide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 94
- *Received treatment (n)*: NA
- *Analysed (n)*: 94
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 55.32
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (methoxyflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major upper abdominal operations

Included criteria: adult patients, elective cases scheduled for major upper abdominal operations

Excluded criteria: NA

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: lactose • *Time point of administration*: approximately 30 minutes before end of each operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 20 mg • *Time point of administration*: approximately 30 minutes before end of each operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Trimethobenzamide • *Dose*: 300 mg • *Time point of administration*: approximately 30 minutes before end of each operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Nausea (0 to 24 hours)*

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Dobkin 1968 *(Continued)*

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** this project was supported by a grant-in-aid from Merck Sharp Dohme Research Laboratories **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Allen B. Dobkin **Institution:** Department of Anesthesiology, State University Hospital, State University of New York, Upstate Medical Center, Syracuse, New York, NY, USA **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the order of assignment of the drugs followed a random number code"
Allocation concealment (selection bias)	Unclear risk	Quote: "the order of assignment of the drugs followed a random number code. The identity of the substance was not known to the anaesthetist, who merely recorded the code number of the drug on his anaesthetic record after he administered the material" Judgement comment: no details on allocation provided
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the identity of the substance was not known to the anaesthetist"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patient's chart was reviewed 24 hours postoperatively to record the incidence of nausea and vomiting and related information. The identity of the compounds administered was not revealed to the principals involved in the study until the study was completed and all the data were tabulated"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "each patient's record was reviewed 24 hours after the operation to obtain follow-up data" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Dobkin 1968 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Doe 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 24 • *Received treatment (n)*: 24 • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 29.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 46 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: various strabismus surgeries Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 21 • *Received treatment (n)*: 21 • *Analysed (n)*: 21 • *Age (mean ± SD, median (IQR), median (range))*: 31.3 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 38 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: various strabismus surgeries

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Doe 1998 *(Continued)*

	Included criteria: 15 to 65 years of age (adult), ASA I to III, scheduled to undergo various strabismus surgeries **Excluded criteria:** morbid obesity (BSA > 35 kg/m^2), history of liver disease or seizures, adverse reaction to any of the study drugs, suspected difficult airway, deviation from the anaesthetic protocol, opioid or antiemetic premedication **Pretreatment:** baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Droperidol • *Dose*: 1.25 mg • *Time point of administration*: after intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 12.5% (metoclopramide 10 mg IV every 15 minutes) Ondansetron • *Dose*: 4 mg • *Time point of administration*: after intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 14.3% (metoclopramide 10 mg IV every 15 minutes)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting ("overnight")* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (PACU, same day surgery)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Perry Jones **Institution:** Brooke Army Medical Center, Department of Surgery, Fort Sam Houston, TX 78234-6200, USA **Email:** NA **Address:** Brooke Army Medical Center, Department of Surgery, 3851 Roger Brooke Drive, Fort Sam Houston, TX 78234-6200, USA **Duration of study:** NA

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Doe 1998 *(Continued)*

	Language: English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: quote: "only the anaesthetist knew which drug was given. The patient, ophthalmologist, and nurse observers were blinded to study drug"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "only the anaesthetist knew which drug was given. The patient, ophthalmologist, and nurse observers were blinded to study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Doo 2016

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 49 • *Received treatment (n)*: NA • *Analysed (n)*: 48 • *Age (mean ± SD, median (IQR), median (range))*: 47.8 ± 9.5

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Doo 2016 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 59.5 ± 8.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 39/9/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 143.9
- *Use of perioperative opioids (if yes, which?)*: 35 mL postoperative morphine via PCA
- *Type of surgery*: thyroidectomy

Ramosetron (group 2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 53
- *Received treatment (n)*: NA
- *Analysed (n)*: 53
- *Age (mean ± SD, median (IQR), median (range))*: 46.6 ± 8.9
- *Weight (mean ± SD, median (IQR), median (range))*: 59.9 ± 8.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 47/6/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 140.5
- *Use of perioperative opioids (if yes, which?)*: 39 mL postoperative morphine via PCA
- *Type of surgery*: thyroidectomy

Included criteria: females with ASA I or II, 20 to 65 years of age, undergoing thyroidectomy; the basic inclusion criteria for patients were female gender, non-smoking, and anticipated use of opioids postoperatively; thus, patients with 3 risk factors for PONV were selected

Excluded criteria: diabetes mellitus, gastrointestinal disease, or history of motion sickness or PONV; smokers; menstruating or had taken an antiemetic medication or steroids within 72 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, non-smoker, history of PONV/motion sickness): no

Interventions	**Intervention characteristics** Placebo (group 1) • *Dose*: saline • *Time point of administration*: after removal of the thyroid • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ramosetron (group 2) • *Dose*: 0.3 mg • *Time point of administration*: after removal of the thyroid • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

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Doo 2016 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Seonghoon Ko **Institution:** Department of Anesthesiology and Pain Medicine, Chonbuk National University Medical School and Hospital, Jeonju, Korea **Email:** shko@jbnu.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Chonbuk National University Medical School and Hospital, 20, Gunji-ro, Deokjin-gu, Jeonju 54907, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** Incidence of no PONV **Trial registry number:** NA
Notes	Two out of 3 groups relevant (continuous administration of antiemetic via PCA)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using computer-generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Low risk	Quote: "the study medications were prepared in identical 2 ml syringes. In a double-blind manner, the placebo (saline), 0.3 mg, or 0.15 mg of ramosetron in

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Doo 2016 *(Continued)*

All outcomes		2 ml preparations were given by a group-blinded anesthesiologist in Group 1, 2, and 3 after removal of the thyroid, respectively"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "PONV during the periods 0 to 2 h, 2 to 6 h, and 6 to 24 h after anesthesia was evaluated by an anesthesiologist blinded to the study group or by spontaneous complaints by the patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 150 patients enrolled in this study, 1 patient in Group 1 was excluded because of protocol violation. In this case, the violation did not affect patient safety and was considered a minor violation. Consequently, 149 patients were included in the study. The final patients comprised 48 in Group 1, 53 in Group 2, and 48 in Group 3"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "...and 48 in Group 3. The 3 groups were comparable in terms of patient characteristics and anesthesia time (Table 1). There were no differences in the consumption of analgesic solution in PCA among the 3 groups during the postoperative 24 h (Group 1; 35 ± 14)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, non-smoker, history of PONV/motion sickness): no

Dsouza 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Dexamethasone (4 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 31 • *Received treatment (n)*: NA • *Analysed (n)*: 31 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg of fentanyl for induction, 1.5 mg/kg tramadol as rescue analgesia • *Type of surgery*: laparoscopic gynaecological surgery Dexamethasone (8 mg group)

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Dsouza 2011 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 31
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg of fentanyl for induction, 1.5 mg/kg tramadol as rescue analgesia
- *Type of surgery*: laparoscopic gynaecological surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 31
- *Received treatment (n)*: NA
- *Analysed (n)*: 31
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg of fentanyl for induction, 1.5 mg/kg tramadol as rescue analgesia
- *Type of surgery*: laparoscopic gynaecological surgery

Included criteria: women aged 20 to 60 years with ASA grade I or II, scheduled for gynaecological laparoscopic surgery (e.g. laparoscopic ovarian cystectomy, adhesiolysis, Burch suspension, ovarian drilling, myomectomy, tubal reanastomosis, tubal patency test) under general anaesthesia with endotracheal intubation

Excluded criteria: physical status ASA III or above; lactating or menstruating; taking any medication, including corticosteroids (except oral contraceptive pills); history of motion sickness; had not complied with 6 hours of preoperative fasting; gastrointestinal disorders; had received opioids, antiemetics, or steroids in the previous month; had previous hypersensitivity to these drugs

Pretreatment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, history of motion sickness): no; (history of PONV, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Dexamethasone (4 mg group) • *Dose*: 4 mg

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Dsouza 2011 *(Continued)*

- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 0% (metoclopramide 10 mg)

Dexamethasone (8 mg group)

- *Dose*: 8 mg
- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 6.7% (metoclopramide 10 mg)

Ondansetron 4 mg

- *Dose*: 4 mg
- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 16.1% (metoclopramide 10 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (overall, exact time point unknown)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Nita D'souza **Institution:** Department of Anesthesia and Intensive care, All India Institute of Medical Sciences, New Delhi, India **Email:** drnita610@yahoo.com **Address:** Doctor's Hostel, Room No. 2, JPNA Trauma Centre, AIIMS, New Delhi-110029, India. Tel.: +91 9953008488 **Language:** English

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Dsouza 2011 *(Continued)*

	Duration of study: NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the participants underwent simple randomization into 3 groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "open-label" Judgement comment: study was not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: study was not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "among the 93 patients enrolled, 1 patient from the Dexa 8 group was excluded because she failed to comply with the nil-per-mouth criterion"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, history of motion sickness): no; (history of PONV, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Dua 2004

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA

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Dua 2004 *(Continued)*

- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 46.3 ± 14.1
- *Weight (mean ± SD, median (IQR), median (range))*: 63.55 ± 14.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 12/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 114.2
- *Use of perioperative opioids (if yes, which?)*: 95.2 µg fentanyl
- *Type of surgery*: modified radical mastectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 50.6 ± 10.9
- *Weight (mean ± SD, median (IQR), median (range))*: 56.9 ± 9.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 11/9/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 114.2
- *Use of perioperative opioids (if yes, which?)*: 106.2 µg fentanyl
- *Type of surgery*: modified radical mastectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 47.7 ± 11.9
- *Weight (mean ± SD, median (IQR), median (range))*: 58.78 ± 11.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 12/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 126.0
- *Use of perioperative opioids (if yes, which?)*: 103.7 µg fentanyl
- *Type of surgery*: modified radical mastectomy

Included criteria: ASA physical status I or II, between 21 and 75 years of age, undergoing general anaesthesia for modified radical mastectomy

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Dua 2004 *(Continued)*

	Excluded criteria: known stomach disorders; history of heart burn, motion sickness, previous PONV, lower oesophageal sphincter disorders; menstruation; uncontrolled hypertension; poorly controlled diabetes; preoperative emesis < 12 hours before surgery **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: just before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (ondansetron 4 mg) Granisetron • *Dose*: 4 mg • *Time point of administration*: just before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 15% (ondansetron 4 mg) Placebo • *Dose*: saline • *Time point of administration*: just before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 40% (ondansetron 4 mg)
Outcomes	*Vomiting (0 to 24 hours, PONV score 2 + 3)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (during 24 hours)* • Outcome type: dichotomous outcome *Headache (overall, exact time point unknown)* • Outcome type: dichotomous outcome *Sedation/drowsiness (overall, exact time point unknown)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, overall, exact time point unknown)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Dr S. Bhatnagar

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Dua 2004 *(Continued)*

Institution: Department of Anesthesiology, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India

Email: NA

Address: 2, North Avenue, I.I.T., New Delhi

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "generated random number list to assign patients into three equal groups (n=20)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "anaesthetists were blinded to the group to which the patients had been assigned" Judgement comment: no statement on blinding of participants
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "postoperatively, all episodes of PONV were recorded for the first 24 hours (0-2, 2-6, 6-24 hours) by direct questioning by the attending anaesthetist or by spontaneous complaint by the patients" Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Dua 2014

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics**

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Dua 2014 *(Continued)*

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 34.26 ± 13.77
- *Weight (mean ± SD, median (IQR), median (range))*: 60.22 ±- 6.876
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 36/14
- *Gender (female in %)*: 48
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 179.44
- *Use of perioperative opioids (if yes, which?)*: 121.3
- *Type of surgery*: tympanoplasty and mastoidectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 32.48 ± 14.56
- *Weight (mean ± SD, median (IQR), median (range))*: 60.66 ± 7.847
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 39/11
- *Gender (female in %)*: 38
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 179.5
- *Use of perioperative opioids (if yes, which?)*: 109.8 µg intraoperative fentanyl
- *Type of surgery*: tympanoplasty and mastoidectomy

Included criteria: ASA I or II, 18 to 65 years of age, undergoing middle ear surgery (tympanoplasty and mastoidectomy) under general anaesthesia

Excluded criteria: history of smoking, gastritis, heartburn, motion sickness; previous PONV; lower oesophageal sphincter disorders; Ellison-Zollinger syndrome; uncontrolled hypertension; poorly controlled diabetes; preoperative emesis < 6 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: 30 minutes before reversal of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 8 mg IV

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Dua 2014 *(Continued)*

	Granisetron • *Dose*: 1 mg • *Time point of administration*: 30 minutes before reversal of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 8 mg IV
Outcomes	*Vomiting (0 to 24 hours, PONV score 2 +3)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours, PONV score 1)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Naresh Dua **Institution:** Department of Anaesthesiology, Pain and Perioperative Medicine, Sir Ganga Ram Hospital, Old Rajinder Nagar, New Delhi, India **Email:** ndua14@yahoo.com **Address:** Department of Anaesthesiology, Pain and Perioperative Medicine, Sir Ganga Ram Hospital, Old Rajinder Nagar, New Delhi 110060, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Dua 2014 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "randomization list was prepared by a random number function in a computer spreadsheet"
Allocation concealment (selection bias)	Unclear risk	Quote: "a randomization list was prepared by a random number function in a computer spreadsheet and identical syringes containing each drug were prepared by personnel not involved in this study" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "a randomization list was prepared by a random number function in a computer spreadsheet and identical syringes containing each drug were prepared by personnel not involved in this study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "by direct questioning by the attending anaesthesiologist without knowledge of which antiemetic the patient had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "there were no significant differences between the groups with regard to age, sex, weight, height, sex, ASA physical status, duration of anaesthesia and surgery, type of surgery (tympanoplasty, mastoidectomy), preoperative PONV, intraoperative analgesic requirements, and time to first feeding" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Dubey 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 38.6 ± 10.0 • *Weight (mean ± SD, median (IQR), median (range))*: 44.4 ± 6.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 42/8/0/0 • *Gender (female in %)*: 64

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Dubey 2003 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 3 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic procedures

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 35.5 ± 8.6
- *Weight (mean ± SD, median (IQR), median (range))*: 47.1 ± 7.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 43/7/0/0
- *Gender (female in %)*: 62
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 3 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic procedures

Included criteria: adult patients, ASA I and II, undergoing day-case laparoscopic procedures under general anaesthesia

Excluded criteria: known sensitivity to lidocaine, propofol, or granisetron; concomitant analgesic or sedative medication; presence of infection on the dorsum of the left hand; indications for rapid sequence intubation; presence of cardiac conduction defects; epilepsy; use of antiarrhythmic medications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: pretreatment • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Granisetron • *Dose*: 2 mg • *Time point of administration*: pretreatment • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Headache (immediate postoperative period)* • Outcome type: dichotomous outcome

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Dubey 2003 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** India **Setting:** outpatient, single-centre **Author's name:** Prakash K. Dubey **Institution:** Departments of Anesthesiology and Surgical Gastroenterology, Indira Gandhi Institute of Medical Sciences, Patna, India **Email:** xscactus@indiatimes.com **Address:** 305, Janpriya Apartments, North S.K. Puri, Patna 800 013, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (lidocaine group)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "by use of sealed envelopes, patients were allocated randomly to one of three groups" Judgement comment: insufficient information on random sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "by use of sealed envelopes, patients were allocated randomly to one of three groups" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes (SNOSE)"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "an independent anesthetist prepared the solutions, and the investigator did not know the contents of the solutions"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "another independent clinician, unaware of the group to which the patients had been allocated, assessed the level of pain on injection of propofol. The patients were asked a standard question"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the study included 150 patients" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the demographic data were comparable among the three groups (Table 1)"

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Dubey 2003 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Eberhart 1999a

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 35 (31 to 45) • *Weight (mean ± SD, median (IQR), median (range))*: 78 (70 to 84) • *BMI (mean ± SD, median (IQR), median (range))*: 24.4 (22.4 to 26.5) • *ASA I/II/III/IV (n)*: 22/13/0/0 • *Gender (female in %)*: 0 • *Non-smoker (%)*: 66 • *History of PONV/motion sickness (%)*: 23/0 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 130 • *Use of perioperative opioids (if yes, which?)*: 10 µg/kg/h remifentanil intraoperative, 23 patients with postoperative piritramide as rescue analgesic • *Type of surgery*: nasal surgery (septoplasty, rhinoplasty, septorhinoplasty) Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 31 (27 to 48) • *Weight (mean ± SD, median (IQR), median (range))*: 82 (73 to 93) • *BMI (mean ± SD, median (IQR), median (range))*: 25.4 (22.9 to 27.5) • *ASA I/II/III/IV (n)*: 25/10/0/0 • *Gender (female in %)*: 0 • *Non-smoker (%)*: 54 • *History of PONV/motion sickness (%)*: 3/6 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 135 • *Use of perioperative opioids (if yes, which?)*: 9 µg/kg/h remifentanil intraoperative, 17 patients with postoperative piritramide as rescue analgesic • *Type of surgery*: nasal surgery (septoplasty, rhinoplasty, septorhinoplasty)

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Eberhart 1999a *(Continued)*

	Included criteria: ASA I or II, males undergoing nasal surgery (septoplasty, rhinoplasty, septorhinoplasty) **Excluded criteria:** receiving antiemetics, having nausea or vomiting in the 2 weeks before surgery **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 23%: metoclopramide 0.2 mg/kg, dolasetron 12.5 mg additional Droperidol • *Dose*: 15 µg/kg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 9%: metoclopramide 0.2 mg/kg, dolasetron 12.5 mg additional
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** L.H.J. Eberhart **Institution:** Department of Anaesthesiology, University of Ulm, Germany **Email:** NA **Address:** Department of Anaesthesiology, University of Ulm, D-89070 Ulm, Germany **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV

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Eberhart 1999a *(Continued)*

	Trial registry number: NA
Notes	Two out of 4 groups relevant (repeated dose of dimenhydrinate).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "a computer-generated randomization plan was used"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "study medication was prepared by a colleague not involved in the study to preserve the double blind aspect of the study"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Eberhart 1999b

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 68 (58 to 74) • *Weight (mean ± SD, median (IQR), median (range))*: 70 (63 to 80) • *BMI (mean ± SD, median (IQR), median (range))*: 26.2 (23.7 to 29.2) • *ASA I/II/III/IV (n)*: 3/19/13/0 • *Gender (female in %)*: 70.9

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Eberhart 1999b *(Continued)*

- *Non-smoker (%)*: 74.3
- *History of PONV/motion sickness (%)*: 22.9/22.9
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg to 1 mg alfentanil, 1 patient received piritramide
- *Type of surgery*: cataract surgery

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 70 (60 to 76)
- *Weight (mean ± SD, median (IQR), median (range))*: 71 (64 to 81)
- *BMI (mean ± SD, median (IQR), median (range))*: 26.0 (24.0 to 29.1)
- *ASA I/II/III/IV (n)*: 5/14/16/0
- *Gender (female in %)*: 70.9
- *Non-smoker (%)*: 88.6
- *History of PONV/motion sickness (%)*: 22.9/17.1
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg to 1 mg alfentanil, 1 patient received piritramide
- *Type of surgery*: cataract surgery

Dolasetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 68 (58 to 74)
- *Weight (mean ± SD, median (IQR), median (range))*: 71 (64 to 78)
- *BMI (mean ± SD, median (IQR), median (range))*: 25.7 (23.4 to 27.7)
- *ASA I/II/III/IV (n)*: 11/14/11/0
- *Gender (female in %)*: 69.4
- *Non-smoker (%)*: 83.3
- *History of PONV/motion sickness (%)*: 25.0/25.0
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg to 1 mg alfentanil, 1 patient received piritramide
- *Type of surgery*: cataract surgery

Droperidol + dolasetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 70 (56 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: 69 (60 to 84)

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Eberhart 1999b *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 25.5 (23.9 to 29.5)
- *ASA I/II/III/IV (n)*: 7/23/5/0
- *Gender (female in %)*: 70.9
- *Non-smoker (%)*: 91.4
- *History of PONV/motion sickness (%)*: 20.0/14.3
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg to 1 mg alfentanil, 1 patient received piritramide
- *Type of surgery*: cataract surgery

Included criteria: scheduled for cataract surgery under general anaesthesia

Excluded criteria: ASA III or IV, senile dementia, psychiatric disease, cerebral circulation disturbances, received antiemetics during the last 2 weeks, adipositas (BMI > 35 kg/m^2), intolerance to or contraindications against 1 of the study medications (e.g. M. Parkinson)

Pretreatment: baseline characteristics (age, weight): no; (ASA): yes. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: NaCl
- *Time point of administration*: 5 to 10 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 20.0% (10 mg metoclopramide or 0.5 mg/kg dimenhydrinate)

Droperidol

- *Dose*: 10 µg/kg
- *Time point of administration*: 5 to 10 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 5.7% (10 mg metoclopramide or 0.5 mg/kg dimenhydrinate)

Dolasetron

- *Dose*: 12.5 mg/kg
- *Time point of administration*: 5 to 10 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 5.6% (10 mg metoclopramide or 0.5 mg/kg dimenhydrinate)

Droperidol + dolasetron

- *Dose*: droperidol 10 µg/kg, dolasetron 12.5 mg
- *Time point of administration*: 5 to 10 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 5.7% (10 mg metoclopramide or 0.5 mg/kg dimenhydrinate)

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

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Eberhart 1999b *(Continued)*

- Outcome type: dichotomous outcome

Extrapyramidal symptoms, restlessness (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (examination room)

- Outcome type: dichotomous outcome

Sedation/drowsiness (at 2 hours, 5 hours, 8 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Leopold Eberhart **Institution:** Klinik für Anästhesiologie Universität Ulm **Email:** leopold.eberhart@medizin.uni-ulm.de **Address:** Klinik für Anästhesiologie Universität Ulm, Steinhövelstraße 9; 89075 Ulm **Duration of study:** NA **Language:** German **Study's primary outcome:** complete response in 24 hours **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "eines computergenerierten Randomisierungsplans" Judgement comment: quote (translated): "computer-generated randomization"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "droperidol in 10 ml NaCl. Die Studienmedikation wurde von einem Mitarbeiter vorbereitet, der nicht in die Studie involviert war. Am Abend vor, und am" Judgement comment: quote (translated): "the study medication was prepared by an employee who was not involved in the study"
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement comment: no statement

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Eberhart 1999b *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "insgesamt konnten die Daten von sieben Patienten nicht ausgewertet werden. Die Gründe dafür waren: Absage oder Terminverschiebung der Operation (n = 5) oder die Nichteinhaltung des vorgesehenen Narkoseverfahrens (n = 2)" Judgement comment: missing outcome data were described and were unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): yes. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): unclear

Eberhart 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: NA • *Analysed (n)*: 78 • *Age (mean ± SD, median (IQR), median (range))*: 62 (57 to 72) • *Weight (mean ± SD, median (IQR), median (range))*: 75 (72 to 81) • *BMI (mean ± SD, median (IQR), median (range))*: 25.9 (23.8 to 28.5) • *ASA I/II/III/IV (n)*: 16/48/14/0 • *Gender (female in %)*: 50.0 • *Non-smoker (%)*: 71.8 • *History of PONV/motion sickness (%)*: 28.2/11.5 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 145 • *Use of perioperative opioids (if yes, which?)*: 7.2 remifentanil (8 to 15 µg/kg/h), 56.4% treatment with opioids (piritramide) • *Type of surgery*: vitreoretinal surgery Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: NA • *Analysed (n)*: 76 • *Age (mean ± SD, median (IQR), median (range))*: 61 (57 to 70)

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Eberhart 2004 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 73 (69 to 79)
- *BMI (mean ± SD, median (IQR), median (range))*: 26.2 (24.4 to 27.8)
- *ASA I/II/III/IV (n)*: 15/41/18/0
- *Gender (female in %)*: 54.1
- *Non-smoker (%)*: 78.4
- *History of PONV/motion sickness (%)*: 25.7/10.8
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 140
- *Use of perioperative opioids (if yes, which?)*: 8 µg/kg/h to 15 µg/kg/h remifentanil, 50.0% treatment with opioids (piritramide)
- *Type of surgery*: vitreoretinal surgery

Dolasetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 74
- *Age (mean ± SD, median (IQR), median (range))*: 64 (57 to 72)
- *Weight (mean ± SD, median (IQR), median (range))*: 71 (66 to 81)
- *BMI (mean ± SD, median (IQR), median (range))*: 26.0 (23.4 to 27.7)
- *ASA I/II/III/IV (n)*: 18/39/19/0
- *Gender (female in %)*: 52.6
- *Non-smoker (%)*: 71.1
- *History of PONV/motion sickness (%)*: 23.7/11.8
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 150
- *Use of perioperative opioids (if yes, which?)*: 8 µg/kg/h to 15 µg/kg/h remifentanil, 48.7% treatment with opioids (piritramide)
- *Type of surgery*: vitreoretinal surgery

Droperidol + dolasetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 76
- *Age (mean ± SD, median (IQR), median (range))*: 65 (55 to 73)
- *Weight (mean ± SD, median (IQR), median (range))*: 76 (71 to 85)
- *BMI (mean ± SD, median (IQR), median (range))*: 25.7 (22.8 to 29.9)
- *ASA I/II/III/IV (n)*: 17/40/19/0
- *Gender (female in %)*: 51.3
- *Non-smoker (%)*: 77.6
- *History of PONV/motion sickness (%)*: 22.4/14.5
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 155
- *Use of perioperative opioids (if yes, which?)*: 8 µg/kg/h to 15 µg/kg/h remifentanil, 51.3% treatment with opioids (piritramide)
- *Type of surgery*: vitreoretinal surgery

Included criteria: ASA I to III patients undergoing vitreoretinal surgery

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Eberhart 2004 *(Continued)*

Excluded criteria: receiving antiemetics or long-term corticoid treatment, having nausea or vomiting during the 2 weeks before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 37.2% (dimenhydrinate 0.5 mg/kg) Droperidol • *Dose*: 10 µg/kg • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 22.4% (dimenhydrinate 0.5 mg/kg) Dolasetron • *Dose*: 12.5 mg • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 28.4% (dimenhydrinate 0.5 mg/kg) Droperidol + dolasetron • *Dose*: droperidol 10 µg/kg, dolasetron 12.5 mg • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 18.4% (dimenhydrinate 0.5 mg/kg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Arrhythmia (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)*

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Eberhart 2004 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** none of the study authors had any financial interests in drugs or methods used in this trial **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Leopold Eberhart **Institution:** Philipps-University of Marburg **Email:** eberhart@mailer.uni-marburg.de **Address:** Department of Anesthesia and Intensive Care, Philipps-University of Marburg, D-35033 Marburg, Germany **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** severity of PONV (rated by a standardized scoring algorithm) was analysed as the main endpoint of the study via the Kruskal–Wallis test
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "two sets of sealed envelopes were used for females and males, respectively, to ensure a homogenous gender distribution between the groups" Quote: "the patients were stratified according to gender to receive 1 of 4 prophylactic antiemetic treatments in a double-blind manner 15 minutes before the end of surgery" Judgement comment: randomized using sealed envelopes
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement on opaque, sequentially numbered envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the syringes were prepared by a third, neutral person not involved in the perioperative care of the patient, immediately before the start of anesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients were visited on the ward 2, 5, 8, and 24 hours postoperatively by a blinded observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: dropouts < 15%, balanced between arms, reasons unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Eberhart 2004 *(Continued)*

Other bias	Low risk	Quote: "the biometric data (Table 2) and anesthetic and surgical parameters (Table 1) of the remaining 151 patients showed no relevant difference among the groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Eberhart 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: 80 • *Analysed (n)*: 76 • *Age (mean ± SD, median (IQR), median (range))*: 40 (30 to 53) • *Weight (mean ± SD, median (IQR), median (range))*: 75 (61 to 82) • *BMI (mean ± SD, median (IQR), median (range))*: 25.3 (22.4 to 28.4) • *ASA I/II/III/IV (n)*: 23/46/7/0 • *Gender (female in %)*: 76 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 105 • *Use of perioperative opioids (if yes, which?)*: 0.3 mg fentanyl, 20 patients received sufentanil, 7.6 µg/kg/h remifentanil, 54 patients received opioids, 10 mg piritramide • *Type of surgery*: gynaecological and ENT procedures Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: 80 • *Analysed (n)*: 80 • *Age (mean ± SD, median (IQR), median (range))*: 39 (28 to 51) • *Weight (mean ± SD, median (IQR), median (range))*: 71 (62 to 81) • *BMI (mean ± SD, median (IQR), median (range))*: 25.0 (22.1 to 28.2) • *ASA I/II/III/IV (n)*: 20/41/19/0 • *Gender (female in %)*: 67 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane)

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Eberhart 2006 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115
- *Use of perioperative opioids (if yes, which?)*: 0.3 mg fentanyl, 21 patients received sufentanil, 7.5 µg/kg/h remifentanil, 47 patients received opioids, 7.5 mg piritramide
- *Type of surgery*: gynaecological and ENT procedures

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: 80
- *Analysed (n)*: 76
- *Age (mean ± SD, median (IQR), median (range))*: 38 (28 to 48)
- *Weight (mean ± SD, median (IQR), median (range))*: 75 (63 to 84)
- *BMI (mean ± SD, median (IQR), median (range))*: 24.7 (21.6 to 27.8)
- *ASA I/II/III/IV (n)*: 16/41/18/0
- *Gender (female in %)*: 71
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105
- *Use of perioperative opioids (if yes, which?)*: 0.3 mg fentanyl, 24 patients received sufentanil, 7.0 µg/kg/h remifentanil, 47 patients received opioids, 7.5 mg piritramide
- *Type of surgery*: gynaecological and ENT procedures

Dexamethasone + tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: 80
- *Analysed (n)*: 79
- *Age (mean ± SD, median (IQR), median (range))*: 43 (32 to 58)
- *Weight (mean ± SD, median (IQR), median (range))*: 70 (64 to 84)
- *BMI (mean ± SD, median (IQR), median (range))*: 25.2 (23.1 to 28.3)
- *ASA I/II/III/IV (n)*: 19/41/19/0
- *Gender (female in %)*: 72
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100
- *Use of perioperative opioids (if yes, which?)*: 0.3 mg fentanyl, 27 patients received sufentanil, 8.0 µg/kg/h remifentanil, 49 patients received opioids, 7.5 mg piritramide
- *Type of surgery*: gynaecological and ENT procedures

Included criteria: ASA I to III, undergoing various gynaecological and ENT procedures enrolled into the study if (a) surgery was expected to be ≥ 60 minutes, and (b) the patient had risk for PONV ≥ 40% according to 2 validated risk scores for PONV using the following established risk factors for PONV: female gender, positive history of previous PONV or motion sickness, postoperative opioid administration or non-smoking status (the latter was defined as complete abstinence from tobacco during the previous 3 months)

Excluded criteria: receiving antiemetics or having nausea or vomiting during the 2 weeks before surgery, receiving long-term corticoid treatment, diabetes mellitus, allergies against one of the intended drug regimens

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Eberhart 2006 *(Continued)*

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

Interventions	**Intervention characteristics** Placebo • *Dose*: lactulose • *Time point of administration*: 1 to 2 hours before surgery • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: first-line droperidol 20 µg/kg; second-line dimenhydrinate 62 mg; 42.1% Tropisetron • *Dose*: 5 mg • *Time point of administration*: 1 to 2 hours before surgery • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: first-line droperidol 20 µg/kg; second-line dimenhydrinate 62 mg; 20% Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 1 to 2 hours before surgery • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: first-line droperidol 20 µg/kg; second-line dimenhydrinate 62 mg; 33.3% Dexamethasone + tropisetron • *Dose*: dexamethasone 8 mg, tropisetron 5 mg • *Time point of administration*: 1 to 2 hours before surgery • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: first-line droperidol 20 µg/kg; second-line dimenhydrinate 62 mg; 12.7%
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (wound infection requiring antibiotic > 3 days)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)*

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Eberhart 2006 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Leopord Eberhart **Institution:** Department of Anaesthesia and Intensive Care, University Hospital Giessen-Marburg, Marburg, Germany **Email:** eberhart@mailer.uni-marburg.de **Address:** Department of Anaesthesia and Intensive Care, University Hospital Giessen-Marburg, D-35033 Marburg, Germany **Duration of study:** NA **Language:** English **Study's primary outcome:** main outcome measures were severity of PONV within first 24 hours (rated by a standardized scoring algorithm) **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the CONSORT Statement (http:// www.consort-statement.org). The patients were randomly selected and given sealed envelopes with one of four interventions 1–2 h before surgery together" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "patients were randomly selected and given sealed envelopes with one of four interventions 1–2 h before surgery together" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes (SNOSE)"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "to ensure double-blind conditions the original medication was coated with indistinguishable cellulose capsules and were prepared by a neutral person not involved in the perioperative care of the patient"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients were visited on the ward at 2 h and 24 h postoperatively by an observer blinded to the study medication"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...are shown in Fig. 1. No patient was excluded from the analysis as a result of side-effects or treatment failure. For this reason and because of the

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Eberhart 2006 *(Continued)*

		low number of drop-outs (n = 10, 3%) no retreatment analysis was performed. The biometric data (Table 1)..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no.Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

Eberhart 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + dolasetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 44 (40 to 49) • *Weight (mean ± SD, median (IQR), median (range))*: 78 (71 to 84) • *BMI (mean ± SD, median (IQR), median (range))*: 26.5 (24.8 to 30.7) • *ASA I/II/III/IV (n)*: 19/25/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 150 • *Use of perioperative opioids (if yes, which?)*: 0.5 mg fentanyl, 1.1 mg remifentanil, postoperative piritramide as rescue analgesic • *Type of surgery*: non-cancer abdominal hysterectomy Dolasetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 45 (42 to 53) • *Weight (mean ± SD, median (IQR), median (range))*: 78 (71 to 85) • *BMI (mean ± SD, median (IQR), median (range))*: 26.9 (25.2 to 29.9) • *ASA I/II/III/IV (n)*: 16/22/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Eberhart 2011 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 145
- *Use of perioperative opioids (if yes, which?)*: 0.48 mg fentanyl, 1.0 mg remifentanil, postoperative piritramide as rescue analgesic
- *Type of surgery*: non-cancer abdominal hysterectomy

Included criteria: non-diabetic ASA I and II women undergoing elective non-cancer abdominal hysterectomy

Excluded criteria: blood glucose > 5.5 mmol/L after a 6-hour fasting period; previous pathological glucose tolerance test; intake of oral antidiabetics, insulin, or beta-blockers; arbitrarily chosen level of BMI > 35 kg/m^2

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Dexamethasone + dolasetron • *Dose*: dexamethasone 8 mg, dolasetron 12.5 mg • *Time point of administration*: dexamethasone 2 hours before scheduled surgery, dolasetron at end of surgery • *Route of administration*: dexamethasone PO, dolasetron IV • *Rescue antiemetics (if yes, which?)*: NA Dolasetron • *Dose*: 12.5 mg • *Time point of administration*: placebo 2 hours before scheduled surgery, dolasetron at end of surgery • *Route of administration*: placebo PO, dolasetron IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** institutional funding **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Leopold H.J. Eberhart **Institution:** Department of Anaesthesiology and Intensive Care Medicine, Philipps University of Marburg, Germany **Email:** eberhart@staff.uni-marburg.de **Address:** Department of Anaesthesiology and Intensive Care Medicine, Philipps University of Marburg, Baldingerstraße, D-35033 Marburg, Germany **Duration of study:** NA

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Eberhart 2011 *(Continued)*

	Language: English **Study's primary outcome:** blood glucose concentration after surgery **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a computer-generated random list"
Allocation concealment (selection bias)	Low risk	Quote: "the latter was stored in a sealed box prepared by the hospital pharmacy prior to the beginning of the study according to a computer-generated random list in order to ensure allocation concealment" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the latter was stored in a sealed box prepared by the hospital pharmacy prior to the beginning of the study according to a computer-generated random list in order to ensure allocation concealment. The box contained a tablet with 8 mg dexamethasone or an undistinguishable placebo tablet"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: blinding ensured due to central allocation and indistinguishable placebo treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: reasons for missing outcome data (< 15%) were described and were unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the biometric data of all patients ('intention to treat sample') are shown in Table 1. There were no statistically significant or clinically relevant differences between the two groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Ebneshahidi 2013

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Haloperidol • *Assessed for eligibility (n)*: -

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Ebneshahidi 2013 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 49
- *Received treatment (n)*: NA
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 36 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 55.1
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative 20 mg morphine via PCA
- *Type of surgery*: laparotomic, orthopaedic, gynaecological, urological

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 51
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 33 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 48
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 67
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative 20 mg morphine via PCA
- *Type of surgery*: laparotomic, orthopaedic, gynaecological, urological

Included criteria: ASA I or II; 21 to 65 years of age; undergoing elective general, gynaecological, or orthopaedic surgery under general anaesthesia

Excluded criteria: known electrolyte imbalance (particularly hypokalaemia and hypomagnesaemia); underlying cardiac abnormalities; significant hepatic or renal dysfunction; hypothyroidism; drug abuse; familial long QT syndrome; taking drugs known to prolong the QT interval

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Haloperidol • *Dose*: 2 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA

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Ebneshahidi 2013 *(Continued)*

	Placebo • *Dose*: 10 mL sterile water • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Extrapyramidal symptoms (NA)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** departmental sources only **Country:** Iran **Setting:** NA **Author's name:** Masood Mohseni **Institution:** Department of Anesthesiology, Tehran University of Medical Sciences, Tehran, Iran **Email:** Masood.mohseni@gmail.com **Address:** Department of Anesthesiology, Rasoul Akram Medical Center Affiliated to Tehran University of Medical Sciences, Niayesh Ave, Sattarkhan St, Tehran, Iran **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** pain
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomization was performed by the hospital pharmacy using a table of random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, anesthetist, and anesthetic technician who were involved in the patients' care and data recording were blinded to the nature of the assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...anesthetic technician who were involved in the patients' care and data recording were blinded to the nature of the assignment"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no statement 98 participants enrolled, but baseline characteristics were presented for 99 participants (49/50)

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Ebneshahidi 2013 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "baseline characteristics and covariates of surgery in the haloperidol and placebo groups were comparable [Table 2]" Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Eidi 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 73 • *Received treatment (n)*: 72 • *Analysed (n)*: 72 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 61/12/0/0 • *Gender (female in %)*: 73.97 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 119 • *Use of perioperative opioids (if yes, which?)*: 1 to 2 µg/kg fentanyl as premedication, intraoperative remifentanil • *Type of surgery*: tympanoplasty Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 73 • *Received treatment (n)*: 72 • *Analysed (n)*: 71 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 64/9/0/0 • *Gender (female in %)*: 67.12 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Eidi 2012 *(Continued)*

- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 121
- *Use of perioperative opioids (if yes, which?)*: 1 to 2 µg/kg fentanyl as premedication, intraoperative remifentanil
- *Type of surgery*: tympanoplasty

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 73
- *Received treatment (n)*: 73
- *Analysed (n)*: 73
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 63/10/0/0
- *Gender (female in %)*: 75.34
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 124
- *Use of perioperative opioids (if yes, which?)*: 1 to 2 µg/kg fentanyl as premedication, intraoperative remifentanil
- *Type of surgery*: tympanoplasty

Included criteria: ASA I or II undergoing tympanoplasty type I (no simultaneous ossiculoplasties or mastoid surgeries)

Excluded criteria: digestive problems, history of treatment with antiemetics, nausea in the preceding 24 hours, obesity (BMI > 40)

Pretreatment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo

- *Dose*: distilled water
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV

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Eidi 2012 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Khosro Kolahdouzan **Institution:** Department of Anesthesiology, Faculty of ParaMedicine, Tabriz University of Medical Sciences, Tabriz, Iran **Email:** kkolahdouzan@yahoo.com **Address:** Department of Anesthesiology, Faculty of ParaMedicine, Tabriz University of Medical Sciences, Daneshghah Street, Postal Code: 51656, Tabriz, Iran **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** IRCT201106154005N4
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "simple randomized sampling procedure was carried out on the basis of study criteria using the “Random Allocation Software” program (practical solution for randomization in clinical trial with different types of formatted output platform windows, version: 1.0, file size: 6.33 MB)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the patients, those administering the drug, and those registering the signs and symptoms of the patients were unaware of the medicine used in each group"
Blinding of outcome assessment (detection bias)	Low risk	Quote: "...and those registering the signs and symptoms of the patients were unaware of the medicine used in each group"

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Eidi 2012 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: study flow diagram: 216 out of 219 enrolled participants were analysed. Dropouts were described and were unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: IRCT201106154005N4 (retrospective registration)
Other bias	Unclear risk	Quote: "was considered statistically significant. There was no significant difference between the three groups in terms of demographic data or physical condition of ASA (table 1). Moreover, there were no statistically significant differences between the three groups in terms of systolic and diastolic pressure, duration of operation, duration of recovery, SPO 2 before induction or SPO 2 at emergence from recovery (%) (table 2). The average systolic or diastolic..." Judgement comment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Ekinci 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 42.25 ± 10.58 • *Weight (mean ± SD, median (IQR), median (range))*: 66.75 ± 9.32 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 81.75 • *Use of perioperative opioids (if yes, which?)*: meperidine 1 mg/kg IM • *Type of surgery*: total abdominal hysterectomy Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20

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Ekinci 2011 *(Continued)*

- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 43.55 ± 10.15
- *Weight (mean ± SD, median (IQR), median (range))*: 66.85 ± 8.68
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90.00
- *Use of perioperative opioids (if yes, which?)*: meperidine 1 mg/kg IM
- *Type of surgery*: total abdominal hysterectomy

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 43.45 ± 8.17
- *Weight (mean ± SD, median (IQR), median (range))*: 67.75 ± 8.21
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93.00
- *Use of perioperative opioids (if yes, which?)*: meperidine 1 mg/kg IM
- *Type of surgery*: total abdominal hysterectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 43.85 ± 11.06
- *Weight (mean ± SD, median (IQR), median (range))*: 66.05 ± 12.51
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 89.50
- *Use of perioperative opioids (if yes, which?)*: meperidine 1 mg/kg IM
- *Type of surgery*: total abdominal hysterectomy

Placebo

- *Assessed for eligibility (n)*: -

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Ekinci 2011 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 42.80 ± 13.01
- *Weight (mean ± SD, median (IQR), median (range))*: 66.75 ± 7.44
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 97.50
- *Use of perioperative opioids (if yes, which?)*: meperidine 1 mg/kg IM
- *Type of surgery*: total abdominal hysterectomy

Included criteria: female, 20 to 72 years of age, scheduled for gynaecological operations where total abdominal hysterectomy was planned, ASA I to III

Excluded criteria: ASA IV or V; antiemetic or glucocorticosteroid use within 24 hours of surgery; intake of opioid drugs; allergy to droperidol, metoclopramide, tropisetron, or ondansetron; pregnancy; current menstrual period; breastfeeding; obesity (body mass index > 34); mental retardation; psychiatric illness; cardiac, renal, neurological, or liver disease; operation anticipated to exceed 2 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Droperidol

- *Dose*: 2.5 mg
- *Time point of administration*: 5 minutes after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: 5 minutes after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Tropisetron

- *Dose*: 2.5 mg
- *Time point of administration*: 5 minutes after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: 5 minutes after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Placebo

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Ekinci 2011 *(Continued)*

	• *Dose*: saline 0.9% • *Time point of administration*: 5 minutes after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (overall, exact time point unknown)* • Outcome type: dichotomous outcome *Sedation/drowsiness (overall, exact time point unknown)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Osman Ekinci **Institution:** Department of Anesthesiology, Haydarpaşa Numune Hospital for Research and Training, Istanbul, Turkey **Email:** droekinci@mynet.com **Address:** Department of Anesthesiology, Haydarpaşa Numune Hospital for Research and Training, TR–34668 Istanbul (Turkey) **Language:** English **Duration of study:** 1 February 2007 to 31 March 2008 **Trial registry number:** NA **Study's primary outcome:** postoperative vomiting
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "we randomized patients by using a computerized randomization table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "given to reverse neuromuscular blockade. The injector with the drug was prepared by the study coordinator according to software which was carefully designed to prevent duplicate injections. The injectors were numbered and given to the staff who did not know the content. Also, patients did not know which agent they were given. The study was designed to..."

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Ekinci 2011 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic characteristics of 100 female patients who were ASA I to II physical status are shown in table 1. There were no statistically significant differences in age and weight (p 1 0.05)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

El Deeb 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Placebo (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 32.1 ± 3.5 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 1.2 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 134 • *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction • *Type of surgery*: thyroidectomy Ondansetron + dexamethasone (group II) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40

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El Deeb 2011 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 29.1 ± 3.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 27 ± 1.2
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 132
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction
- *Type of surgery*: thyroidectomy

Included criteria: ASA I or II, undergoing general anaesthesia for elective thyroidectomy, 3 or more risk factors for PONV (adult female gender, previous history of PONV, history of motion sickness, non-smoking status, duration of surgery longer than 1 hour)

Excluded criteria: younger than 17 years or older than 60 years of age, smoking, surgery lasting less than 1 hour, and known allergy or previous adverse reaction to any of the study drugs

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (duration of anaesthesia, non-smoker, perioperative opioids): no; (gender, history of PONV/motion sickness): unclear, but inclusion criteria was three or more risk factors)

Interventions	**Intervention characteristics** Placebo (group I) • *Dose*: saline • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 1 mg IV; 24 h: 22.5% Ondansetron + dexamethasone (group II) • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 1 mg IV; 24 h: 5%
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA

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El Deeb 2011 *(Continued)*

Country: Egypt

Setting: inpatient, single-centre

Author's name: Alaa El-Deeb

Institution: Department of Anesthesia, Faculty of Medicine, Mansoura University, Egypt

Email: alaaeldeep9@hotmail.com

Address: NA

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	Two out of 3 groups relevant (comparator midazolam)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated using computer-generated code to receive"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all solutions were 5 ml volume, looked identical, prepared by personnel blinded to the study and were given immediately after the induction of anesthesia. After the placement of standard"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperatively, nausea and vomiting were evaluated every 3 h for 6 h then every 6 h up to 24 h by an observer who is blinded to group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the three groups showed no significant differences regarding patient characteristics such as age, body mass index and duration of anesthesia (Table 1)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (duration of anaesthesia, non-smoker, perioperative opioids): no; (gender, history of PONV/motion sickness): unclear, but inclusion criterion was 3 or more risk factors)

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Elhakim 1995

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 46.6 ± 9.1 • *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 8.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 17/8/0/0 • *Gender (female in %)*: 68 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 28/NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 70 • *Use of perioperative opioids (if yes, which?)*: 0.25 mg/kg nalbuphine at induction, 30.9 mg nalbuphine postoperatively (number of patients requesting: 15) • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 47 ± 11.2 • *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 8.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 16/9/0/0 • *Gender (female in %)*: 72 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 28/NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 69 • *Use of perioperative opioids (if yes, which?)*: 0.25 mg/kg nalbuphine at induction, 30.5 mg nalbuphine postoperatively (number of patients requesting: 5) • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** scheduled for laparoscopic cholecystectomy **Excluded criteria:** symptoms of gastrointestinal reflux **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker): unclear; (perioperative opioids): yes

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Elhakim 1995 *(Continued)*

Interventions	**Intervention characteristics** Placebo (group 1) • *Dose*: saline • *Time point of administration*: before induction of anaesthesia, over a period of 10 minutes • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Ondansetron (group 2) • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia, over a period of 10 minutes • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Egypt **Setting:** inpatient, single-centre **Author's name:** M. Elhakim **Institution:** Departments of Anaesthesia end Surgery, Faculty of Medicine, Ain-Sbams and Cairo Universities, Cairo, Egypt **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (group 3 with additional tenoxicam not included)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly allocated" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "prepared preciously by the hospital pharmacy department" No further information on allocation concealment

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Elhakim 1995 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: administration of study drugs was done by an independent operator who was blinded to the solution given
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: outcomes were recorded by nursing staff who were unaware of the antiemetic medication
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker): unclear; (perioperative opioids): yes

Elhakim 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 41 (32 to 58) • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 20/5/0/0 • *Gender (female in %)*: 84 • *Non-smoker (%)*: 53.33 • *History of PONV/motion sickness (%)*: 10/20 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 104 • *Use of perioperative opioids (if yes, which?)*: 5.8 µg/kg intraoperative fentanyl, 78.7 mg postoperative nalbuphine • *Type of surgery*: laparoscopic cholecystectomy Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30

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Elhakim 2002 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 43 (30 to 56)
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 20/5/0/0
- *Gender (female in %)*: 84
- *Non-smoker (%)*: 56.67
- *History of PONV/motion sickness (%)*: 13.33/13.33
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 103
- *Use of perioperative opioids (if yes, which?)*: 6.0 µg/kg intraoperative fentanyl, 66.0 mg postoperative nalbuphine
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron + dexamethasone (2 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 42 (30 to 55)
- *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 21/4/0/0
- *Gender (female in %)*: 88
- *Non-smoker (%)*: 46.67
- *History of PONV/motion sickness (%)*: 16.67/20
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 106
- *Use of perioperative opioids (if yes, which?)*: 5.7 µg/kg intraoperative fentanyl, 59.1 mg postoperative nalbuphine
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron + dexamethasone (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 41 (32 to 61)
- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 20/5/0/0
- *Gender (female in %)*: 88
- *Non-smoker (%)*: 50
- *History of PONV/motion sickness (%)*: 13.33/26.67
- *Type of general anaesthesia*: Inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 108
- *Use of perioperative opioids (if yes, which?)*: 5.9 µg/kg intraoperative fentanyl, 57.0 mg postoperative nalbuphine
- *Type of surgery*: laparoscopic cholecystectomy

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Elhakim 2002 *(Continued)*

Ondansetron + dexamethasone (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 42 (28 to 59)
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/3/0/0
- *Gender (female in %)*: 84
- *Non-smoker (%)*: 60
- *History of PONV/motion sickness (%)*: 16.67/23.33
- *Type of general anaesthesia*: Inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 106
- *Use of perioperative opioids (if yes, which?)*: 5.6 µg/kg intraoperative fentanyl, 56.3 mg postoperative nalbuphine
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron + dexamethasone (16 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 43 (25 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 20/5/0/0
- *Gender (female in %)*: 88
- *Non-smoker (%)*: 53.33
- *History of PONV/motion sickness (%)*: 16.67/20
- *Type of general anaesthesia*: Inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100
- *Use of perioperative opioids (if yes, which?)*: 5.7 µg/kg intraoperative fentanyl, 54.7 mg postoperative nalbuphine
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: undergoing general anaesthesia for elective laparoscopic cholecystectomy

Excluded criteria: received opioid, non-steroidal anti-inflammatory drugs, steroids, or antiemetic agents during the week before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes (use of nalbuphine was stated as similar among groups, but Group P 39.4 mg vs Group OD16 20.1 mg at 24 hours -> difference of about 50%)

Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: before induction of anaesthesia

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Elhakim 2002 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 30%; metoclopramide 10 mg IV

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 17%; metoclopramide 10 mg IV

Ondansetron + dexamethasone (2 mg group)

- *Dose*: ondansetron 4 mg, dexamethasone 2 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 17%; metoclopramide 10 mg IV

Ondansetron + dexamethasone (4 mg group)

- *Dose*: ondansetron 4 mg, dexamethasone 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 7%; metoclopramide 10 mg IV

Ondansetron + dexamethasone (8 mg group)

- *Dose*: ondansetron 4 mg, dexamethasone 8 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 0%; metoclopramide 10 mg IV

Ondansetron + dexamethasone (16 mg group)

- *Dose*: ondansetron 4 mg, dexamethasone 16 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 1%; metoclopramide 10 mg IV

Outcomes

Vomiting (0 to 6 hours)

- Outcome type: dichotomous outcome

Vomiting (12 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Egypt

Setting: inpatient, single-centre

Author's name: Mokhtar Elhakim

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Elhakim 2002 *(Continued)*

Institution: Department of Anaesthesia, Faculty of Medicine, Ain-Shams University, Cairo, Egypt

Email: mokhtare_h@hotmail.com

Address: Al Horreya Heliopolis, Code No: 11361, P.O. Box: 2361, Cairo, Egypt

Duration of study: NA

Language: English

Study's primary outcome: incidence of vomiting

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "allocated randomly to one of six groups (n = 30 each) using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications were prepared by a single nurse anesthetist in two identical syringes with 2 mL of solution to ensure blinding"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all nurses were blinded to the study groups"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "patients' characteristics, factors related to operation and anesthesia, and simplified Apfel score, 12 did not differ between groups (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Entezariasl 2010

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics**

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Entezariasl 2010 *(Continued)*

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 67 ± 9.3
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 52
- *Non-smoker (%)*: 88
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 36.2
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: cataract surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 61.5 ± 10.1
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 40
- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 38.5
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: cataract surgery

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 65.9 ± 11.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 44
- *Non-smoker (%)*: 88
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 35.4

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Entezariasl 2010 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: cataract surgery

Metoclopramide + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 71 ± 5.9
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 56
- *Non-smoker (%)*: 88
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 37.2
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: cataract surgery

Included criteria: cataract surgery under general anaesthesia, ASA I or II

Excluded criteria: diabetes mellitus or other underlying disorders, use of antiemetics during past 24 hours, positive history of motion sickness or PONV

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: 1 minute before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: 1 minute before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: 1 minute before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide + dexamethasone

- *Dose*: metoclopramide 10 mg, dexamethasone 8 mg
- *Time point of administration*: 1 minute before induction of anaesthesia

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Entezariasl 2010 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (recovery room)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** M. Khoshbaten **Institution:** Drug Applied Research Centre, Tabriz, Islamic Republic of Iran **Email:** mkhoshbaten@yahoo.com **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly assigned by block randomization to one of 4 groups of 25 patients: placebo..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...kg) and atracurium (0.5 mg/kg). They were given by the anaesthetist who was unaware of the drug allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...of those needing treatment for PONV were evaluated by nurses, who were blind to the patient's group as the drug administered was not recorded on the patient's anaesthesia chart. The occurrence of PONV was also recorded 24 hours following..."

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Entezariasl 2010 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "in the final analysis. There were no significant differences between the background characteristics of patients in the 4 groups in terms of age, sex, duration of surgery or history of smoking (Table 1)" Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Erhan 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 52.5 ± 13.9 • *Weight (mean ± SD, median (IQR), median (range))*: 63.9 ± 11.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 70 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 93 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 50.3 ± 14.6 • *Weight (mean ± SD, median (IQR), median (range))*: 62.1 ± 7.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Erhan 2008 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 85
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 82
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction
- *Type of surgery*: laparoscopic cholecystectomy

Granisetron (group 3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 50.1 ± 13.0
- *Weight (mean ± SD, median (IQR), median (range))*: 61.2 ± 5.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 85
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction
- *Type of surgery*: laparoscopic cholecystectomy

Dexamethasone (group 4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 53.4 ± 7.6
- *Weight (mean ± SD, median (IQR), median (range))*: 62.9 ± 5.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 65
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 85.8
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: scheduled for laparoscopic cholecystectomy with general anaesthesia, between 21 and 75 years of age (mean 51.5 years)

Excluded criteria: ASA III or IV; over 75 years of age; body mass index > 30; pregnancy; smoking; signs of gastrointestinal, endocrine, renal, hepatic, or immunological disease; use of opioids or tranquillizers less than 1 week before the operation; treatment with steroids; history of alcohol or drug abuse; history of motion sickness; preoperative diagnosis of gallbladder empyema and previous endoscopic sphincterotomy for common bile duct stones; conversion to open cholecystectomy

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Erhan 2008 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness, perioperative opioids): no; (history of PONV): unclear
Interventions	**Intervention characteristics** Placebo (group 1) • *Dose*: 0.9% NaCl • *Time point of administration*: 15 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron (group 2) • *Dose*: 4 mg • *Time point of administration*: 15 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Granisetron (group 3) • *Dose*: 3 mg • *Time point of administration*: 15 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone (group 4) • *Dose*: 8 mg • *Time point of administration*: 15 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre

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Erhan 2008 *(Continued)*

Author's name: Yamac Erhan

Institution: Department of Surgery, Faculty of Medicine, Celal Bayar University, Manisa 45040, Turkey

Email: yamacerhan@yahoo.com

Address: Department of Anesthesiology, Faculty of Medicine, Ege University, 35100 Izmir, Turkey

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly divided into four groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications were prepared by a technician anesthetist in identical 5 ml syringes and administered in a double-blind fashion"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the incidence of nausea and vomiting was recorded during three assessment periods, 0–6 h, 6–12 h, and 12–24 h, by nursing staff without knowledge of which antiemetic the patients had received. Both..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all 80 patients enrolled in the study had their surgical procedures completed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the mean values for age, weight, height, time of surgery, and time of anesthesia are given in Table 1. Groups were comparable with respect to demographic data, time of surgery, and time of anesthesia" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness, perioperative opioids): no; (history of PONV): unclear

Eriksson 1996

Study characteristics

Methods	**Study design:** randomized controlled trial

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Eriksson 1996 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Placebo (group DS) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 31 (20 to 46) • *Weight (mean ± SD, median (IQR), median (range))*: 59 (42 to 75) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 59 • *Use of perioperative opioids (if yes, which?)*: 50 µg fentanyl in PACU, 1 patient received oxycodone due to persistent pain • *Type of surgery*: diagnostic or operative gynaecological laparoscopy Ondansestron (group DO) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 33 (24 to 46) • *Weight (mean ± SD, median (IQR), median (range))*: 61 (47 to 81) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 57 • *Use of perioperative opioids (if yes, which?)*: 50 µg fentanyl in PACU, 1 patient received oxycodone due to persistent pain • *Type of surgery*: diagnostic or operative gynaecological laparoscopy **Included criteria:** non-pregnant women undergoing diagnostic or operative gynaecological laparoscopy (tubal ligations excluded), 18 to 50 years of age, ASA I or II **Excluded criteria:** 30% normal weight (Metropolitan Life Insurance, 1983), with contraindications to the anaesthetics used; had taken drugs with known antiemetic potency during 24 hours before anaesthesia; tubal ligation **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Placebo (group DS)

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Eriksson 1996 *(Continued)*

- *Dose*: saline
- *Time point of administration*: 1 minute before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol 0.1 mg/10 kg IV, twice, if necessary; thereafter ondansetron 4 mg IV

Ondansestron (group DO)

- *Dose*: 4 mg
- *Time point of administration*: 1 minute before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol 0.1 mg/10 kg IV, twice, if necessary; thereafter ondansetron 4 mg IV

Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (discharge to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** study was supported by Pharmacia Pharmaceuticals, Sweden **Country:** Finland **Setting:** outpatient, single-centre **Author's name:** Heidi Eriksson **Institution:** Anaesthesia Research, Departments I and II of Obstetrics and Gynaecology, Helsinki University Central Hospital, Helsinki, Finland **Email:** NA **Address:** Anaesthesia Research, Departments I and II of Obstetrics and Gynaecology, Helsinki University Central Hospital, Haartmaninkatu 2, FIN-00290 Helsinki, Finland **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	Two out of 3 groups relevant (propofol group)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "according to randomization, the patients were allocated to three groups" Judgement comment: no further information on sequence generation provided

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Eriksson 1996 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "in a double-blind fashion" Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the anesthetic technique used). However, all recovery variables were assessed by the same research nurse to avoid person-to-person variation in assessments. No preanesthetic medication was used" Judgement comment: no information on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "three patients were excluded from the study (two from Group DO and one from Group PROP) due to surgical complications"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Ersayli 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, different time points of administration
Participants	**Baseline characteristics** Methylprednisolone (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 46.1 ± 11.1 • *Weight (mean ± SD, median (IQR), median (range))*: 80.7 ± 18.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 12/3/0/0 • *Gender (female in %)*: 40 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 102.6 • *Use of perioperative opioids (if yes, which?)*: 108.3 µg fentanyl, 12.8 mg morphine postoperative • *Type of surgery*: lumbar discectomy Control (group II)

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Ersayli 2006 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 45.4 ± 10.6
- *Weight (mean ± SD, median (IQR), median (range))*: 76.2 ± 12.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 13/2/0/0
- *Gender (female in %)*: 40
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 109.6
- *Use of perioperative opioids (if yes, which?)*: 98.3 µg fentanyl, 13.4 mg morphine postoperative
- *Type of surgery*: lumbar discectomy

Methylprednisolone (group III)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 55.6 ± 9.5
- *Weight (mean ± SD, median (IQR), median (range))*: 75.6 ± 9.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 10/5/0/0
- *Gender (female in %)*: 20
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115.3
- *Use of perioperative opioids (if yes, which?)*: 120 µg fentanyl, 11.2 mg morphine postoperative
- *Type of surgery*: lumbar discectomy

Control (group IV)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 48.8 ± 11.3
- *Weight (mean ± SD, median (IQR), median (range))*: 69.8 ± 11.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 10/5/0/0
- *Gender (female in %)*: 53.33
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102.6
- *Use of perioperative opioids (if yes, which?)*: 110 µg fentanyl, 13.2 mg morphine postoperative

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Ersayli 2006 *(Continued)*

- *Type of surgery*: lumbar discectomy

Included criteria: scheduled for surgery under general anaesthesia for unilateral lumbar disc herniation; first lumbar disc surgery; 17 to 70 years of age; ASA I or II; no benefit from a 4-week course of conservative treatment

Excluded criteria: spinal stenosis, known allergy to local anaesthetics and pregnancy, use of systemic steroids

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear; (gender): yes

Interventions	**Intervention characteristics** Methylprednisolone (group I) • *Dose*: 40 mg • *Time point of administration*: just before wound closure • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Control (group II) • *Dose*: placebo or no treatment (NA) • *Time point of administration*: just before wound closure • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Methylprednisolone (group III) • *Dose*: 40 mg • *Time point of administration*: just before incision • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Control (group II) • *Dose*: placebo or no treatment (NA) • *Time point of administration*: just before incision • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM
Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** no funds were received in support of this work. **Country:** Turkey **Setting:** NA, single-centre **Author's name:** Alp Gurbet **Institution:** Department of Anesthesiology and Reanimation, Uludag University Medical Faculty, Bursa, Turkey

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Ersayli 2006 *(Continued)*

Email: agurbet@uludag.edu.tr

Address: Uludag University Medical Faculty, Department of Anesthesiology and Reanimation, Gorukle, Bursa, Turkey

Duration of study: September 2004 to March 2005

Language: English

Study's primary outcome: pain intensity in VAS score

Trial registry number: NA

Notes	Four out of 5 groups relevant (group C without bupivacaine infiltration), control groups II and IV combined, experimental groups I and III combined for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "each individual was randomly assigned to one of five groups by envelopes" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "by envelopes that identified the treatment to be received" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the parameters were recorded at 1, 4, 8, 16, 20, and 24 hours after surgery by a pain clinic nurse who visited each patient" Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there were no significant differences among the five study groups with respect to mean age, sex distribution, mean weight, proportions of ASA classifications, mean operating time, or mean amount of fentanyl used during the operation (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear; (gender): yes

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Esmaili 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Betamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: morphine 0.1 mg/kg for induction • *Type of surgery*: elective gynaecological surgeries Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: morphine 0.1 mg/kg for induction • *Type of surgery*: elective gynaecological surgeries **Included criteria:** over 20 years of age, ASA I or II, undergoing elective gynaecological surgeries **Excluded criteria:** corticosteroids long term or within a week before the operation; use of analgesics of any type the week before the operation; having pain, nausea, or vomiting before induction of anaesthesia; history of active gastric ulcer or presence of allergy to any kind of drug **Pretreatment:** baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (perioperative opioids): no; (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): unclear

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Esmaili 2004 *(Continued)*

Interventions	**Intervention characteristics** Betamethasone • *Dose*: 8 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** NA **Author's name:** Mohammad-Hasan Esmaili **Institution:** Department of Anesthesiology, Shiraz University of Medical Sciences, Shiraz, Iran **Email:** mhesm@yahoo.com **Address:** Department of Anesthesiology, Nemazee Hospital, Shiraz, Iran **Language:** English **Duration of study:** February to May 2000 **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly assigned into 2 equal control and study groups of 30 members each" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no placebo intervention in the control group. Anaesthesiologists unblinded

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Esmaili 2004 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "members of both groups were questioned with regard to the intensity of pain, nausea, and vomiting they experienced" Judgement comment: no information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (perioperative opioids): no; (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): unclear

Fabling 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 47 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 76 ± 18 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 55 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 328 • *Use of perioperative opioids (if yes, which?)*: 1250 µg intraoperative fentanyl, codeine as rescue analgesic • *Type of surgery*: supratentorial craniotomy Droperidol + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 52 ± 12

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Fabling 2000 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 82 ± 22
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 281
- *Use of perioperative opioids (if yes, which?)*: 1189 µg intraoperative fentanyl, codeine as rescue analgesic
- *Type of surgery*: supratentorial craniotomy

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 85 ± 19
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 45
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 312
- *Use of perioperative opioids (if yes, which?)*: 1169 µg intraoperative fentanyl, codeine as rescue analgesic
- *Type of surgery*: supratentorial craniotomy

Included criteria: 18 to 75 years of age, scheduled for elective supratentorial craniotomy for mass lesion

Excluded criteria: ASA IV or V, antiemetic use preoperatively or intraoperatively, allergy to ondansetron or droperidol, pregnancy, breastfeeding, morbid obesity, mental retardation, psychiatric illness

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, "large dose" dexamethasone • *Time point of administration*: on surgical commencement of skin closure, dexamethasone intraoperatively • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 40% (trimethobenzamide 200 mg, ondansetron 4 mg) Droperidol + dexamethasone • *Dose*: droperidol 0.625 mg, "large dose" dexamethasone

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Fabling 2000 *(Continued)*

	• *Time point of administration*: on surgical commencement of skin closure, dexamethasone intraoperatively • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 40% (trimethobenzamide 200 mg, ondansetron 4 mg) Dexamethasone • *Dose*: "large dose" dexamethasone • *Time point of administration*: intraoperatively • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 50% (trimethobenzamide 200 mg, ondansetron 4 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours) or PONV* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Cecil O. Borel **Institution:** Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina, USA **Email:** borel001@mc.duke.edu **Address:** Department of Anesthesiology, DUMC Box 3094, Duke University, Durham, NC 27710, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	Dexamethasone given perioperatively; dose unknown but stated "was not different between groups"

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned to one of three groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Fabling 2000 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "study drugs were prepared by a pharmacist and administered by the anesthesia staff not involved in data collection. Study..." Judgement comment: no information on blinding of anaesthesiologists
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "all groups were demographically similar, and there was no difference in duration of anesthesia or total fentanyl dose administered (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Fabling 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 23 • *Age (mean ± SD, median (IQR), median (range))*: 55 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 16 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 52.17 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 282 • *Use of perioperative opioids (if yes, which?)*: 1196 µg intraoperative fentanyl, 104 mg postoperative codeine IM • *Type of surgery*: infratentorial craniotomy Dexamethasone + ondansetron

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Fabling 2002 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 23
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 80 ± 19
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 47.82
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 325
- *Use of perioperative opioids (if yes, which?)*: 1464 µg intraoperative fentanyl, 160 mg postoperative codeine IM
- *Type of surgery*: infratentorial craniotomy

Included criteria: 18 to 75 years of age, scheduled for elective infratentorial craniotomy

Excluded criteria: ASA IV or V, antiemetic use preoperatively or intraoperatively, allergy to ondansetron, pregnancy, breastfeeding, morbid obesity, mental retardation, psychiatric illness

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: NA, 0.9% saline • *Time point of administration*: dexamethasone intraoperatively, saline at skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 65% (trimethobenzamide 200 mg IM, ondansetron 4 mg IV, promethazine 12.5 mg) Dexamethasone + ondansetron • *Dose*: dexamethasone NA, ondansetron 8 mg • *Time point of administration*: dexamethasone intraoperatively, ondansetron at skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 65% (trimethobenzamide 200 mg IM, ondansetron 4 mg IV, promethazine 12.5 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours) or PONV* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** supported in part by a grant from Glaxo Smith Kline, Research Triangle Park, North Carolina

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Fabling 2002 *(Continued)*

Country: USA

Setting: inpatient, NA

Author's name: Jennifer M. Fabling

Institution: Department of Anesthesia, Sir Charles Gairdner Hospital, Nedlands, Australia

Email: NA

Address: Department of Anesthesia, Sir Charles Gairdner Hospital, Nedlands, WA 6009, Australia

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: incidence of postoperative nausea

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized to one of two groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study drugs were prepared by a pharmacist in a syringe labeled by number only and administered by anesthesia staff not involved in data collection"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "emetic episodes and analgesic requirements were documented by nursing staff who were blinded to group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "fifty patients were enrolled. Four patients were excluded because of protocol violations, leaving 46 patients for analysis (n 23 ondansetron, n 23 placebo group)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "both groups were similar demographically and there was no difference in duration of anesthesia, total fentanyl dose, and postoperative codeine administered (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

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Fahlenkamp 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (xenon group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 43 • *Received treatment (n)*: 43 • *Analysed (n)*: 43 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (xenon) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 0.19 µg/kg/min remifentanil, 0.08 mg/kg piritramide during anaesthesia, 0.08 mg/kg piritramide during PACU • *Type of surgery*: elective abdominal surgery Placebo (xenon group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (xenon) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 0.19 µg/kg/min remifentanil, 0.08 mg/kg piritramide during anaesthesia, 0.08 mg/kg piritramide during PACU • *Type of surgery*: elective abdominal surgery Dexamethasone (sevoflurane group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 44 • *Received treatment (n)*: 44 • *Analysed (n)*: 44

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Fahlenkamp 2016 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0.18 µg/kg/min remifentanil, 0.07 mg/kg piritramide during anaesthesia, 0.09 mg/kg piritramide during PACU
- *Type of surgery*: elective abdominal surgery

Placebo (sevoflurane group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0.18 µg/kg/mg remifentanil, 0.07 mg/kg piritramide during anaesthesia, 0.09 mg/kg piritramide during PACU
- *Type of surgery*: elective abdominal surgery

Included criteria: scheduled for elective abdominal surgery (i.e. gynaecological, urological, or abdominal surgery through open or laparoscopic approach) with planned duration of at least 60 minutes and planned admission to the ward after postanaesthesia care unit (PACU) stay, 18 to 75 years of age, ASA I or II, Apfel's simplified PONV predicting score of 2 to 4 (i.e. a PONV likelihood of about 40% to 80%)

Excluded criteria: severe cardiac, respiratory, liver, or kidney function disorders; known or suspected allergic reaction to one of the study medications; suspicion of malignant hyperthermia; pregnancy/lactation period; legal incapacity to give informed consent; refusal to participate

Pretreatment: no data on baseline characteristics nor potential effect modifiers for subgroups (antiemetic prophylaxis) provided

Interventions	**Intervention characteristics** Dexamethasone (xenon group) • *Dose*: 4 mg • *Time point of administration*: within first hour of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo (xenon group) • *Dose*: 0.9% NaCl

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Fahlenkamp 2016 *(Continued)*

- *Time point of administration*: within first hour of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone (sevoflurane group)

- *Dose*: 4 mg
- *Time point of administration*: within first hour of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo (sevoflurane group)

- *Dose*: 0.9% NaCl
- *Time point of administration*: within first hour of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** work was supported by a project grant (financial support, drug supply) from Air Liquide Santé International to MC. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Mark Coburn **Institution:** Department of Anesthesiology, University Hospital Aachen, Aachen, Germany **Email:** mcoburn@ukaachen.de **Address:** Department of Anesthesiology, University Hospital Aachen, Aachen, Germany **Language:** English **Duration of study:** November 2008 to March 2011 **Trial registry number:** EUCTR2008-004132-20, NCT00793663 **Study's primary outcome:** Nausea during PACU stay
Notes	Four groups, factorial design (different anaesthesia regimen with or without prophylaxis). Groups with same interventions pooled for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...size 10; allocation ratio 1:1). The randomization lists were generated by computer allocation using a randomization-software (RandList version 1.2, DatInf) by a member of the clinic staff independent from the study team and sealed in an opaque..."

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Fahlenkamp 2016 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "to a serious adverse event. Randomization codes for the type of anesthesia were sealed in opaque envelopes parameterized with the corresponding study number on the outside, and were opened by the study physician on the day of surgery shortly before the start of intervention. Anesthesia technique was blinded to..."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...with the individual study number. Participants, study physicians, and outcome assessors were blinded to the type of prophylactic treatment. Trial Procedure A sketch of..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...with the individual study number. Participants, study physicians, and outcome assessors were blinded to the type of prophylactic treatment. Trial Procedure A sketch of..."
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "occurred in seven cases (¥): One patient withdrew his consent; two were excluded after randomization for safety reasons. Two patients did not receive the scheduled surgery; two did not receive the allocated intervention for administrative reasons. Post interventional drop-out in the sevoflurane group occurred in nine cases (&): One patient dropped out due to a serious adverse event not associated with the study intervention. Eight patients of the sevoflurane group were excluded from data analysis because of violation of the study protocol. 94 patients in the sevoflurane group received the allocated intervention and data analysis, with 44 cases of dexamethasone as randomized prophylactic treatment and 50 placebo. Two patients (#) did not complete the 24h-follow-up because of withdrawal due to severe nausea. Their data until the time of dropout was included into the final analysis. doi:10.1371/journal.pone.0153807.g002 Nausea and Vomiting following" Judgement comment: dropout rate at 24 hours > 15%. Seven participants withdrew due to severe nausea, and data only until the time of dropout were recorded
Selective reporting (reporting bias)	High risk	Judgement comment: EUCTR2008-004132-20 (prospective registration), NCT00793663 (prospective registration). One of the prospectively registered primary outcomes (1. hypnosis, 2. nausea, 3. reduction of VRS nausea) was omitted in the final study report (hypnosis). Assessment of timing differs between protocol and study report
Other bias	Unclear risk	Quote: "...completed the 24h follow-up. The groups were not different with respect to patient age, height, body mass index, gender, ASA status, PONV history and Apfel Score (Table 1). The mean Apfel Score was lower than expected (Table 1). The study groups did not differ with respect to type of surgery, anesthesia duration, additional epidural, and ongoing and post anesthesia piritramide doses (Table 2). Relevant differences were observed in the total dose of propofol administered for induction, and the use of oxygen and remifentanil during maintenance of anesthesia (Table 2). The PACU stay..." Judgement comment: no data on baseline characteristics nor potential effect modifiers for subgroups (antiemetic prophylaxis) provided

Feng 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial

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Feng 2009 *(Continued)*

Study grouping: 3 groups, monoprophylaxis and combination prophylaxis

Participants	**Baseline characteristics** Haloperidol (group H) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 70 • *Received treatment (n)*: NA • *Analysed (n)*: 64 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 26/38/0/0 • *Gender (female in %)*: 75 • *Non-smoker (%)*: 83 • *History of PONV/motion sickness (%)*: 20/31 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 111 • *Use of perioperative opioids (if yes, which?)*: 152 µg intraoperative fentanyl, 25.4 mg postoperative meperidine • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 70 • *Received treatment (n)*: NA • *Analysed (n)*: 65 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/41/0/0 • *Gender (female in %)*: 70.77 • *Non-smoker (%)*: 77 • *History of PONV/motion sickness (%)*: 23/29 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 111 • *Use of perioperative opioids (if yes, which?)*: 148 µg intraoperative fentanyl, 25.4 mg postoperative meperidine • *Type of surgery*: laparoscopic cholecystectomy Haloperidol + ondansetron (group HO) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 70 • *Received treatment (n)*: NA • *Analysed (n)*: 63 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 23/40/0/0

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Feng 2009 *(Continued)*

- *Gender (female in %)*: 76.19
- *Non-smoker (%)*: 76
- *History of PONV/motion sickness (%)*: 14/25
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 113
- *Use of perioperative opioids (if yes, which?)*: 146 µg intraoperative fentanyl, 25.4 mg postoperative meperidine
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, undergoing elective laparoscopic cholecystectomy

Excluded criteria: clinical evidence of a difficult airway, obesity (body mass index > 35 kg/m^2), pregnancy, psychiatric illness, clinically significant major organic disease, preoperative QTc interval > 440 ms, consumption of a drug with antiemetic properties within 24 hours of the study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Haloperidol (group H) • *Dose*: 2 mg • *Time point of administration*: about 30 minutes before conclusion of surgery, saline at induction • *Route of administration*: IM (saline IV) • *Rescue antiemetics (if yes, which?)*: 27%: metoclopramide 10 mg IM (diphenhydramine hydrochloride 30 mg IV as rescue medication for MPS) Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: after induction of general anaesthesia, saline 30 minutes before conclusion of surgery • *Route of administration*: IV (saline IM) • *Rescue antiemetics (if yes, which?)*: 22%: metoclopramide 10 mg IM (diphenhydramine hydrochloride 30 mg IV as rescue medication for MPS) Haloperidol + ondansetron (group HO) • *Dose*: haloperidol 2mg, ondansetron 4 mg • *Time point of administration*: ondansetron after induction of general anaesthesia, haloperidol about 30 minutes before conclusion of surgery • *Route of administration*: ondansetron IV, haloperidol IM • *Rescue antiemetics (if yes, which?)*: 8%: metoclopramide 10 mg IM (diphenhydramine hydrochloride 30 mg IV as rescue medication for MPS)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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Feng 2009 *(Continued)*

	QT prolongation, QTc > 470 ms (PACU) • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan (ROC) **Setting:** inpatient, single-centre **Author's name:** Chin-Chen Chu **Institution:** Department of Anesthesiology, Chi-Mei Medical Center, Tainan, Taiwan, R.O.C. **Email:** mikechu62@seed.net.tw **Address:** Department of Anesthesiology, Chi-Mei Medical Center, Tainan, Taiwan, R.O.C. **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response and patient satisfaction scores **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number table (n = 70 in each)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the study medications diluted with 2 mL saline were prepared by a nurse anesthetist in two syringes labeled “i.m.” or “i.v.”. Each patient was given the test drug i.v. after in- duction of general anesthesia and another dose of test drug at the completion of gallbladder resection, about 30 minutes before the conclusion of surgery. Patients and the investigators who collected the postoperative data were blinded to the drugs given" Judgement comment: blinding of anaesthesiologists unclear
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the investigators who collected the postoperative data were blinded to the drugs given"

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Feng 2009 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "eighteen of the 210 patients enrolled in the study were excluded from the analysis, of whom 10 required an exploratory laparotomy, and eight had incomplete data collected. The data obtained from the remaining 192 patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "patients' characteristics such as age, weight, height, history of PONV and motion sickness, durations of surgery and anesthesia were not different between the three groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Feo 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 49 • *Received treatment (n)*: 49 • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg to 4 µg/kg for induction, mean dose of fentanyl during surgery 10.5 ± 3.3 µg/kg • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 52 • *Received treatment (n)*: 52 • *Analysed (n)*: 52 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA

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Feo 2006 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg to 4 µg/kg for induction, mean dose of fentanyl during surgery 10.5 ± 3.3 µg/kg
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: patients undergoing elective laparoscopic cholecystectomy

Excluded criteria: ASA IV; age over 75 years; body mass index > 30; pregnancy; signs of endocrine, renal, hepatic, or immunological disease; use of opioids or tranquillizers less than 1 week before the operation; treatment with steroids; history of alcohol or drug abuse; preoperative diagnosis of gallbladder empyema; previous endoscopic sphincterotomy for common bile duct stones

Pretreatment: baseline characteristics (age, weight, ASA): unclear (data not shown). Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear (data not shown)

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: 90 minutes before skin incision
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg; 10%

Placebo group

- *Dose*: saline
- *Time point of administration*: 90 minutes before skin incision
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg; 44%

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours) or PONV

- Outcome type: dichotomous outcome

Postoperative wound infection (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Italy

Setting: single-centre

Author's name: C.V. Feo

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Feo 2006 *(Continued)*

Institution: Sezione di Chirurgia Generale, Azienda Ospedaliera Universitaria di Ferrara, Italy

Email: cvfeo@unife.it

Address: Sezione di Chirurgia Generale, Azienda Ospedaliera Universitaria di Ferrara, Corso Giovecca 203, 44100 Ferrara, Italy

Duration of study: March to December 2004

Language: English

Study's primary outcome: degree of postoperative nausea and vomiting

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomized to receive..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "both the patients and the data collector were blinded with respect to the study group" Judgement comment: no information about blinding of anaesthesiologists provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "both the patients and the data collector were blinded with respect to the study group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "six patients (6 per cent) were excluded from the study because of preoperative treatment with steroids (two patients) and previous endoscopic sphincterotomy (four patients)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no difference in sex distribution, age, body mass index, ASA score, pathology, or median operation and anaesthesia times between the dexamethasone and placebo groups" Judgement comment: baseline characteristics (age, weight, ASA): unclear (data not shown). Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear (data not shown)

Feroci 2011

Study characteristics

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Feroci 2011 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range))*: 53.8 ± 14.73 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 68.63 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 84.40 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, no postoperative opioids • *Type of surgery*: extracapsular total thyroidectomy or lobectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range))*: 57.37 ± 13.15 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 66.67 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 88.65 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, no postoperative opioids • *Type of surgery*: extracapsular total thyroidectomy or lobectomy **Included criteria:** underwent thyroid surgery for benign disease categorized as ASA I and II, weighed 50 kg to 100 kg **Excluded criteria:** younger than 18 years of age, previous malignant disease, previous thyroid surgery or neck surgery, had received antiemetic therapy within 48 hours before surgery, chronic pain disorder, insulin-dependent diabetes mellitus, history of severe and/or repeated PONV after previous minor surgery, pregnancy **Pretreatment:** baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Feroci 2011 *(Continued)*

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 20 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: first-line 10 mg/2 mL metoclopramide IV up to 3 times a day; second-line 4 mg ondansetron IV up to 3 times a day Placebo • *Dose*: NaCl • *Time point of administration*: 20 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: first-line 10 mg/2 mL metoclopramide IV up to 3 times a day; second-line 4 mg ondansetron IV up to 3 times a day
Outcomes	*Mortality (0 to 48 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (0 to 30 days)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** Francesco Feroci **Institution:** General Surgery Unit, Misericordia and Dolce Hospital, Prato, Italy **Email:** fferoci@yahoo.it **Address:** NA **Language:** English **Duration of study:** January to December 2009 **Trial registry number:** NCT00888303 **Study's primary outcome:** primary outcome measure was PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed by a computer-generated list of random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Feroci 2011 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "identical syringes were prepared by staff who were not involved in the study according to the random number list. The patients, anesthetists, and investigators who collected the postoperative data were blinded to the randomization process and to the types of drugs administered"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "investigators who collected the postoperative data were blinded to the randomization process and to the types of drugs administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "between January 2009 and December 2009, 114 patients underwent surgery for thyroid disease at our institution. Ten patients were excluded from the randomization according to the following exclusion criteria: 2 patients who had a previous malignant disease, 2 patients who had undergone previous thyroid surgery, 4 patients who had insulin-dependent diabetes mellitus, and 2 patients because of the lack of any comprehension of the Italian language. Two patients in the control arm were excluded from all analyses due to a postoperative hemorrhage requiring an urgent reparative operation. Therefore, data from 102 patients (51 for each group) were available for the analysis per protocol. One other patient in the dexamethasone group was excluded from subjective voice function analysis due to a verified lesion on the recurrent laryngeal nerve"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00888303 (retrospective registration)
Other bias	Unclear risk	Quote: "there were no statistically significant differences between the 2 groups with regard to patient demographics, operation type, postoperative morbidity, and length of stay (Table 1)" Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Forrester 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Meclizine + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 35.5 ± 9.4 • *Weight (mean ± SD, median (IQR), median (range))*: 68.05 ± 10.33 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 92.31 • *Non-smoker (%)*: 92.31

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Forrester 2007 *(Continued)*

- *History of PONV/motion sickness (%)*: 69.23/74.36
- *Type of general anaesthesia*: inhalational anaesthesia (iso-/sevo-/desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 129.79
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: NA

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 39.8 ± 11.2
- *Weight (mean ± SD, median (IQR), median (range))*: 76.47 ± 13.52
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 81.58
- *Non-smoker (%)*: 89.47
- *History of PONV/motion sickness (%)*: 68.42/89.47
- *Type of general anaesthesia*: inhalational anaesthesia (iso-/sevo-/desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 136.21
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: NA

Included criteria: consented for surgery under general anaesthesia scheduled for 60 minutes or longer, ASA I or II, 18 to 65 years of age, English language proficiency, presence of 4 of 5 risk factors for PONV (general anaesthesia, female gender, non-smoker, history of motion sickness, history of PONV)

Excluded criteria: contraindications to receiving general anaesthesia, history of sensitivity to ondansetron or meclizine, antiemetic use within 24 hours of surgery, pregnancy, gastro-oesophageal reflux disease, obesity with a body mass index > 35

Pretreatment: baseline characteristics (age, ASA): no; (weight): yes. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Meclizine + ondansetron • *Dose*: meclizine 50 mg, ondansetron 4 mg • *Time point of administration*: meclizine within 15 to 30 minutes before surgery, ondansetron 15 to 30 minutes before end of surgical procedure • *Route of administration*: meclizine PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, metoclopramide 10 to 20 mg IV, promethazine 12.5 to 25 mg IV Ondansetron • *Dose*: placebo tablets, ondansetron 4 mg • *Time point of administration*: placebo within 15 to 30 minutes before surgery, ondansetron 15 to 30 minutes before end of surgical procedure • *Route of administration*: placebo PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, metoclopramide 10 to 20 mg IV, promethazine 12.5 to 25 mg IV
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)*

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Forrester 2007 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient and outpatient, single-centre **Author's name:** Carry M. Forrester **Institution:** Naval Medical Center, Portsmouth, Virginia **Email:** NA **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of nausea
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the enrolled subjects then were randomly assigned by the pharmacy to 1 of 2 groups using a computer-generated random numbers process"
Allocation concealment (selection bias)	Low risk	Quote: "group 2 (placebo and ondansetron). The pharmacist placed two 25 mg meclizine tablets (50 mg total) or 2 placebo tablets in an opaque brown plastic bag. The bag labeled 'meclizine study'..."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the opaque bag was used to ensure that the investigators were blinded to the study drug because a placebo with an appearance identical to that of meclizine was unavailable. Negative pregnancy test results were verified for all female subjects before study enrollment. Within 15 to 30 minutes before surgery, patients were given the “study drug” with no more than 2 ounces of water by a staff member. When taking the study drug, patients were asked to close their eyes so they would remain blinded to the physical characteristics of the pills. The staff member who administered the study medication preoperatively was not allowed to participate in the care of the patient postoperatively to maintain the integrity of the double-blind study" Judgement comment: participants may be able to recognize their allocation (different physical appearance of the pills)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "on arrival in the PACU, the data collection tools were delivered to the PACU personnel, who were also blinded to the treatment group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 84 subjects were enrolled, but 7 were removed from the study because of breaches in protocol or a change in anesthetic management, leaving a total of 77 subjects (group 1, 39; group 2, 38) for the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Forrester 2007 *(Continued)*

Other bias	Unclear risk	Quote: "with the exception of patient weight, there were no significant differences in relation to demographic variables, including surgical time, anesthesia time, smoking history, or history of motion sickness or PONV between groups (Table)" Judgement comment: baseline characteristics (age, ASA): no; (weight): yes. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Fortney 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 518 • *Received treatment (n)*: NA • *Analysed (n)*: 508 (efficacy)/518 (safety) • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 17 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 87 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 86/61 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 56.2 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/alfentanil, 75% postoperative opioids • *Type of surgery*: gynaecological, breast, urological, musculoskeletal, other outpatient surgery Droperidol (0.625 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 518 • *Received treatment (n)*: NA • *Analysed (n)*: 509 (efficacy)/518 (safety) • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 17 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 87 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 85/60 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)

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Fortney 1998 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 57.8
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/alfentanil, 69% postoperative opioids
- *Type of surgery*: gynaecological, breast, urological, musculoskeletal, other outpatient surgery

Droperidol (1.25 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 510
- *Received treatment (n)*: NA
- *Analysed (n)*: 503 (efficacy)/510 (safety)
- *Age (mean ± SD, median (IQR), median (range))*: 35 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 91
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 88/60
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 54
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/alfentanil, 65% postoperative opioids
- *Type of surgery*: gynaecological, breast, urological, musculoskeletal, other outpatient surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 515
- *Received treatment (n)*: NA
- *Analysed (n)*: 505 (efficacy)/515 (safety)
- *Age (mean ± SD, median (IQR), median (range))*: 36 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 16
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 89
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 85/62
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 57.3
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/alfentanil, 73% postoperative opioids
- *Type of surgery*: gynaecological, breast, urological, musculoskeletal, other outpatient surgery

Included criteria: ASA I or II, between 18 and 65 years of age, history of motion sickness or PONV after general anaesthesia, scheduled for general anaesthesia for outpatient procedures planned to last no longer than 2 hours. Additionally, study patients were limited to those undergoing procedures considered to have high emetogenic potential (laparoscopic, genitourinary, lower extremity orthopaedics, umbilical or ventral herniorrhaphies, partial mastectomies, or lumpectomies)

Excluded criteria: major organ disease, ASA II or greater, weight > 100% over ideal, pregnancy or breastfeeding, history of alcohol or drug abuse, receipt of an investigational drug within 30 days of the study, receipt of an agent with antiemetic properties within 24 hours of the study, known hypersensitivity to 5-HT3 antagonists

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Fortney 1998 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes
Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 20 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 45% (not specified, discretion of attending anaesthesiologist) Droperidol (0.625 mg group) • *Dose*: 0.625 mg • *Time point of administration*: 20 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 32% (not specified, discretion of attending anaesthesiologist) Droperidol (1.25 mg group) • *Dose*: 1.25 mg • *Time point of administration*: 20 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 26% (not specified, discretion of attending anaesthesiologist) Ondansetron • *Dose*: 4 mg • *Time point of administration*: 20 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 34% (not specified, discretion of attending anaesthesiologist)
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any AE (overall, exact time point unknown)* • Outcome type: dichotomous outcome *Headache (overall, exact time point unknown)* • Outcome type: dichotomous outcome *Sedation/drowsiness (overall, exact time point unknown)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this work was supported by a grant from Glaxo Wellcome Inc. **Country:** USA **Setting:** outpatient, multi-centre (50) **Author's name:** Jennifer T. Fortney **Institution:** Department of Anesthesiology, Duke University, Durham, North Carolina, USA **Email:** NA **Address:** Box 3094, Duke University Medical Center, Durham, NC 27710, USA

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Fortney 1998 *(Continued)*

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: complete response (no emetic episodes, no requirement for rescue antiemetic medications)

Notes	Data from 2 identical studies at 50 centres were merged (combined data were extracted)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "each patient was then randomized to one of four treatments" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "...or ondansetron 4 mg. All drugs were mixed with 0.9% saline to a final volume of 10 mL and administered in a double-blind fashion no more than 20 min before the induction of anesthesia. After study drug administration..." Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "study personnel recorded episodes of nausea or vomiting and adverse events during the study period" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...than in the placebo group. Follow-up data after discharge from the ambulatory surgery unit were available for 2025 patients. Of those patients who returned the evaluation, not all completed the nausea assessment. The results in Table 3..." Judgement comment: missing data were balanced across all treatment groups and reasons for missing data were reported
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "were therefore combined and reanalyzed. The treatment groups were similar with respect to age, weight, gender, history of susceptibility to motion sickness, history of nausea with general anesthetics, duration of anesthesia, and emergence times (Table 1). There was also no significant difference among the treatment groups in the type of surgery performed (Table 2), with most patients undergoing gynecological..." Quote: "group (69%, P < 0.05). In an u posteriori analysis of postoperative analgesic use, the proportion of patients to whom opioid analgesics were administered was significantly less in the droperidol 1.25 mg group (65%, P < 0.001) compared with the ondansetron group (73%) and the placebo group (75%). The proportion of patients to whom opioid analgesics were administered was also significantly less in the droperido10.625 mg group (69%, P < 0.05) compared with that in the placebo group. Follow-up data after discharge from..."

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Fortney 1998 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes

Foster 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 38 ± 11.9 • *Weight (mean ± SD, median (IQR), median (range))*: 64.2 ± 11.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 15.3 • *Use of perioperative opioids (if yes, which?)*: 50 µg fentanyl at induction • *Type of surgery*: minor gynaecological surgery Droperidol (0.5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 12.9 • *Weight (mean ± SD, median (IQR), median (range))*: 62.7 ± 9.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 15.4 • *Use of perioperative opioids (if yes, which?)*: 50 µg fentanyl at induction • *Type of surgery*: minor gynaecological surgery Droperidol (1 mg group)

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Foster 1996 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 8.3
- *Weight (mean ± SD, median (IQR), median (range))*: 62.3 ± 8.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 15.5
- *Use of perioperative opioids (if yes, which?)*: 50 µg fentanyl at induction
- *Type of surgery*: minor gynaecological surgery

Included criteria: ASA I or II, undergoing minor gynaecological surgery as day cases

Excluded criteria: women with a history of psychotic illness or taking psychotropic medication, as well as those requiring intubation or overnight stay

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: "no droperidol" (placebo or no treatment unclear) • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: any patients requiring antiemetic treatment or opioid analgesia were to be treated and then excluded from the study Droperidol (0.5 mg group) • *Dose*: 0.5 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: any patients requiring antiemetic treatment or opioid analgesia were to be treated and then excluded from the study Droperidol (1 mg group) • *Dose*: 1 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: any patients requiring antiemetic treatment or opioid analgesia were to be treated and then excluded from the study
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours) or PONV* • Outcome type: dichotomous outcome

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Foster 1996 *(Continued)*

	Extrapyramidal symptoms, restlessness (0 to 24 hours) • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** outpatient, single-centre **Author's name:** P.N. Foster **Institution:** Department of Anaesthetics, Royal Preston Hospital, Preston PR2 4HT **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly allocated by a sealed envelope system" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "...by a sealed envelope system" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "both the patient and the investigators were blind to the patient's study group" Judgement comment: no information on blinding of the anaesthesiologist. No details on preparation and identical appearance of study drugs
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the investigators were blind to the patient's study group" Judgement comment: outcome assessment was made by the investigators
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "seven patients, two controls and five from the droperidol 0.5 mg group, could not be contacted after discharge; the presented data therefore relates to 113 women"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Foster 1996 *(Continued)*

Other bias	Unclear risk	Quote: "the three groups were comparable for age, weight, type and duration of procedure and the administration of syntocinon (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Fukami 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 58 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24.4 ± 4.5 • *ASA I/II/III/IV (n)*: 37/2/1/0 • *Gender (female in %)*: 42.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 130 • *Use of perioperative opioids (if yes, which?)*: 0.1 mg fentanyl at induction • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 56 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24.7 ± 3.4 • *ASA I/II/III/IV (n)*: 35/4/1/0 • *Gender (female in %)*: 37.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 130 • *Use of perioperative opioids (if yes, which?)*: 0.1 mg fentanyl at induction

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Fukami 2009 *(Continued)*

- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: undergoing laparoscopic cholecystectomy

Excluded criteria: ASA IV, older than 80 years of age, pregnancy, treatment with steroids, severe diabetes mellitus (HbA1c > 8.5%), use of opioids or tranquilizers less than 1 week before LC, history of alcohol or drug abuse, preoperative diagnosis of gallbladder carcinoma, acute pancreatitis, emergency operation, conversion from LC to an open procedure

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 90 minutes before skin incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo • *Dose*: saline • *Time point of administration*: 90 minutes before skin incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Postoperative wound infection* (postoperative complications were recorded during hospitalization, and patients were followed up at least once after discharge) • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Y. Fukami **Institution:** Department of Surgery, Shizuoka Saiseikai General Hospital, Shizuoka 422-8527, Japan **Email:** yasuyuki490225@yahoo.co.jp **Address:** Department of Surgery, Shizuoka Saiseikai General Hospital, Shizuoka 422-8527, Japan **Duration of study:** January 2006 to May 2008 **Language:** English **Study's primary outcome:** incidence of nausea and vomiting **Trial registry number:** NA
Notes	None
Risk of bias	

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Fukami 2009 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...using an equal number of blind envelopes" Judgement comment: insufficient information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "...using an equal number of blind envelopes" Judgement comment: not stated; "sequentially numbered, opaque, sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "eighteen patients were excluded from the study, because of age more than 80 years (n = 8), lack of consent (n = 2), bile duct injury (n = 1), acute pancreatitis (n = 1) and conversion from LC to an open procedure (n = 6; 6%). A total of 80 LC patients were enrolled (Fig. 1), 40 being randomized to intravenous dexamethasone (8 mg) and 40 to placebo"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...the hospital for 3 days. There were no significant differences between the two groups with regard to mean age, gender, BMI, preoperative CRP level, ASA score, or anesthesia and operation times (Tables 1, 2). Seven patients..." Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Gallinger 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: NA • *Age (mean ± SD, median (IQR), median (range))*: 34 ± 2.5

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Gallinger 2007 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 116 ± 7
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic surgery

Ondansetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 32 ± 3.1
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 123 ± 9.4
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic surgery

Ondansetron + dexamethasone + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 35 ± 2.7
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 130 ± 10.0
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic surgery

Included criteria: laparoscopic surgery under general anaesthesia

Excluded criteria: NA

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Gallinger 2007 *(Continued)*

	Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (duration of anaesthesia): no; (gender, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Ondansetron + droperidol • *Dose*: ondansetron 8 mg, droperidol 1.25 mg • *Time point of administration*: ondansetron at induction, droperidol during anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20 mg metoclopramide, 1 mg to 2 mg ondansetron Ondansetron + dexamethasone • *Dose*: ondansetron 8 mg, dexamethasone 8 mg • *Time point of administration*: ondansetron at induction, dexamethasone during anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20 mg metoclopramide, 1 mg to 2 ondansetron Ondansetron + dexamethasone + droperidol • *Dose*: ondansetron 8 mg, dexamethasone 8 mg, droperidol 1.25 mg • *Time point of administration*: ondansetron at induction, dexamethasone and droperidol during anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20 mg metoclopramide, 1 mg to 2 ondansetron
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Russia **Setting:** inpatient, single-centre **Author's name:** E. Gallinger **Institution:** NA **Email:** NA **Address:** NA **Duration of study:** NA **Language:** Russian (translated by Alena Rudenko) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Number of participants per group unclear; no information on missing data. No author contact information available

Risk of bias

Bias	Authors' judgement	Support for judgement

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Gallinger 2007 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" (Translation). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessor
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: number of participants per group unclear, no information on missing data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (duration of anaesthesia): no; (gender, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Gan 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 57 (16 to 76) • *Weight (mean ± SD, median (IQR), median (range))*: 62.3 ± 0.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 58 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 105 • *Use of perioperative opioids (if yes, which?)*: 0.005% fentanyl 10 mL for postoperative analgesia, no intraoperative opioids

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Gan 1994 *(Continued)*

- *Type of surgery*: total hip or knee replacement or femoral resection

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 38
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 61 (18 to 78)
- *Weight (mean ± SD, median (IQR), median (range))*: 63.4 ± 9.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 55
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102
- *Use of perioperative opioids (if yes, which?)*: 0.005% fentanyl 10 mL for postoperative analgesia, no intraoperative opioids
- *Type of surgery*: total hip or knee replacement or femoral resection

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 42
- *Received treatment (n)*: NA
- *Analysed (n)*: 42
- *Age (mean ± SD, median (IQR), median (range))*: 59 (19 to 82)
- *Weight (mean ± SD, median (IQR), median (range))*: 63.8 ± 0.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 55
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 118
- *Use of perioperative opioids (if yes, which?)*: 0.005% fentanyl 10 mL for postoperative analgesia, no intraoperative opioids
- *Type of surgery*: total hip or knee replacement or femoral resection

Included criteria: ASA I or II, undergoing total hip or knee replacement or femoral resection

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 0.9% saline • *Time point of administration*: recovery suite (before onset of PONV) • *Route of administration*: IV

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Gan 1994 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM (38%) Droperidol • *Dose*: 1.25 mg droperidol • *Time point of administration*: recovery suite (before onset of PONV) • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM (34%) Ondansetron • *Dose*: 4 mg ondansetron • *Time point of administration*: recovery suite (before onset of PONV) • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM (17%)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Glaxo provided ondansetron **Country:** UK **Setting:** inpatient, single-centre **Author's name:** T.J. Gan **Institution:** Department of Anaesthesia, Royal National Orthopaedic Hospital Trust, Brockley Hill, Stanmore, Middlesex, UK **Email:** tong.gan@stonybrookmedicine.edu **Address:** Department of Anaesthesia, Royal National Orthopaedic Hospital Trust, Brockley Hill, Stanmore, Middlesex, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Gan 1994 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "to the recovery suite where they were allocated randomly to receive i.v. a 25-ml..." Quote: "randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "1.25 mg or saline only. This was administered over a period of 10 min by the recovery staff who were blinded to the solution given. A continuous infusion of 0.5..." Quote: "double-blind comparison"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "nausea and vomiting were recorded hourly for 24 h by the nursing staff, commencing from the time of arrival in the post-operative recovery room" Quote: "double-blind" Judgement comment: insufficient information on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences in patient characteristics (table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Gan 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 26 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 47 ± 10

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Gan 2004 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 18
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 6/16/3/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 36
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 199
- *Use of perioperative opioids (if yes, which?)*: 343 µg fentanyl intraoperative, 76 µg postoperative fentanyl
- *Type of surgery*: major breast surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 7/16/1
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 46
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 222
- *Use of perioperative opioids (if yes, which?)*: 376 µg fentanyl intraoperative, 91 µg postoperative fentanyl
- *Type of surgery*: major breast surgery

Included criteria: undergoing major breast surgery

Excluded criteria: pregnant, experiencing menstrual symptoms, using a permanent cardiac pacemaker, had previous experience with acupuncture therapies, had received any antiemetic medication or had experienced nausea, vomiting, or retching within 24 hours of surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg; 28% Placebo • *Dose*: saline • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg; 54%

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Gan 2004 *(Continued)*

Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Tong J. Gan **Institution:** Departments of Anesthesiology and Plastic Surgery, Duke University Medical Center, Durham, North Carolina, USA **Email:** gan00001@mc.duke.edu **Address:** Department of Anesthesiology, Duke University Medical Center, Box 3094, Durham, NC 2771, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of nausea **Trial registry number:** NA
Notes	Two out of 3 groups relevant (electro-acupoint stimulation)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was achieved using a random number generator"
Allocation concealment (selection bias)	Unclear risk	Quote: "in a sealed envelope technique..." Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the anesthesiologists and care providers were blinded to the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperative data were collected by a separate research nurse not involved in the preoperative or intraoperative management of patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "seventy-seven patients were enrolled in the study. One patient from the O group did not have her scheduled surgery and one patient from the P

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Gan 2004 *(Continued)*

		group withdrew from participation before the administration of study procedure. Seventy-five patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no difference in patient demographics among the groups..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Gan 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Granisetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 101 • *Received treatment (n)*: 89 • *Analysed (n)*: 87 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 84 • *History of PONV/motion sickness (%)*: 28/28 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 123 • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine • *Type of surgery*: abdominal hysterectomy Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 109 • *Received treatment (n)*: 89 • *Analysed (n)*: 89 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 79

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Gan 2005 *(Continued)*

- *History of PONV/motion sickness (%)*: 26/25
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 127
- *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine
- *Type of surgery*: abdominal hysterectomy

Included criteria: females over 18 years of age, ASA I to III, scheduled to undergo abdominal hysterectomy requiring general anaesthesia

Excluded criteria: known hypersensitivity or contraindication to study medications; chronic nausea and vomiting or experienced retching, vomiting, or moderate or severe nausea in the 24 hours before anaesthesia; had received an antiemetic drug or a drug with antiemetic properties during the 24 hours before anaesthesia; body mass index > 36, pregnant or breastfeeding, condition requiring long-term opioid use

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Granisetron + dexamethasone • *Dose*: granisetron 0.1 mg, dexamethasone 8 mg • *Time point of administration*: granisetron approximately 15 minutes before tracheal extubation, dexamethasone immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 55% (granisetron 0.1 mg IV) Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: ondansetron approximately 15 minutes before tracheal extubation, dexamethasone immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 47% (granisetron 0.1 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours, 0 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours) or PONV* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Mortality (0 to 24 hours)*

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Gan 2005 *(Continued)*

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this research was sponsored by Roche Laboratories Inc., Nutley, NJ **Country:** USA **Setting:** inpatient, multi-centre (19 centres in the USA) **Author's name:** Tong J. Gan **Institution:** Duke University Medical Center, Durham, North Carolina, USA **Email:** gan00001@mc.duke.edu **Address:** Box 3094, Department of Anesthesiology, Duke University Medical Center, Durham, NC, USA **Language:** English **Duration of study:** 30 October 2003 to 27 April 2004 **Trial registry number:** NA **Study's primary outcome:** primary efficacy endpoint was proportion of patients with no vomiting during 0 to 2 hours after tracheal extubation
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomization lists were computer-generated, centrally determined..."
Allocation concealment (selection bias)	Low risk	Quote: "the randomization lists were computer-generated, centrally determined, and the randomization numbers were allocated sequentially in the order in which patients were enrolled"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications were prepared by the site pharmacist, who was not involved in any other part of the study, and presented to blinded investigators as identical 2-mL filled syringes"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: outcome assessors were blinded due to study design
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "...considered evaluable for efficacy. The 34 patients excluded from efficacy analyses either did not receive at least 1 dose of study medication (GD, n6; OD, n10), received D but not either G or O (GD, n6; OD, n10), or had no 2-h nausea/vomiting assessment (GD, n2); no patient was excluded for reasons related to nausea or vomiting. Treatment groups were generally similar..."

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Gan 2005 *(Continued)*

		Judgement comment: rate of missing outcome data > 15%. Reasons described and unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "treatment groups were generally similar with regard to baseline characteristics (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Gan 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Aprepitant (40 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 272 • *Received treatment (n)*: 261 • *Analysed (n)*: 248 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 11.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 55/171/35/0 • *Gender (female in %)*: 94 • *Non-smoker (%)*: 75 • *History of PONV/motion sickness (%)*: 30/29 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, volatile agent) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 120 • *Use of perioperative opioids (if yes, which?)*: 99.6% participants with postoperative opioid use 0 to 24 hours • *Type of surgery*: gynaecological procedure, prostatectomy, intestinal resection, hernia repair, bladder surgery, cholecystectomy, nephrectomy Aprepitant (125 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 263 • *Received treatment (n)*: 252 • *Analysed (n)*: 239 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 9.4 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 64/152/36/0

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Gan 2007 *(Continued)*

- *Gender (female in %)*: 94
- *Non-smoker (%)*: 82
- *History of PONV/motion sickness (%)*: 33/25
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, volatile agent)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: 99.6% of participants with postoperative opioid use 0 to 24 hours
- *Type of surgery*: gynaecological procedure, prostatectomy, intestinal resection, hernia repair, bladder surgery, cholecystectomy, nephrectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 270
- *Received treatment (n)*: 253
- *Analysed (n)*: 246
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 11.2
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 61/160/32/0
- *Gender (female in %)*: 95
- *Non-smoker (%)*: 79
- *History of PONV/motion sickness (%)*: 32/25
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, volatile agent)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 132
- *Use of perioperative opioids (if yes, which?)*: 99% of participants with postoperative opioid use 0 to 24 hours
- *Type of surgery*: gynaecological procedure, prostatectomy, intestinal resection, hernia repair, bladder surgery, cholecystectomy, nephrectomy

Included criteria: 18 years of age or older, scheduled to undergo open abdominal surgery requiring an overnight hospital stay, ASA I to III, scheduled to receive general anaesthesia including nitrous oxide with volatile anaesthetics

Excluded criteria: pregnant or breastfeeding, undergoing surgery requiring routine placement of a nasogastric or oral-gastric tube, receiving spinal regional or propofol-maintained anaesthesia, vomiting of any organic aetiology, vomiting for any reason within 24 hours of surgery, abnormal laboratory values as specified by the protocol (alanine aminotransferase or aspartate aminotransferase > 2.5× upper limit of normal, bilirubin > 1.5× upper limit of normal, creatinine > 1.5× upper limit of normal), medications metabolized by CYP3A4 and known to have a narrow therapeutic index were prohibited, people taking such medications and unable to discontinue them for the duration of the study were excluded

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics**

Aprepitant (40 mg group)

- *Dose*: 40 mg
- *Time point of administration*: 1 to 3 hours before anticipated induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: 55% NA

Aprepitant (125 mg group)

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Gan 2007 *(Continued)*

- *Dose*: 125 mg
- *Time point of administration*: 1 to 3 hours before anticipated induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: 56% NA

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 54% NA

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 14 days)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 14 days)* • Outcome type: dichotomous outcome *QT prolongation (at 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 14 days)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 14 days)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 14 days' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was funded by Merck and Co., Inc. **Country:** USA **Setting:** inpatient, multi-centre (29) **Author's name:** Tong J. Gan **Institution:** Department of Anesthesiology, Duke University Medical Centre, Durham, North Carolina, USA **Email:** gan00001@mc.duke.edu **Address:** Department of Anesthesiology, Duke University Medical Centre, Durham, NC 27710, USA **Language:** English **Duration of study:** 26 September 2003 to 24 November 2004 **Trial registry number:** NCT00090155

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Gan 2007 *(Continued)*

	Study's primary outcome: primary efficacy endpoint was proportion of patients with complete response, defined as no vomiting and no use of rescue therapy, in the 24 hours after surgery, to be tested for superiority of aprepitant
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...using a computer-generated random allocation schedule stratified according to gender"
Allocation concealment (selection bias)	Low risk	Quote: "to ensure blinding among staff employed by the sponsor who were involved with the study, the randomization schedule was generated by a statistician who was otherwise uninvolved with the study. On the day of surgery, patients were randomized to one of three preoperative treatments: oral aprepitant 40 mg, oral aprepitant 125 mg, or IV ondansetron 4 mg. Matching placebos were used to maintain blinding. Blinded allocation schedules and supplies of aprepitant were provided by the sponsor, and each study site designated an unblinded pharmacist to receive, store, and prepare the ondansetron and saline placebo"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "each study site designated an unblinded pharmacist to receive, store, and prepare the ondansetron and saline placebo"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: outcome assessors were blinded due to study design
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "disposition of the 805 patients randomized into the study is shown in Figure 1. All randomized patients who received study drug (n 766) were included in the tolerability assessments; data were excluded from 39 patients who either did not receive any study drug (n 34) or who, due to incorrect preparation of the vial for IV administration at the study site, received either placebo for aprepitant and placebo for ondansetron, or active aprepitant and active ondansetron (n 5). The efficacy analyses excluded these 39 patients plus another 14 patients who either did not undergo surgery but did receive drug (n 1), did not have posttreatment efficacy assessments (n 2), or did not receive Vial B but received active drug in Bottle A (n 11). An additional 19 patients, for whom significant violations of study conduct and data collection occurred at one site, were also excluded from the efficacy analyses before unblinding occurred, although safety data from these 19 patients were included in the safety assessments"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00090155 (retrospective registration)
Other bias	Unclear risk	Quote: "the treatment groups also did not differ in terms of patient baseline characteristics, including risk factors for PONV (Table 1)" Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

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Gan 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Transdermal scopolamine + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 310 • *Received treatment (n)*: 308 • *Analysed (n)*: 304 • *Age (mean ± SD, median (IQR), median (range))*: 38.1 ± 11.2 • *Weight (mean ± SD, median (IQR), median (range))*: 75.4 ± 20.5 • *BMI (mean ± SD, median (IQR), median (range))*: 29.1 ± 15.8 • *ASA I/II/III/IV (n)*: 142/143/19/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 42/52 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane/ isoflurane/ sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 78 • *Use of perioperative opioids (if yes, which?)*: postoperative fentanyl • *Type of surgery*: gynaecological laparoscopy, laparoscopic cholecystectomy, breast augmentation surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 310 • *Received treatment (n)*: 310 • *Analysed (n)*: 304 • *Age (mean ± SD, median (IQR), median (range))*: 38.9 ± 10-6 • *Weight (mean ± SD, median (IQR), median (range))*: 76.5 ± 21.1 • *BMI (mean ± SD, median (IQR), median (range))*: 28.6 ± 7.7 • *ASA I/II/III/IV (n)*: 123/158/23/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 47/47 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane/ isoflurane/ sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 78 • *Use of perioperative opioids (if yes, which?)*: postoperative fentanyl • *Type of surgery*: gynaecological laparoscopy, laparoscopic cholecystectomy, breast augmentation surgery **Included criteria:** ASA I to III; adult females undergoing outpatient gynaecological laparoscopy, laparoscopic cholecystectomy, or breast augmentation surgery with anticipated duration of 1 to 3 hours; based on Apfel 4-point risk scoring system for identifying high-risk patients, female patients were recruited to participate in the study if they had at least 2 of 3 high-risk factors associated with PONV: (1) history of PONV and/or motion sickness, (2) non-smoker, and (3) expectation to receive intraoperative and postoperative opioids

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Gan 2009 *(Continued)*

	Excluded criteria: symptoms of nausea and vomiting, received an antiemetic within 48 hours of surgery, closed angle-glaucoma, allergic to study drugs **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Transdermal scopolamine + ondansetron • *Dose*: scopolamine 1.5 mg over 72 hours, ondansetron 4 mg • *Time point of administration*: scopolamine two hours before entering the operating room and remained in place until 24 hours after the end of surgery, ondansetron two to five minutes min before induction of anaesthesia • *Route of administration*: scopolamine transdermal, ondansetron IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg Ondansetron • *Dose*: placebo sham patch, ondansetron 4 mg • *Time point of administration*: placebo two hours before entering the operating room and remained in place until 24 hours after the end of surgery, ondansetron two to five minutes min before induction of anaesthesia • *Route of administration*: placebo transdermal, ondansetron IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (postdischarge to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by Baxter Healthcare Corporation

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Gan 2009 *(Continued)*

Country: USA

Setting: outpatient, multi-centre (24)

Author's name: Tong J. Gan

Institution: Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina, USA

Email: GAN00001@mc.duke.edu

Address: Department of Anesthesiology, Duke University Medical Center, PO Box 3094, Durham, NC 27710, USA

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: primary efficacy endpoint was complete antiemetic response through 24 hours after end of surgery

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "independent research personnel not associated with the study used a random number generator in a sealed envelope technique to randomly assign patients to one of two treatment groups"
Allocation concealment (selection bias)	Low risk	Quote: "...in a sealed envelope technique to randomly assign patients to one of two treatment groups" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE), but randomization was performed by research personnel not associated with the study
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "patients received either an active TDS patch or a similar appearing sham over the mastoid area 2 h before entering the operating room" Judgement comment: no information on blinding of personnel. TDS patches and sham patches only called "similar" - not identical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 620 patients who were randomly assigned to treatment, 618 were treated (two patients were withdrawn by the investigator and did not receive study medication). Figure 1 illustrates the patient screening and random assignment process. The treatment groups were comparable with respect to demographic data and clinical characteristics (Table 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the treatment groups were comparable with respect to demographic data and clinical characteristics (Table 1)"

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Gan 2009 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Gan 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 103 • *Received treatment (n)*: 103 • *Analysed (n)*: 103 • *Age (mean ± SD, median (IQR), median (range))*: 45.8 ± 10.1 • *Weight (mean ± SD, median (IQR), median (range))*: 76.1 ± 15.4 • *BMI (mean ± SD, median (IQR), median (range))*: 28.5 ± 5.2 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 71 • *History of PONV/motion sickness (%)*: 30/32 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane/isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 132 • *Use of perioperative opioids (if yes, which?)*: morphine equivalent • *Type of surgery*: elective open abdominal surgery Rolapitant (5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 103 • *Received treatment (n)*: 103 • *Analysed (n)*: 103 • *Age (mean ± SD, median (IQR), median (range))*: 44.6 ± 10.1 • *Weight (mean ± SD, median (IQR), median (range))*: 76.4 ± 17.4 • *BMI (mean ± SD, median (IQR), median (range))*: 28.5 ± 6.1 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 64 • *History of PONV/motion sickness (%)*: 37/24 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane/isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 132 • *Use of perioperative opioids (if yes, which?)*: morphine equivalent • *Type of surgery*: elective open abdominal surgery Rolapitant (20 mg group)

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Gan 2011 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 102
- *Received treatment (n)*: 102
- *Analysed (n)*: 102
- *Age (mean ± SD, median (IQR), median (range))*: 47.1 ± 12.6
- *Weight (mean ± SD, median (IQR), median (range))*: 75.6 ± 16.4
- *BMI (mean ± SD, median (IQR), median (range))*: 28.1 ± 5.8
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 73
- *History of PONV/motion sickness (%)*: 32/32
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 132
- *Use of perioperative opioids (if yes, which?)*: morphine equivalent
- *Type of surgery*: elective open abdominal surgery

Rolapitant (70 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 103
- *Received treatment (n)*: 103
- *Analysed (n)*: 103
- *Age (mean ± SD, median (IQR), median (range))*: 44.1 ± 10.1
- *Weight (mean ± SD, median (IQR), median (range))*: 79.1 ± 17.3
- *BMI (mean ± SD, median (IQR), median (range))*: 29.6 ± 5.9
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 65
- *History of PONV/motion sickness (%)*: 37/30
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 126
- *Use of perioperative opioids (if yes, which?)*: morphine equivalent
- *Type of surgery*: elective open abdominal surgery

Rolapitant (200 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 104
- *Received treatment (n)*: 104
- *Analysed (n)*: 104
- *Age (mean ± SD, median (IQR), median (range))*: 47.4 ± 10.9
- *Weight (mean ± SD, median (IQR), median (range))*: 77.7 ± 15.4
- *BMI (mean ± SD, median (IQR), median (range))*: 29.2 ± 5.3
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 70
- *History of PONV/motion sickness (%)*: 38/33
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: morphine equivalent

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Gan 2011 *(Continued)*

- *Type of surgery*: elective open abdominal surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 104
- *Received treatment (n)*: 104
- *Analysed (n)*: 104
- *Age (mean ± SD, median (IQR), median (range))*: 47.9 ± 12.6
- *Weight (mean ± SD, median (IQR), median (range))*: 79.3 ± 16.2
- *BMI (mean ± SD, median (IQR), median (range))*: 29.4 ± 5.6
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 62
- *History of PONV/motion sickness (%)*: 34/27
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138
- *Use of perioperative opioids (if yes, which?:* morphine equivalent
- *Type of surgery*: elective open abdominal surgery

Included criteria: adult women with ASA I to III scheduled to undergo elective open abdominal surgery under general anaesthesia who were expected to be hospitalized for at least 24 hours and to require postoperative IV patient-controlled analgesia (PCA)

Excluded criteria: clinically significant or unstable cardiac, respiratory, hepatic, or renal disease; allergies to study medications; retching/vomiting or moderate to severe nausea 24 hours before anaesthesia; chronic nausea or vomiting; antiemetic treatment within previous 5 days; need for opioid adjuncts during study period; body mass index > 40; any condition requiring daily opioid use within 7 days before surgery; expected need for placement of a nasogastric tube for gastric suction (a nasogastric tube could be inserted at end of surgery for decompression only)

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

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Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: placebo no later than 30 minutes before induction of anaesthesia, placebo immediately before induction of anaesthesia
- *Route of administration*: IV, PO
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV or up to 8 mg PO, additional rescue therapy at investigator's discretion

Rolapitant (5 mg group)

- *Dose*: 5 mg
- *Time point of administration*: rolapitant no later than 30 minutes before induction of anaesthesia, placebo immediately before induction of anaesthesia
- *Route of administration*: rolapitant PO, placebo IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV or up to 8 mg PO, additional rescue therapy at investigator's discretion

Rolapitant (20 mg group)

- *Dose*: 20 mg

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Gan 2011 *(Continued)*

- *Time point of administration*: rolapitant no later than 30 minutes before induction of anaesthesia, placebo immediately before induction of anaesthesia
- *Route of administration*: rolapitant PO, placebo IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV or up to 8 mg PO, additional rescue therapy at investigator's discretion

Rolapitant (70 mg group)

- *Dose*: 70 mg
- *Time point of administration*: rolapitant no later than 30 minutes before induction of anaesthesia, placebo immediately before induction of anaesthesia
- *Route of administration*: rolapitant PO, placebo IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV or up to 8 mg PO, additional rescue therapy at investigator's discretion

Rolapitant (200 mg group)

- *Dose*: 200 mg
- *Time point of administration*: rolapitant no later than 30 minutes before induction of anaesthesia, placebo immediately before induction of anaesthesia
- *Route of administration*: rolapitant PO, placebo IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV or up to 8 mg PO, additional rescue therapy at investigator's discretion

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: ondansetron immediately before induction of anaesthesia, placebo no later than 30 minutes before induction of anesthesia
- *Route of administration*: rolapitant PO, placebo IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV or up to 8 mg PO, additional rescue therapy at investigator's discretion

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 0 to 30 to 60 days' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** study was funded by Schering Plough, Inc. (now acquired by Merck, Inc.) **Country:** USA, Canada **Setting:** inpatient, multi-centre (45 in USA and Canada, 37 of these enrolled patients) **Author's name:** Tong J. Gan **Institution:** Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina, USA **Email:** tjgan@duke.edu

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Gan 2011 *(Continued)*

Address: Department of Anesthesiology, Duke University Medical Center, CB 3094, Durham, NC 27710, USA

Language: English

Duration of study: NA

Trial registry number: NCT00539721

Study's primary outcome: primary endpoint was response rate of subjects who did not experience any emetic episodes (regardless of rescue medication use) for 0 to 24 hours

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed before surgery according to a computer-generated randomization schedule"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...of PONV or motion sickness. Blinding was ensured with matching placebo capsules. Intravenous ondansetron (2 mL) and saline placebo (2 mL) were prepared by the pharmacists in a blinded 3-mL syringe. Oral rolapitant or placebo..."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on outcome assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "six hundred nineteen subjects were randomized from 37 centers; of these, 532 subjects completed the trial through 30- to 60-day follow-up (Fig. 1). Of the 87 patients who did not complete the study, 30 were lost to follow-up, 26 withdrew for reasons unrelated to study medication, 12 discontinued the study because of protocol ineligibility, 11 were discontinued because of non-compliance with the protocol, 4 were discontinued because of administrative reasons, 3 were discontinued because of AEs, and 1 was discontinued because of incisional pain" Judgement comment: rate of missing outcome data > 15%. Three participants discontinued due to AEs
Selective reporting (reporting bias)	Low risk	Judgement comment: NCT00539721 (prospective registration). The prospectively registered primary outcome was reported in the pre-specified way in the final study report
Other bias	Low risk	Quote: "there were no differences in the distribution of the discontinued patients among the groups. Demographic data and patient characteristics were no different among groups (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

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Gan 2017

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Amisulpride • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 345 • *Received treatment (n)*: 345 • *Analysed (n)*: 315 • *Age (mean ± SD, median (IQR), median (range))*: 52 (19 to 88) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27.5 (16.2 to 62.1) • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 74.9 • *Non-smoker (%)*: 82.9 • *History of PONV/motion sickness (%)*: 41.6 • *Type of general anaesthesia*: general anaesthesia at discretion of investigator (no TIVA) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 127.0 • *Use of perioperative opioids (if yes, which?)*: expected use of postoperative opioid use • *Type of surgery*: abdominal, breast, axillary, endoscopic, head, neck, integumentary, musculoskeletal, superficial procedures Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 344 • *Received treatment (n)*: 344 • *Analysed (n)*: 311 • *Age (mean ± SD, median (IQR), median (range))*: 53 (18 to 86) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27.8 (16.6 to 66.2) • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 77.5 • *Non-smoker (%)*: 84.2 • *History of PONV/motion sickness (%)*: 36.3 • *Type of general anaesthesia*: general anaesthesia at discretion of investigator (no TIVA) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 133.4 • *Use of perioperative opioids (if yes, which?)*: expected use of postoperative opioid use • *Type of surgery*: abdominal, breast, axillary, endoscopic, head, neck, integumentary, musculoskeletal, superficial procedures **Included criteria:** 18 years of age or older; had given written, informed consent; had at least 2 of the 4 Apfel risk factors for PONV (history of PONV or motion sickness, habitual non-smoking status, female sex, and expectation of receiving postoperative opioids for analgesia); scheduled to undergo any elective surgery during general anaesthesia; expected to last at least 1 hour from induction of anaesthesia to wound closure; requiring overnight hospitalization **Excluded criteria:** scheduled for outpatient/ambulatory, intrathoracic, transplant, or central nervous system surgery; expected to remain ventilated or to need a nasogastric or orogastric tube in situ for

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Gan 2017 *(Continued)*

	a period after surgery; pre-existing vestibular disorder or history of dizziness or preexisting nausea or vomiting in the 24 hours before surgery; being treated with regular antiemetic therapy including systemic corticosteroids **Pretreatment:** baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Amisulpride • *Dose*: 5 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 45.1% (choice at investigator's discretion) Placebo • *Dose*: identical placebo • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 56.9% (choice at investigator's discretion)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 7 days)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 7 days)* • Outcome type: dichotomous outcome *Mortality (0 to 7 days)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 7 days)* • Outcome type: dichotomous outcome *Headache (0 to 7 days)* • Outcome type: dichotomous outcome *Constipation (0 to 7 days)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 7 days)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 0 to 7 days' observation)*

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Gan 2017 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** supported by Acacia Pharma Ltd, Cambridge, United Kingdom **Country:** France, Germany, United States **Setting:** inpatient, multi-centre (4 sites in France, 6 in Germany, 9 in the USA) **Author's name:** Tong J. Gan **Institution:** Department of Anesthesiology, Stony Brook University Medical Center, Stony Brook, New York, USA **Email:** tong.gan@stonybrookmedicine.edu **Address:** Department of Anesthesiology, Stony Brook University, HSC Level 4, Rm 060, Stony Brook, New York 11794, USA **Language:** English **Duration of study:** July 2013 to January 2014 **Trial registry number:** NCT01991821, NCT01991860 **Study's primary outcome:** primary endpoint was complete response, defined as no vomiting/retching and no use of antiemetic rescue medication in the 24 hour postoperative period
Notes	Two essentially identical studies (EU, USA): pooled results were used for this systematic review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated on a 1:1 basis to receive a single iv dose of either 5 mg amisulpride or an identical placebo via a web-based randomization service, which automatically provided the next patient number from a predetermined randomization list created by an independent statistician. The list was stratified according to whether the patient had two, three, or four risk factors"
Allocation concealment (selection bias)	Low risk	Quote: "each subject number provided by the system matched a vial of study drug held at the study site, the identity of which was blinded to everyone except the contract manufacturer responsible for clinical packaging"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...the identity of which was blinded to everyone except the contract manufacturer responsible for clinical packaging. The study drug was given by slow iv administration during 1 to 2 min at induction of anesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "each subject number provided by the system matched a vial of study drug held at the study site, the identity of which was blinded to everyone except the contract manufacturer responsible for clinical packaging..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "in total, 689 subjects were randomized in the two studies and received active or placebo study treatment, 342 in the United States and 347 in Europe, of whom 626 were evaluable per protocol. Of the 63 subjects excluded from the pp population, all but one had either inadvertently received an antiemetic before, during, or after their operation, but before any event of PONV, or had a very short operation of 20 min or less"

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Gan 2017 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01991821, NCT01991860 (retrospective registration)
Other bias	Unclear risk	Quote: "the study arms were well balanced in terms of risk of PONV as estimated by prospectively ascertained risk factors" Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Gandhi 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Promethazine (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 35.92 ± 10.98 • *Weight (mean ± SD, median (IQR), median (range))*: 51.78 ± 12.61 • *BMI (mean ± SD, median (IQR), median (range))*: 21.76 ± 4.89 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 96 • *Non-smoker (%)*: 98 • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 145.30 • *Use of perioperative opioids (if yes, which?)*: pethidine 1 mg/kg before surgery • *Type of surgery*: major gynaecological surgery, laparoscopic surgery, middle ear surgery Promethazine + ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 35.44 ± 9.55 • *Weight (mean ± SD, median (IQR), median (range))*: 53.72 ± 10.48 • *BMI (mean ± SD, median (IQR), median (range))*: 22.91 ± 4.48 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 98 • *Non-smoker (%)*: 98 • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O)

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Gandhi 2009 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 149.70
- *Use of perioperative opioids (if yes, which?)*: pethidine 1 mg/kg before surgery
- *Type of surgery*: major gynaecological surgery, laparoscopic surgery, middle ear surgery

Promethazine + dexamethasone (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 37.32 ± 10.67
- *Weight (mean ± SD, median (IQR), median (range))*: 54.76 ± 11.00
- *BMI (mean ± SD, median (IQR), median (range))*: 23.73 ± 4.26
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 98
- *Non-smoker (%)*: 98
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 160.90
- *Use of perioperative opioids (if yes, which?)*: pethidine 1 mg/kg before surgery
- *Type of surgery*: major gynaecological surgery, laparoscopic surgery, middle ear surgery

Included criteria: ASA I and II; adult patients of either gender; between 18 and 60 years of age; undergoing elective gynaecological, laparoscopic, or middle ear surgery under general anaesthesia

Excluded criteria: history of motion sickness, or gastrointestinal, hepatic, or renal disease, or cardiovascular, metabolic, or endocrine dysfunction; any antiemetic medication 24 hours before surgery; preoperative nausea or vomiting; pregnancy or lactation; scheduled to have a nasogastric tube in situ after surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness): no; (history of PONV, perioperative opioids): unclear

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Interventions

Intervention characteristics

Promethazine (group P)

- *Dose*: promethazine 0.5 mg/kg, placebo 5 mL normal saline
- *Time point of administration*: promethazine 5 minutes before surgery, placebo immediately after induction of anaesthesia
- *Route of administration*: IM, IV
- *Rescue antiemetics (if yes, which?)*: 10 mg IV metoclopramide

Promethazine + ondansetron (group O)

- *Dose*: promethazine 0.5 mg/kg, ondansetron 4 mg
- *Time point of administration*: promethazine 5 minutes before surgery, ondansetron immediately after induction of anaesthesia
- *Route of administration*: IM, IV
- *Rescue antiemetics (if yes, which?)*: 10 mg IV metoclopramide

Promethazine + dexamethasone (group D)

- *Dose*: promethazine 0.5 mg/kg, dexamethasone 8 mg
- *Time point of administration*: promethazine 5 minutes before surgery, dexamethasone immediately after induction of anaesthesia

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Gandhi 2009 *(Continued)*

	• *Route of administration*: IM, IV • *Rescue antiemetics (if yes, which?)*: 10 mg IV metoclopramide
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** NA **Author's name:** Ranju Gandhi **Institution:** Department of Anaesthesiology and intensive care, Lady Hardinge Medical College, New Delhi, India **Email:** icu_era@.yahoo.co.in **Address:** Department of Anaesthesiology and intensive care, Lady Hardinge Medical College, New Delhi, India 110001 **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned to three groups of 50 patients each" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Low risk	Quote: "personnel not involved in the study prepared identical syringes containing the study drugs"

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Gandhi 2009 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all observations were made by an observer who was unaware of the treatment regimen each patient had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no significant difference between the three groups with respect to demographic data (mean age, height, weight and BMI), the distribution of pre-operative risk factors (gender, type of surgery, personal habits, phase of menstrual cycle and previous exposure to anaesthesia) and mean duration of surgery and anaesthesia (Table 1, 2 and 3)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness): no; (history of PONV, perioperative opioids): unclear

Ganem 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 27 • *Received treatment (n)*: NA • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: TIVA (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 54 • *Use of perioperative opioids (if yes, which?)*: sufentanil for induction • *Type of surgery*: diagnostic or surgical gynaecological laparoscopy Alizapride • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Ganem 2001 *(Continued)*

- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 32 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: TIVA (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 53
- *Use of perioperative opioids (if yes, which?)*: sufentanil for induction
- *Type of surgery*: diagnostic or surgical gynaecological laparoscopy

Included criteria: female, 21 to 50 years of age, ASA I or II, BMI < 30, submitted to diagnostic or surgical gynaecological laparoscopy

Excluded criteria: current or previous gastric complaints, history of nausea and vomiting with previous anaesthesia, movement kinetosis, psychiatric disease, menstruating, alcohol and drug abusers

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: Intravenous ondansetron (4 mg) Alizapride • *Dose*: 50 mg • *Time point of administration*: immediately before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: Intravenous ondansetron (4 mg)
Outcomes	*Vomiting (0 to 1 hour, PACU)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Brazil **Setting:** inpatient **Author's name:** Eliana Marisa Ganem **Institution:** Departamento de Anestesiologiada FMB - UNESP **Email:** NA **Address:** Dept° de Anestesiologia da FMB - UNESP, Distrito de Rubião Júnior, 18618-970 - Botucatu, SP **Language:** English

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Ganem 2001 *(Continued)*

	Duration of study: NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly distributed in two groups according to the antiemetic drug, that is, group 1, ondansetron (4 mg) and group 2 alizapride (50 mg)" Judgement comment: no information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "groups were homogeneous as to age, weight, height and surgery and anesthesia duration (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Ganem 2002

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Ganem 2002 *(Continued)*

- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol, sufentanil), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, tramadol as rescue analgesic
- *Type of surgery*: gynaecological laparoscopy

Dexamethasone (group 2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 30 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol, sufentanil), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 87
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, tramadol as rescue analgesic
- *Type of surgery*: gynaecological laparoscopy

Included criteria: women, 18 to 46 years of age, ASA I or II, body mass index < 30, undergoing diagnostic or surgical gynaecological laparoscopy

Excluded criteria: current or previous gastric complaints, history of nausea and vomiting with previous anaesthesia, motion sickness, psychiatric disease, menstruating, alcohol or drug users

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, duration of anaesthesia): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo (group 1) • *Dose*: saline • *Time point of administration*: immediately before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Dexamethasone (group 2) • *Dose*: 8 mg • *Time point of administration*: immediately before anaesthetic induction

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Ganem 2002 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*Vomiting (PACU, 0 to 1 hour)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Brazil **Setting:** NA **Author's name:** Eliana Marisa Ganem **Institution:** Departamento de Anestesiologia da Faculdade de Medicina de Botucatu (FMB - UNESP), Botucatu, SP **Email:** NA **Address:** Deptº de Anestesiologia da FMB - UNESP, Distrito de Rubião Júnior, 18618-970 Botucatu, SP **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly distributed in two groups according to the antiemetic scheme" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Ganem 2002 *(Continued)*

Other bias	Unclear risk	Quote: "...for nausea and vomiting. Both groups were homogeneous in age, weight and height, as well as anesthesia and surgery duration (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, duration of anaesthesia): no; (non-smoker, perioperative opioids): unclear

Gauchan 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 33.42 ± 6.87 • *Weight (mean ± SD, median (IQR), median (range))*: 53.26 ± 7.12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 45/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 76 • *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl for induction • *Type of surgery*: laparoscopic cholecystectomy Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 6.49 • *Weight (mean ± SD, median (IQR), median (range))*: 49.64 ± 11.17 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 45/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 67 • *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl for induction

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Gauchan 2014 *(Continued)*

- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I, female, 20 to 45 years of age, weighing 40 kg to 65 kg, undergoing elective laparoscopic cholecystectomy

Excluded criteria: history of drug allergy, gastrointestinal disease, smoking, motion sickness, and/ or PONV; pregnant or menstruating; had taken antiemetic medication within last 24 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 100 µg/kg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 40 µg/kg Granisetron • *Dose*: 40 µg/kg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 40 µg/kg
Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 12 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Nepal **Setting:** inpatient, single-centre **Author's name:** Sabin Gauchan **Institution:** Department of Anesthesia, Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu, Nepal **Email:** sabingauchan@gmail.com **Address:** Department of Anesthesia, Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu, Nepal, : +977-9851058474 **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA

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Gauchan 2014 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...were randomly divided" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind study" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all patients were observed postoperatively by doctors who were unaware of the study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "total 90 patients were included in the study" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "there was no significant difference in age, weight and duration of surgery in two groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Gautam 2008

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 48 • *Age (mean ± SD, median (IQR), median (range))*: 38.21 ± 9.22 • *Weight (mean ± SD, median (IQR), median (range))*: 59.92 ± 7.098

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Gautam 2008 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 91.67
- *Non-smoker (%)*: 58.33
- *History of PONV/motion sickness (%)*: 2.08/8.33
- *Type of general anaesthesia*: balanced anaesthesia (halothane, meperidine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95.54
- *Use of perioperative opioids (if yes, which?)*: 60.23 mg meperidine intraoperatively, 189.58 mg meperidine postoperatively
- *Type of surgery*: laparoscopic cholecystectomy

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 47
- *Age (mean ± SD, median (IQR), median (range))*: 39.21 ± 8.56
- *Weight (mean ± SD, median (IQR), median (range))*: 61.26 ± 5.70
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 89.36
- *Non-smoker (%)*: 55.32
- *History of PONV/motion sickness (%)*: 6.38/10.64
- *Type of general anaesthesia*: balanced anaesthesia (halothane, meperidine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 97.89
- *Use of perioperative opioids (if yes, which?)*: 61.17 mg meperidine intraoperatively, 178.72 mg meperidine postoperatively
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 47
- *Age (mean ± SD, median (IQR), median (range))*: 38.89 ± 11.12
- *Weight (mean ± SD, median (IQR), median (range))*: 58.68 ± 6.74
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 91.49
- *Non-smoker (%)*: 55.32
- *History of PONV/motion sickness (%)*: 2.13/4.26
- *Type of general anaesthesia*: balanced anaesthesia (halothane, meperidine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90.19
- *Use of perioperative opioids (if yes, which?)*: 59.53 mg meperidine intraoperatively, 178.19 mg meperidine postoperatively
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, between 23 and 65 years of age, undergoing general anaesthesia for elective laparoscopic cholecystectomy

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Gautam 2008 *(Continued)*

Excluded criteria: nausea and/or vomiting, had taken any antiemetic medication within 48 hours before surgery, history of allergy to any of the study drugs. Patients who received any investigational drug within 30 days before surgery and those who required conversion from laparoscopic technique to open approach were excluded retrospectively

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 29.2% (metoclopramide 10 mg) Dexamethasone • *Dose*: 8 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 31.9% (metoclopramide 10 mg) Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8.5% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (overall, during hospital stay)* • Outcome type: dichotomous outcome *Sedation/drowsiness (overall, during hospital stay)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects

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Gautam 2008 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** Nepal **Setting:** inpatient, single-centre **Author's name:** Binod Gautam **Institution:** Department of Anaesthesiology and Intensive Care, Kathmandu Medical College, Sinamangal, Nepal **Email:** gautambinod2060@hotmail.com **Address:** Dept. of Anaesthesiology and Intensive Care, Kathmandu Medical College, Sinamangal, PO Box 23760, Nepal **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response in 24 hours (no episode of PONV)
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization list was prepared before anaesthesia using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "identical syringes containing each treatment regimen were diluted with normal saline to make a volume of 5 ml by a personnel not involved in the study. Drug preparations were administered IV just before induction of anaesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all observations were recorded by direct questioning (with only two possible answers of yes/no) by trained on-duty doctors blinded to the group assignment, or based on spontaneous complaint by the patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "out of 150 patients enrolled, eight patients required conversion to open cholecystectomy because of surgical reasons and were excluded from the study. Data obtained from the remaining 142 patients were analyzed for interpretation"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "patient characteristics and the factors related to surgery and anaesthesia did not differ between the groups (Table 1). Time to first meperidine demand, VAS pain scores and meperidine consumption during 24 hour period were similar among all groups (Table 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

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Gautam 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Methylprednisolone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 44.1 ± 10.9 • *Weight (mean ± SD, median (IQR), median (range))*: 56.2 ± 10.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 36.67 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.9 • *Use of perioperative opioids (if yes, which?)*: 165.7 mg fentanyl intraoperatively, 538.9 mg postoperatively via PCA • *Type of surgery*: laparoscopic cholecystectomy Placebo + etoricoxib • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 41.7 ± 8.4 • *Weight (mean ± SD, median (IQR), median (range))*: 56.2 ± 9.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 33.3 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 119.3 • *Use of perioperative opioids (if yes, which?)*: 157.6 mg fentanyl intraoperatively, 496.7 mg postoperatively via PCA • *Type of surgery*: laparoscopic cholecystectomy Methylprednisolone + etoricoxib • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30

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Gautam 2014 *(Continued)*

- *Received treatment (n)*: 30
- *Analysed (n)*: 28
- *Age (mean ± SD, median (IQR), median (range))*: 45.8 ± 9.7
- *Weight (mean ± SD, median (IQR), median (range))*: 55.5 ± 9.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 30
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 123.1
- *Use of perioperative opioids (if yes, which?)*: 166.6 mg fentanyl intraoperatively, 328.2 mg postoperatively via PCA
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 28
- *Age (mean ± SD, median (IQR), median (range))*: 44.5 ± 8.8
- *Weight (mean ± SD, median (IQR), median (range))*: 55.7 ± 9.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 43.33
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 119.1
- *Use of perioperative opioids (if yes, which?)*: 167.6 mg fentanyl intraoperatively, 776.4 mg postoperatively via PCA
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: adults, 20 to 65 years of age, either sex, ASA I or II, scheduled for laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: impaired kidney or liver functions, history of drug or alcohol abuse, history of chronic pain or daily intake of analgesics, uncontrolled medical disease (diabetes mellitus and hypertension), history of intake of NSAIDs within 24 hours before surgery, inability to operate a patient-controlled analgesia device

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics**

Methylprednisolone

- *Dose*: 125 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Placebo + etoricoxib

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Gautam 2014 *(Continued)*

- *Dose*: placebo tablet, 120 mg
- *Time point of administration*: 1 hour before induction
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Methylprednisolone + etoricoxib

- *Dose*: methylprednisolone 125 mg, etoricoxib 120 mg
- *Time point of administration*: 1 hour before induction, before induction of anaesthesia
- *Route of administration*: PO, IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Placebo

- *Dose*: placebo tablet, sterile water
- *Time point of administration*: 1 hour before induction, before induction of anaesthesia
- *Route of administration*: PO, IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Outcomes

PONV (probably 0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (probably 0 to 24 hours)

- Outcome type: dichotomous outcome

Identification

Sponsorship source: NA

Country: India

Setting: NA

Author's name: Sujeet Gautam

Institution: Department of Anesthesiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences

Email: docsksg@gmail.com

Address: Department of Anaesthesiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Road, Lucknow 226 014, India

Duration of study: October 2012 to September 2013

Language: English

Study's primary outcome: severity of postoperative pain both at rest (static pain) and while coughing (dynamic pain), apostoperative fentanyl consumption

Trial registry number: NA

Notes

Groups with methylprednisolone ± etoricoxib were pooled as experimental group for analysis. Groups with placebo ± etoricoxib were pooled as control group for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients meeting the inclusion criteria during the pre-anesthetic checkup were randomly assigned into four equal groups of 30 each with the

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Gautam 2014 *(Continued)*

		help of a computer-generated table of random numbers. A random allocation sequence concealed in 120 consecutively numbered, sealed envelopes..."
Allocation concealment (selection bias)	Unclear risk	Quote: "random allocation sequence concealed in 120 consecutively numbered, sealed envelopes, determining group distribution, was computer-generated by a project nurse not otherwise involved in the trial" Judgement comment: not stated' "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all study personnel and participants were blind to the group allocation for the duration of the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all of these measures were assessed by an anesthesia registrar blind to group allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the reasons for patients not being randomized were refusal to participate in the study (18 patients), chronic analgesic consumption (2 patients) and an inability to operate the patient-controlled analgesia device (3 patients). Eight patients were excluded from the study following the initial randomization process and were therefore not subjected to further analysis (7 underwent a conversion to open cholecystectomy and 1 needed re-exploration on account of postoperative bleeding)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "postoperative pain (static and dynamic) and fentanyl consumption were significantly reduced by methylprednisolone, etoricoxib and the combination groups as compared with the placebo ($P < 0.05$) (Table 2). The methylprednisolone + etoricoxib combination caused a significant reduction in postoperative pain and fentanyl consumption as compared to methylprednisolone or etoricoxib alone ($P < 0.05$) (Table 2)" Quote: "there were no differences amongst the groups with regard to age, sex, weight distribution, the duration of anesthesia, the duration of surgery or the level of intra-operative fentanyl consumption ($P > 0.05$) (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Gesztesi 2000-1

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping: 4** groups, dose-finding study, monoprophylaxis
Participants	**Baseline characteristics** Placebo (to 100 mg) • *Assessed for eligibility (n)*: -

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Gesztesi 2000-1 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 21
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 97
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 4 µg/kg fentanyl at induction, 50 mg morphine intraoperatively and postoperatively via PCA
- *Type of surgery*: total abdominal hysterectomy

CP-122,721 (100 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 21
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 4 µg/kg fentanyl at induction, 53 mg morphine intraoperatively and postoperatively via PCA
- *Type of surgery*: total abdominal hysterectomy

Placebo (to 200 mg)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 18
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 81

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Gesztesi 2000-1 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 4 µg/kg fentanyl at induction, 47 mg morphine intraoperatively and postoperatively via PCA
- *Type of surgery*: total abdominal hysterectomy

CP-122,721 (200 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 78 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 108
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 4 µg/kg fentanyl at induction, 45 mg morphine intraoperatively and postoperatively via PCA
- *Type of surgery*: total abdominal hysterectomy

Included criteria: healthy, ASA I or II, nonpregnant women presenting for total abdominal hysterectomy procedures

Excluded criteria: had received any antiemetic medications within 24 hours before induction of anaesthesia, had received an investigational drug within the past 30 days, had vomited or retched within the preceding 24 hours, more than 60% above their ideal body weight

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo (to 100 mg) • *Dose*: placebo • *Time point of administration*: 60 to 90 minutes before induction of general anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: droperidol CP-122,721 (100 mg group) • *Dose*: 100 mg • *Time point of administration*: 60 to 90 minutes before induction of general anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: droperidol Placebo (to 200 mg) • *Dose*: placebo • *Time point of administration*: 60 to 90 minutes before induction of general anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: droperidol CP-122,721 (200 mg group)

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Gesztesi 2000-1 *(Continued)*

	• *Dose*: 200 mg • *Time point of administration*: 60 to 90 minutes before induction of general anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: droperidol
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 72 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by Pfizer Central Research, Groton, Connecticut, USA **Country:** USA **Setting:** inpatient, multi-centre **Author's name:** Paul F. White **Institution:** Departments of Anaesthesiology, Departments of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, USA **Email:** pwhite@mednet.swmed.edu **Address:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5363 Harry Hines Boulevard, F 2.208, Dallas, Texas, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of postoperative emesis **Trial registry number:** NA
Notes	Two studies: dose-ranging study (study I), interaction study (study II) Groups with same interventions pooled for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "in the interaction study, patients were randomly assigned to one of three treatment groups using a computer-generated random number table" Judgement comment: "low risk of bias" for the interaction study. Missing information for the dose-ranging study, but we assume similar performance
Allocation concealment (selection bias)	Unclear risk	Quote: "all study medications were prepared by the manufacturer (Pfizer, Inc., Groton, CT) in identical capsules" Quote: "the oral study drug was supplied by Pfizer Inc., in blinded containers, whereas the parenteral (intravenous) solution was prepared by a local pharmacist who was not otherwise involved in the conduct of the study" Judgement comment: insufficient information on allocation concealment

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Gesztesi 2000-1 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the patients, anesthesiologists, and observers were all blinded to the study medications being administered"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients, anesthesiologists, and observers were all blinded to the study medications being administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 277 patients enrolled in the two studies, 34 were withdrawn because of protocol violations (e.g., inadvertent administration of a drug with antiemetic properties during surgery), failure to receive the study medication at the appropriate time, or cancellation of the surgical procedure"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the treatment groups were comparable with respect to age, weight, height, history of PONV and motion sickness, day of menstrual cycle, duration of surgery, and PCA morphine usage during the first 72 h postoperatively (tables 1 and 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Gesztesi 2000-2

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 52 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 18/NA • *Type of general anaesthesia*: standardized general anaesthetic technique • *Duration of anaesthesia or surgery (in min; as mean or median)*: 162 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: total abdominal hysterectomy

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Gesztesi 2000-2 *(Continued)*

CP-122,721

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 52
- *Age (mean ± SD, median (IQR), median (range))*: 44 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 18/NA
- *Type of general anaesthesia*: standardized general anaesthetic technique
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 146
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: total abdominal hysterectomy

CP-122,721 + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 53
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 16
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 20/NA
- *Type of general anaesthesia*: standardized general anaesthetic technique
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 139
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: total abdominal hysterectomy

Included criteria: healthy, ASA I or II, non-pregnant women presenting for total abdominal hysterectomy procedures

Excluded criteria: had received any antiemetic medication within 24 hours before induction of anaesthesia, had received an investigational drug within the past 30 days, had vomited or retched within the preceding 24 hours, more than 60% above ideal body weight

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: ondansetron 15 to 30 minutes before end of surgical procedure, placebo 60 to 90 minutes before induction of anaesthesia
- *Route of administration*: ondansetron IV, placebo PO

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Gesztesi 2000-2 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: droperidol CP-122,721 • *Dose*: 200 mg • *Time point of administration*: CP-122,721 60 to 90 minutes before induction of anaesthesia, placebo 15 to 30 minutes before end of surgery • *Route of administration*: placebo: IV, CP-122,721: PO • *Rescue antiemetics (if yes, which?)*: droperidol CP-122,721 + ondansetron • *Dose*: CP-122,721 200 mg, ondansetron 4 mg • *Time point of administration*: CP-122,721 60 to 90 minutes before induction of anaesthesia, ondansetron 15 to 30 minutes before end of surgical procedure • *Route of administration*: ondansetron: IV, CP-122,721: PO • *Rescue antiemetics (if yes, which?)*: droperidol
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 72 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 72 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by Pfizer Central Research, Groton, Connecticut, USA **Country:** USA **Setting:** inpatient, multi-centre **Author's name:** Paul F. White **Institution:** Departments of Anaesthesiology, Departments of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, USA **Email:** pwhite@mednet.swmed.edu **Address:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5363 Harry Hines Boulevard, F 2.208, Dallas, Texas, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of postoperative emesis **Trial registry number:** NA
Notes	Two studies: dose-ranging study (study I), interaction study (study II)

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Gesztesi 2000-2 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "in the interaction study, patients were randomly assigned to one of three treatment groups using a computer-generated random number table" Judgement comment: "low risk of bias" for the interaction study. Missing information for the dose-ranging study, but we assume similar performance
Allocation concealment (selection bias)	Unclear risk	Quote: "all study medications were prepared by the manufacturer (Pfizer, Inc., Groton, CT) in identical capsules" Quote: "the oral study drug was supplied by Pfizer Inc., in blinded containers, whereas the parenteral (intravenous) solution was prepared by a local pharmacist who was not otherwise involved in the conduct of the study" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the patients, anesthesiologists, and observers were all blinded to the study medications being administered"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients, anesthesiologists, and observers were all blinded to the study medications being administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 277 patients enrolled in the two studies, 34 were withdrawn because of protocol violations (e.g., inadvertent administration of a drug with antiemetic properties during surgery), failure to receive the study medication at the appropriate time, or cancellation of the surgical procedure"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the treatment groups were comparable with respect to age, weight, height, history of PONV and motion sickness, day of menstrual cycle, duration of surgery, and PCA morphine usage during the first 72 h postoperatively (tables 1 and 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Ghosh 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Palonosetron • *Assessed for eligibility (n)*: -

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Ghosh 2011 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 36.33 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 57.47 ± 8.25
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 25/5/0/0
- *Gender (female in %)*: 90
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 59
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 1 µg/kg every 30 minutes, tramadol 100 mg IV
- *Type of surgery*: laparoscopic cholecystectomy

Palonosetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 35.03 ± 10.15
- *Weight (mean ± SD, median (IQR), median (range))*: 56.67 ± 9.81
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 25/5/0/0
- *Gender (female in %)*: 83
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 61.33
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 1 µg/kg every 30 minutes, tramadol 100 mg IV
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, 18 to 60 years of age, weighing 40 to 70 kg, scheduled for elective laparoscopic surgery under general anaesthesia

Excluded criteria: pregnant or menstruating, gastrointestinal or renal disease, received cancer chemotherapy within past 4 weeks, emetogenic radiotherapy within past 8 weeks, had experienced nausea or vomiting, had taken antiemetic medication within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics**

Palonosetron

- *Dose*: 0.075 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 0% (ondansetron 4 mg)

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Ghosh 2011 *(Continued)*

	Palonosetron + dexamethasone • *Dose*: palonosetron 0.075 mg, dexamethasone 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% (ondansetron 4 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** departmental funding only **Country:** India **Setting:** Inpatient, single-centre **Author's name:** Dr. Anirban Pal **Institution:** Department of Anesthesiology, Calcutta National Medical College (CNMC), Kolkata, India **Email:** pal.anirban1@gmail.com **Address:** 43/6/5 Jheel Road, Kolkata - 700 031, West Bengal, India **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the patients were randomly (computer-generated numbers inserted into opaque envelope) allocated to two groups P and PD"
Allocation concealment (selection bias)	Unclear risk	Quote: "the patients were randomly (computer-generated numbers inserted into opaque envelope) allocated to two groups P and PD..." Judgement comment: not stated if envelopes were sequentially numbered and sealed (SNOSE)

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Ghosh 2011 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "a consultant anesthesiologist who performed general anesthesia and used the study drug, was unaware of the type of study drug used and did not participate in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...paracetamol 1 g (100 ml). Patients were asked about nausea, vomiting, retching and any side-effects, at 2, 6, 24, 48 h by an investigator. The investigator and the patients were blinded to the study drug used. The severity of PONV..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Gijzels 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Haloperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 37.6 (18 to 55) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 9/16 patients received postoperative opioids • *Type of surgery*: NA Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Gijzels 2006 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 18
- *Age (mean ± SD, median (IQR), median (range))*: 39.7 (21 to 55)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 16/18 patients received postoperative opioids
- *Type of surgery*: NA

Included criteria: women undergoing surgery with general inhalational anaesthesia, between 18 and 55 years of age, at least 3 risk factors for PONV according to Apfel score, written informed consent

Excluded criteria: pregnancy or breastfeeding, liver insufficiency, extrapyramidal disorders, postoperative use of PCA with morphine derivatives

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Haloperidol • *Dose*: 1 mg • *Time point of administration*: 30 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 5 participants (dexamethasone or granisetron) Placebo • *Dose*: saline 0.9% • *Time point of administration*: 30 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 12 participants (dexamethasone or granisetron)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Netherlands

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Gijzels 2006 *(Continued)*

Setting: NA, single-centre

Author's name: M.J. Gijzels

Institution: Deventer Ziekenhuis, Deventer, Netherlands

Email: miekegijzels@hotmail.com

Address: NA

Duration of study: NA

Language: Dutch

Study's primary outcome: PONV

Trial registry number: NA

Notes	Study was reported as an interim analysis (for 39 patients out of 170)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomised". No other statement on random sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: in this interim analysis, 39 patients were included. In 5 cases, propofol/TIVA was given instead of inhalational anaesthesia. Results for these 5 women were not included
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a trial registry and no published study protocol
Other bias	High risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear; (perioperative opioids): yes

Glaser 2004

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis

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Glaser 2004 *(Continued)*

Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: NA • *Analysed (n)*: 99 • *Age (mean ± SD, median (IQR), median (range))*: 56.5 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 16 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 63.64 • *Non-smoker (%)*: 66.67 • *History of PONV/motion sickness (%)*: 14.14/7.07 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 77 • *Use of perioperative opioids (if yes, which?)*: 290 µg intraoperative fentanyl, 61 patients needed piritramide as rescue analgesic • *Type of surgery*: laparoscopic cholecystectomy Dixyrazine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: NA • *Analysed (n)*: 98 • *Age (mean ± SD, median (IQR), median (range))*: 54.5 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 70.41 • *Non-smoker (%)*: 69.39 • *History of PONV/motion sickness (%)*: 16.33/5.10 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 81 • *Use of perioperative opioids (if yes, which?)*: 294 µg intraoperative fentanyl, 75 patients needed piritramide as rescue analgesic • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** undergoing elective laparoscopic cholecystectomy, ASA I to III, 18 to 85 years old **Excluded criteria:** pregnancy, intolerance to neuroleptics, akinetic disorders, morbid obesity (twice the ideal body weight or > 130 kg), susceptibility to vomiting or retching even before surgery, ongoing antiemetic or psychotropic medication **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes
Interventions	**Intervention characteristics** Placebo

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Glaser 2004 *(Continued)*

- *Dose*: saline
- *Time point of administration*: near end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: tropisetron 2 mg

Dixyrazine

- *Dose*: 10 mg
- *Time point of administration*: near end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: tropisetron 2 mg

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Austria **Setting:** outpatient, single-centre **Author's name:** Christian Glaser **Institution:** Division of Anesthesiology and Intensive Care, Vienna City Hospital, Floridsdorf **Email:** NA **Address:** KH Floridsdorf, Division of Anesthesiology and Intensive Care, Hinaysgasse 1, A-1210 Vienna, Austria **Duration of study:** NA

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Glaser 2004 *(Continued)*

	Language: English **Study's primary outcome:** incidence of nausea **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the participants were randomly allocated to receive 100 ml of saline (0.9% NaCl) i.v. with or without dixyrazine 10 mg (Esucos 1, UCB, Brussels, Belgium) in accordance with a computer-generated randomization table using sealed envelopes"
Allocation concealment (selection bias)	Unclear risk	Quote: "...using sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the dixyrazine was diluted by a research nurse and handed over to an anesthesiologist not otherwise involved in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all postoperative episodes of nausea, retching and vomiting as well as adverse events occurring within the first 24 h were recorded every 15 min in the PACU and every 2-4 h in the ward by specially trained nurses who were unaware of which treatment each patient had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "excluded after the laparoscopic approach had to be switched to laparotomy because of surgical problems. One patient in the placebo group was excluded due to postoperative bleeding"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "besides a small difference in patients' height, which might have been caused by a 20% higher number of males in the placebo group (36 vs. 29), there were no significant differences in demographics and in data related to surgery and anesthesia (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Goksu 2002

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics**

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Goksu 2002 *(Continued)*

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 36.3 (20 to 50)
- *Weight (mean ± SD, median (IQR), median (range))*: 67.2 (52 to 85)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 167.5
- *Use of perioperative opioids (if yes, which?)*: did not use opioids that have emetic activity
- *Type of surgery*: mastoidectomy, tympanoplasty

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 38.3 (20 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: 69.8 (57 to 81)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 40
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 171.5
- *Use of perioperative opioids (if yes, which?)*: did not use opioids that have emetic activity
- *Type of surgery*: mastoidectomy, tympanoplasty

Granisetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 34.8 (20 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: 69.3 (45 to 93)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 45
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 166.5

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Goksu 2002 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: did not use opioids that have emetic activity
- *Type of surgery*: mastoidectomy, tympanoplasty

Included criteria: ASA I and II, 20 to 60 years of age, underwent surgery for chronic otitis media

Excluded criteria: history of motion sickness and antiemetic drug use in the last 24 hours, gastrointestinal disorder, menstruation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (non-smoker, history of PONV): unclear

Interventions	**Intervention characteristics** Granisetron • *Dose*: 3 mg • *Time point of administration*: preceding induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 1.25 mg • *Time point of administration*: preceding induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Granisetron + dexamethasone • *Dose*: granisetron 3 mg, dexamethasone 8 mg • *Time point of administration*: preceding induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Sitki Goksu **Institution:** University of Gaziantep, Turkey **Email:** sitkigoksu@turk.net **Address:** Department of Anesthesiology and Reanimation, Faculty of Medicine, University of Gaziantep, 27310 Gaziantep, Turkey **Language:** English

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Goksu 2002 *(Continued)*

	Duration of study: NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were divided into three equal groups" Judgement comment: no information on randomization method
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: stated "double-blind"; no further description provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no information on blinding of outcome assessors provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the demographic and operative data of the patients were similar and are summarized in Table 1" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (non-smoker, history of PONV): unclear

Goll 2001

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 out of 3 groups relevant, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: NA

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Goll 2001 *(Continued)*

- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 32/44/4/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 81
- *History of PONV/motion sickness (%)*: 14/23
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 349 µg fentanyl, 2.9 mg piritramide
- *Type of surgery*: gynaecological laparoscopy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 81
- *Received treatment (n)*: NA
- *Analysed (n)*: 81
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 31/46/4/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 70
- *History of PONV/motion sickness (%)*: 12/17
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 371 µg fentanyl, 2.4 mg piritramide
- *Type of surgery*: gynaecological laparoscopy

Included criteria: 19 to 70 years of age, ASA I to III, undergoing gynaecological laparoscopy with expected surgical duration exceeding 1 hour and anticipated overnight hospitalization

Excluded criteria: pregnancy, breastfeeding, menopausal status, obesity (> 150% normal weight), eating disorder, renal or liver malfunction, central nervous system injury, vertebrobasilar artery insufficiency, vestibular disease, cytostatic therapy, preoperative vomiting or antiemetic therapy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Control

- *Dose*: no treatment
- *Time point of administration*: -
- *Route of administration*: -
- *Rescue antiemetics (if yes, which?)*: 28.75% (ondansetron 4 mg)

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV

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Goll 2001 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: 18.52% (ondansetron 4 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** supported by National Institutes of Health Grant GM58273, the Bürgermeister Fond der Stadt Wien (Vienna, Austria), the Austrian National Bank Fund (Vienna, Austria), and the Joseph Drown Foundation (Los Angeles, California, USA) **Country:** Austria **Setting:** inpatient, NA **Author's name:** Daniel I. Sessler **Institution:** Institute and Department of Anesthesiology, University of Louisville, Kentucky, USA **Email:** sessler@louisville.edu **Address:** University of Louisville, Abell Administration Center, Room 217, 323 East Chestnut Street, Louisville, KY 40202-3866, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of nausea and/or vomiting over first 24 postoperative hours
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the computer-generated assignments..."
Allocation concealment (selection bias)	Unclear risk	Quote: "the computer-generated assignments were kept in sealed envelopes until used" Judgement comment: not stated; "sequentially numbered, opaque" envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the anesthesiologists were not blinded as to group assignment" Judgement comment: "patients were not informed of their group assignments"

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Goll 2001 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "however, patients, surgeons, and the nurses reporting PONV were blinded as to group assignments and intraoperative management"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "morphometric and demographic factors, hemodynamic responses, and anesthetic management, including intraoperative fluid regimen and duration of anesthesia, were comparable in all three groups (Table 1). Potential confounding factors, including smoking history, alcohol intake, history of motion sickness and PONV, were also comparable in the three treatment groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Gomez Hernandez 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 49.89 ± 10.58 • *Weight (mean ± SD, median (IQR), median (range))*: 67.94 ± 9.91 • *BMI (mean ± SD, median (IQR), median (range))*: 27.20 ± 4.29 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 94.3 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 140.71 • *Use of perioperative opioids (if yes, which?)*: 3 to 5 µg/kg fentanyl at induction, postoperative tramadol infusion • *Type of surgery*: radical mastectomy or breast conservative surgery with lymph node axillary dissection Dexamethasone • *Assessed for eligibility (n)*: -

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Gomez Hernandez 2010 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 50.11 ± 12.37
- *Weight (mean ± SD, median (IQR), median (range))*: 69.52 ± 13.63
- *BMI (mean ± SD, median (IQR), median (range))*: 28.20 ± 6.38
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 88.6
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 139.60
- *Use of perioperative opioids (if yes, which?)*: 3 to 5 µg/kg fentanyl at induction, postoperative tramadol infusion
- *Type of surgery*: radical mastectomy or breast conservative surgery with lymph node axillary dissection

Included criteria: undergoing mastectomy with axillary dissection

Excluded criteria: ASA III or IV; older than 80 years of age; pregnancy; active menstruation; treatment with steroids; severe diabetes mellitus (serum HbA1c > 8%); use of opioids, sedatives, or any kind of analgesics less than 1 week before mastectomy; history of alcohol or drug abuse, motion sickness, and/or PONV after any surgical procedure

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 60 minutes before skin incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg to 8 mg IV Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 60 minutes before skin incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg to 8 mg IV
Outcomes	*Mortality (0 to 7 days)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, observation period unclear)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this work was supported with financial resources of the participant institutions and in part by a grant of the Health Research Found of the Mexican Institute of Social Security (IMSS, Mexico, D.F.) **Country:** Mexico **Setting:** inpatient, single-centre

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Gomez Hernandez 2010 *(Continued)*

Author's name: Alejandro González-Ojeda

Institution: Research Unit in Clinical Epidemiology, Specialties Hospital, Western Medical Center, Mexican Institute of Social Security, Guadalajara, Jalisco, México

Email: avygail5@yahoo.com.mx

Address: Research Unit in Clinical Epidemiology, Specialties Hospital, Western Medical Center. Mexican Institute of Social Security, Avenida Belisario Domínguez 1000, Colonia Independencia, Postal code 44340, Guadalajara, Jalisco, México

Duration of study: June to August 2009

Language: English

Study's primary outcome: incidence of nausea and vomiting

Trial registry number: NCT01116713

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "...using an equal number of blinded envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01116713 (retrospective registration)
Other bias	High risk	Quote: "analgesics were required in more patients of the control group than in the dexamethasone group (21 vs. 10; p = 0.008). The mean dose of intravenous tramadol was lower in the study group (36.01 ± 12.62 vs. 55.74 ± 27.36; p = 0.03)" Quote: "...inclusion in the study. There were no significant differences between the two groups with regard to mean age, weight, height, BMI, neoadjuvant chemotherapy, type of surgical procedure, length of surgical procedures, length of anesthesia or operative bleeding (Table 1). Figure 1 shows the median..."

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Gomez Hernandez 2010 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Graczyk 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 157 • *Received treatment (n)*: 157 • *Analysed (n)*: 157 • *Age (mean ± SD, median (IQR), median (range))*: 32 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 57/43/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 26/NA • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 72 • *Use of perioperative opioids (if yes, which?)*: 167 µg intraoperative fentanyl • *Type of surgery*: outpatient laparoscopic surgery Dolasetron (12.5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 159 • *Received treatment (n)*: 159 • *Analysed (n)*: 159 • *Age (mean ± SD, median (IQR), median (range))*: 32 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 58/42/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 21/NA • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 66 • *Use of perioperative opioids (if yes, which?)*: 170 µg intraoperative fentanyl • *Type of surgery*: outpatient laparoscopic surgery Dolasetron (25 mg group)

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Graczyk 1997 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 157
- *Received treatment (n)*: 157
- *Analysed (n)*: 157
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 60/40/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 24/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66
- *Use of perioperative opioids (if yes, which?)*: 169 µg intraoperative fentanyl
- *Type of surgery*: outpatient laparoscopic surgery

Dolasetron (50 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 162
- *Received treatment (n)*: 162
- *Analysed (n)*: 162
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 63/37/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 24/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66
- *Use of perioperative opioids (if yes, which?)*: 169 µg intraoperative fentanyl
- *Type of surgery*: outpatient laparoscopic surgery

Included criteria: females scheduled for outpatient laparoscopic gynaecologic surgery with general anaesthesia, 18 years of age and older, not pregnant, ASA I or II

Excluded criteria: experienced preoperative nausea and/or vomiting within 24 hours of surgery or had taken any drug with antiemetic activity within that time; had taken an investigational drug within 30 days; significant cardiac conduction abnormalities; major organ dysfunction; exceeded ideal body weight by > 75%. No surgical procedures other than the primary gynaecologic procedure were allowed in patients who took part in the study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline 0.9% • *Time point of administration*: approximately 15 minutes before end of anaesthesia • *Route of administration*: IV

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Graczyk 1997 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: yes (not specified)

Dolasetron (12.5 mg group)

- *Dose*: 12.5 mg
- *Time point of administration*: approximately 15 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: yes (not specified)

Dolasetron (25 mg group)

- *Dose*: 25 mg
- *Time point of administration*: approximately 15 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: yes (not specified)

Dolasetron (50 mg group)

- *Dose*: 50 mg
- *Time point of administration*: approximately 15 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: yes (not specified)

Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, multi-centre (25) **Author's name:** Sarena G. Graczyk **Institution:** Anesthesiologists of Columbia, PA, Columbia, South Carolina, tMagee-Womens Hospital, Pittsburgh, Pennsylvania, USA **Email:** NA **Address:** Anaesthesiologists of Columbia, PA, Columbia, SC 29220, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response in 24 hours (no emetic episodes, no rescue medication)
Notes	None

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Graczyk 1997 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding method
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding method ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...intent-to-treat population), 612 (96%) had no major protocol deviations and were evaluable for efficacy"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a trial registry and no published study protocol available
Other bias	Unclear risk	Quote: "...and were evaluable for efficacy. No statistically significant differences among the treatment groups were observed at baseline for any patient characteristic (Table 1). Overall, the study population was 70% Caucasian and had a mean age of 32 yr. Approximately 25% of the patients had a previous history of PONV. The anesthesia procedures, including use of muscle relaxants, induction, and reversal drugs were statistically comparable among the treatment groups (Table 2). In addition, there were no differences among the groups in concomitant medications or use of postoperative analgesics that would be expected to influence efficacy or safety data. Adverse event data were summarized" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Grecu 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Grecu 2008 *(Continued)*

- *Randomized (n)*: 135
- *Received treatment (n)*: NA
- *Analysed (n)*: 133
- *Age (mean ± SD, median (IQR), median (range))*: 51.9 ± 13.9
- *Weight (mean ± SD, median (IQR), median (range))*: 78.7 ± 18.9
- *BMI (mean ± SD, median (IQR), median (range))*: 28.1 ± 6.2
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 70.4
- *Non-smoker (%)*: 76.3
- *History of PONV/motion sickness (%)*: 22.2/NA
- *Type of general anaesthesia*: general or combined epidural-general (3.7%) anaesthesia, propofol infusions not allowed (no other restrictions on anaesthesia, surgery, or postoperative care)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 156.0
- *Use of perioperative opioids (if yes, which?)*: 70.4% of patients with opioids in PACU
- *Type of surgery*: intra-abdominal/pelvic surgery, superficial/extremity surgery

Haloperidol + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 133
- *Received treatment (n)*: NA
- *Analysed (n)*: 130
- *Age (mean ± SD, median (IQR), median (range))*: 51.0 ± 13.5
- *Weight (mean ± SD, median (IQR), median (range))*: 80.1 ± 21.2
- *BMI (mean ± SD, median (IQR), median (range))*: 28.0 ± 6.6
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 69.2
- *Non-smoker (%)*: 82.3
- *History of PONV/motion sickness (%)*: 23.2/NA
- *Type of general anaesthesia*: general or combined epidural-general (3.7%) anaesthesia, propofol infusions not allowed (no other restrictions on anaesthesia, surgery, or postoperative care)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142.1
- *Use of perioperative opioids (if yes, which?)*: 67.7% of patients with opioids in PACU
- *Type of surgery*: intra-abdominal/pelvic surgery, superficial/extremity surgery

Included criteria: 18 years of age or older; ASA I to III; scheduled for general or combined epidural-general anaesthesia; unlike our first trial, those at high risk for PONV were included

Excluded criteria: adverse reactions to haloperidol or ondansetron, cardiac dysrhythmias, seizure disorder, Parkinson's disease, long-term treatment with dopamine antagonists or dexamethasone. At the request of the study sponsor, a screening electrocardiogram was obtained, and those with a QTc interval > 450 ms were excluded

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

Interventions	**Intervention characteristics**

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: approximately 1 hour before anticipated end of surgery
- *Route of administration*: IV

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Grecu 2008 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: postanaesthesia care unit nurses gave antiemetic rescue treatment for any episode of emesis or nausea score > 2

Haloperidol + ondansetron

- *Dose*: ondansetron 4 mg, haloperidol 1 mg
- *Time point of administration*: approximately 1 hour before anticipated end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: postanaesthesia care unit nurses gave antiemetic rescue treatment for any episode of emesis or nausea score > 2

Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *QT prolongation (PACU)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (PACU)* • Outcome type: dichotomous outcome *Sedation/drowsiness (PACU)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, PACU)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported, in part, by a grant from Glaxo Smith Kline Pharmaceuticals **Country:** USA **Setting:** inpatient and outpatient **Author's name:** Carl Rosow **Institution:** Department of Anesthesia and Critical Care, Massachusetts General Hospital, Boston, USA **Email:** crosow@partners.org **Address:** Department of Anesthesia and Critical Care, Massachusetts General Hospital, 55 Fruit St., Boston, MA 02114, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete responders
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "this randomized..."

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Grecu 2008 *(Continued)*

		Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "each patient received 4 mg of ondansetron plus the contents of a coded syringe containing either 1 mg haloperidol (5 mg/mL, Ben Venue Laboratories, Inc.) or 0.2 mL saline" Judgement comment: no information on blinding of personnel and whether or not coded syringes are identical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "two-hundred and sixty-eight subjects were enrolled, and 263 could be evaluated for efficacy" Judgement comment: no information on reasons for missing outcome data provided
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the groups for any demographic variable (Table 1). The difference in smokers (fewer for the combination) nearly reached significance (P 0.07)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

Green 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Aprepitant • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: 58 • *Analysed (n)*: 57 • *Age (mean ± SD, median (IQR), median (range))*: NA (21 to 65) • *Weight (mean ± SD, median (IQR), median (range))*: 84.3 ± 24.82 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 9/41/8/0 • *Gender (female in %)*: 91

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Green 2012 *(Continued)*

- *Non-smoker (%)*: 72
- *History of PONV/motion sickness (%)*: 55
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, desflurane, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 145.4
- *Use of perioperative opioids (if yes, which?)*: intraoperative and postoperative fentanyl, postoperative morphine
- *Type of surgery*: NA

Aprepitant + scopolamine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 61
- *Analysed (n)*: 58
- *Age (mean ± SD, median (IQR), median (range))*: NA (20 to 65)
- *Weight (mean ± SD, median (IQR), median (range))*: 78.7 ± 21.36
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 7/39/15/0
- *Gender (female in %)*: 88
- *Non-smoker (%)*: 66
- *History of PONV/motion sickness (%)*: 54
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, desflurane, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 150.4
- *Use of perioperative opioids (if yes, which?)*: intraoperative and postoperative fentanyl, postoperative morphine
- *Type of surgery*: NA

Included criteria: age at least 18 years, ASA I to III, elective high-risk PONV surgery expected to last at least 60 minutes requiring general anaesthesia, 2 or more Apfel 4-point risk factors for PONV

Excluded criteria: pregnant or breastfeeding patients, those treated with antiemetic medication within 24 hours of their procedure, history of vomiting from identified non-surgical causes, possession of an allergy or other contraindication to study medications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness): no; (duration of anaesthesia, perioperative opioids): unclear

Interventions	**Intervention characteristics** Aprepitant • *Dose*: 40 mg • *Time point of administration*: at least 1 hour before anaesthesia induction • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 37% (ondansetron 4 mg IV, ondansetron 4 mg oral, and metoclopramide 10 mg oral) Aprepitant + scopolamine • *Dose*: aprepitant 40 mg, scopolamine • *Time point of administration*: aprepitant at least 1 hour before anaesthesia induction; TDS remained for 24 hours from PACU arrival time • *Route of administration*: aprepitant PO, scopolamine transdermal • *Rescue antiemetics (if yes, which?)*: 40% (ondansetron 4 mg IV, ondansetron 4 mg oral, and metoclopramide 10 mg oral)
Outcomes	*Vomiting (0 to 24 hours)*

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Green 2012 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (home vomiting)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 24 hours)

- Outcome type: dichotomous outcome

Visual disturbances (e.g. blurred vision) (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** a small project grant from Merck Co. (M.S.G.): "The concept of the project was originated by M.S.G., DO, who served as the Principal Investigator. Merck Co. reviewed the protocol before issuing any funding. Funds received paid for medications administered, research personnel, pharmacy administrative fees, Western IRB fees, and statistical analysis. Merck Co. had no involvement in the analysis of the data or the preparation of the manuscript. The manuscript was reviewed and approved by Merck Co. before submission with no changes made. M.S.G. has received a small project grant from Merck Co. for the completion of this research project. P.G.'s husband has received a small Project grant from Merck Co. for the completion of this Research project" **Country:** USA **Setting:** inpatient and outpatient surgery, single-centre **Author's name:** M.S. Green **Institution:** Department of Anesthesiology, Drexel University College of Medicine, Hahnemann University Hospital, Philadelphia, PA, USA **Email:** michael.green@drexelmed.edu **Address:** Department of Anesthesiology and Perioperative Medicine, 245 North 15th Street, Mail Stop 310, Philadelphia, PA 19102, USA **Language:** English **Duration of study:** NA **Trial registry number:** NCT00717054, NCT00659737 **Study's primary outcome:** complete response (no emesis, no rescue therapy in 24 hours)
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated process randomly assigned subjects"
Allocation concealment (selection bias)	Unclear risk	Quote: "using a sealed envelope technique"

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Green 2012 *(Continued)*

		Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "depending on the assigned group, the transdermal patch was either a placebo or active medication. All clinicians were blinded to the assigned group"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "trained investigators blinded to the treatment group collected nausea and vomiting information at PACU admission and every 15 min for 1 h, at 2 h, and again at 24 h after operation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of 120 patients randomized, 119 received study medications and 115 completed the trial. Figure 1 illustrates the patient..." Quote: "prior participation in the study excluded one randomized subject before medication administration. The use of a neuraxial anaesthesia technique after medication administration excluded three patients. One patient had surgery postponed due to an upper respiratory tract infection after medication administration"
Selective reporting (reporting bias)	High risk	Judgement comment: NCT00717054 (prospective registration), NCT00659737 (prospective registration). The prospectively registered primary outcome (PONV within 0 to 24 hours) was changed in the published article (complete response in 0 to 24 hours)
Other bias	Unclear risk	Quote: "the two treatment groups did not differ with regard to patient characteristic variables, including number and type of risk factors, and clinical characteristics (Table 1). The type of surgical procedures did not differ between groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness): no; (duration of anaesthesia, perioperative opioids): unclear

Grimsehl 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Cyclizine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 37 • *Received treatment (n)*: NA • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 31 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Grimsehl 2002 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 27/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 26
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl, 7 patients with morphine IV and 16 patients with codeine PO as rescue analgesics
- *Type of surgery*: diagnostic laparoscopy or laparoscopic sterilisation

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 37
- *Received treatment (n)*: NA
- *Analysed (n)*: 37
- *Age (mean ± SD, median (IQR), median (range))*: 33 ± 5
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 16/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 25
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl, 9 patients with morphine IV and 19 patients with codeine PO as rescue analgesics
- *Type of surgery*: diagnostic laparoscopy or laparoscopic sterilisation

Included criteria: ASA I and II, written informed consent, scheduled to undergo diagnostic laparoscopy or laparoscopic sterilization

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Cyclizine • *Dose*: 50 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 11%, prochlorperazine 12.5 mg IM Ondansetron • *Dose*: 4 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 14%, prochlorperazine 12.5 mg IM
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to time to discharge)*

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Grimsehl 2002 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (discharge to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** UK **Setting:** outpatient, single-centre **Author's name:** K. Grimsehl **Institution:** Ninewells Hospital, Dundee DD1 9SY, UK **Email:** NA **Address:** Ninewells Hospital, Dundee DD1 9SY, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of nausea **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned by closed envelope technique" Judgement comment: insufficient information on random sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...mg diclofenac suppository was inserted. All assessments were carried out by a blinded investigator, who was unaware of the anti-emetic given. Anaesthetic time was recorded as..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "(Research Solutions Ltd, UK). Seventy-four patients were recruited to the study and peri-operative data were obtained for all subjects. Both groups were comparable for..." Judgement comment: at 24-hour follow-up: 12 patients were omitted (did not return questionnaire, required escape antiemetic, inadequate analgesia)

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Grimsehl 2002 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...obtained for all subjects. Both groups were comparable for patient characteristics, menstrual cycle, previous PONV and type of operation (Table 1). Anaesthetic times were similar in both groups, but mean (SD) time to..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Grond 1995

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 36 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 22.5/27.5 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 43 • *Use of perioperative opioids (if yes, which?)*: 0.13 mg fentanyl, 17 patients with tramadol • *Type of surgery*: dilation and curettage, diagnostic laparoscopy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 33 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 35/22.5

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Grond 1995 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 45
- *Use of perioperative opioids (if yes, which?)*: 0.13 mg fentanyl, 14 patients with tramadol
- *Type of surgery*: dilation and curettage, diagnostic laparoscopy

Included criteria: ASA I and II, 18 to 65 years of age, presenting for elective diagnostic procedures of the uterus or adnexa

Excluded criteria: pregnancy, drug dependence, psychiatric illness, intolerance to ondansetron or droperidol, pre-existing nausea, intake of antiemetics 24 hours before the study, as well as respiratory, cardiovascular, hepatic, renal, or metabolic disorders

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 8 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV; in case of failure, dimenhydrinate 150 mg IV Droperidol • *Dose*: 2.5 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV; in case of failure, dimenhydrinate 150 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Stefan Grond **Institution:** Department of Anesthesiology and Operative Intensive Care, University of Cologne, Cologne, Germany

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Grond 1995 *(Continued)*

Email: NA

Address: Klinik für Anaesthesiologie und Operative Intensivmedizin, Universität zu Köln, D-50924 Köln, Germany

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were prospectively randomized to receive either ondansetron or droperidol in a double-blind..." Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the syringes containing the study medication were prepared by a nurse otherwise not participating in the study" Judgement comment: no further information on blinding of personnel and identical appearance of syringes provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "all patients were observed by the same recovery room nurse, who did not otherwise participate in the study. During the following 22 h, the patients were monitored on the general ward by nurses who were familiar with the study" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "forty patients received ondansetron and 40 received droperidol. All of them completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the groups with respect to patient characteristics, type of surgery, duration of anesthesia, and doses of anesthetics (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Grover 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different route of administration
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 37 • *Received treatment (n)*: 37 • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 43.4 ± 13.8 • *Weight (mean ± SD, median (IQR), median (range))*: 57.9 ± 8.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 27/9/0/0 • *Gender (female in %)*: 83.33 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: TIVA (propofol), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 111.7 • *Use of perioperative opioids (if yes, which?)*: 0.15 mg/kg morphine at induction, 4 patients with rescue analgesic • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (IV group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: 36 • *Analysed (n)*: 33 • *Age (mean ± SD, median (IQR), median (range))*: 39.2 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 62.8 ± 11.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/9/0/0 • *Gender (female in %)*: 78.79 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: TIVA (propofol), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 100.8 • *Use of perioperative opioids (if yes, which?)*: 0.15 mg/kg morphine at induction, 2 patients with rescue analgesic • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (PO group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: 36 • *Analysed (n)*: 34

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Grover 2009 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 44 ± 8.5
- *Weight (mean ± SD, median (IQR), median (range))*: 58.4 ± 7.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/12/0/0
- *Gender (female in %)*: 73.53
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 96.1
- *Use of perioperative opioids (if yes, which?)*: 0.15 mg/kg morphine at induction, 3 patients with rescue analgesic
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, individuals of either sex, 18 to 65 years of age, scheduled for elective laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: previous history of PONV, motion sickness, antiemetic therapy within 24 hours preoperatively, receiving opioid treatment, pregnancy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: placebo tablet, saline • *Time point of administration*: 30 minutes before surgery, following tracheal intubation • *Route of administration*: PO, IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.15 mg/kg IV Ondansetron (IV group) • *Dose*: 4 mg, placebo tablet • *Time point of administration*: placebo 30 minutes before surgery, ondansetron following tracheal intubation • *Route of administration*: ondansetron IV, placebo PO • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.15 mg/kg IV Ondansetron (PO group) • *Dose*: 8 mg, saline • *Time point of administration*: ondansetron 30 minutes before surgery, placebo following tracheal intubation • *Route of administration*: ondansetron PO, saline IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.15 mg/kg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)*

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Grover 2009 *(Continued)*

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** India **Setting:** outpatient, single-centre **Author's name:** Preethy J. Mathew **Institution:** Department of Anaesthesia and Intensive Care, Postgraduate Institute of Medical Education and Research, Chandigarh, India **Email:** tjpreethy@rediffmail.com **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomised into three groups: placebo, intravenous ondansetron and oral ondansetron groups, using computer generated random numbers"
Allocation concealment (selection bias)	Low risk	Quote: "serially numbered, opaque, sealed envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...were administered the placebo tablet 30 min before surgery by one of the investigators not involved in intra-operative and postoperative outcome assessments" Quote: "...the placebo, orally disintegrating tablets were prepared by the hospital pharmacy"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patient requested pain relief. In the postoperative period, nausea and vomiting were assessed in two epochs of 0–6 and 6–24 h by an anaesthetist who was unaware of the group allocations. The patients were asked to..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...randomisation and was excluded. Since surgery was converted to an open cholecystectomy in six patients, data of 103 patients were analysed (Fig. 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Grover 2009 *(Continued)*

Other bias	Unclear risk	Quote: "patients were analysed (Fig. 1). Demographic data were comparable among the groups (Table 2). Duration of surgery, duration of anaesthesia and time to recovery were also comparable. Time to oral intake was..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Gugale 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 39.26 ± 13.20 • *Weight (mean ± SD, median (IQR), median (range))*: 62.86 ± 10.07 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: none • *Type of surgery*: laparoscopic surgery (appendectomy or cholecystectomy) Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 38.03 ± 12.00 • *Weight (mean ± SD, median (IQR), median (range))*: 63.16 ± 10.50 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 57 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA

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Gugale 2016 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: laparoscopic surgery (appendectomy or cholecystectomy)

Included criteria: 60 patients (18 to 65 years of age), ASA I and II, undergoing elective laparoscopic surgeries, either appendectomy or cholecystectomy

Excluded criteria: gynaecological laparoscopic surgeries

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Granisetron • *Dose*: 0.05 mg/kg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 70% (ondansetron 0.08 mg/kg) Palonosetron • *Dose*: 1.5 µg/kg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (ondansetron 0.08 mg/kg)
Outcomes	*Subjects with any AE (0 to 72 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, overall, exact time point unknown)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** nil **Country:** India **Setting:** inpatient, single-centre **Author's name:** Pradnya Milind Bhalerao **Institution:** Department of Anaesthesiology and Critical Care, B.J. Government Medical College and Sassoon General Hospital, Pune, Maharashtra, India **Email:** dr.pradnyabhalerao@gmail.com **Address:** D-15/10-11, Saritanagari-2, Off, Sinhagad Road, Pune - 411 030, Maharashtra, India **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response at 24 to 72 hours
Notes	None
Risk of bias	

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Gugale 2016 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...were enrolled in each group. Patients were randomly assigned to one of the two prophylactic interventions by a computer-generated number table. This prospective, randomized, double-blinded, comparative study..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "this prospective, randomized, double-blinded, comparative study was..." Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear

Guldogus 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 1.5 • *Weight (mean ± SD, median (IQR), median (range))*: 72.4 ± 3.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 101.3

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Guldogus 1994 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major gynaecological surgery

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 44.8 ± 1.4
- *Weight (mean ± SD, median (IQR), median (range))*: 73.5 ± 2.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105.6
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major gynaecological surgery

Ondansetron + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 13
- *Received treatment (n)*: NA
- *Analysed (n)*: 13
- *Age (mean ± SD, median (IQR), median (range))*: 44.2 ± 1.8
- *Weight (mean ± SD, median (IQR), median (range))*: 73.6 ± 3.34
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 109.4
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major gynaecological surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 41.3 ± 0
- *Weight (mean ± SD, median (IQR), median (range))*: 75.3 ± 0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA

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Guldogus 1994 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104.3
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major gynaecological surgery

Included criteria: ASA I or II, women undergoing major gynaecological surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 8 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 5 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron + droperidol • *Dose*: ondansetron 4 mg, droperidol 5 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: saline • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre

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Guldogus 1994 *(Continued)*

Author's name: Fuat Güldogus

Institution: NA

Email: NA

Address: NA

Duration of study: NA

Language: Turkish (translated by Emine Yesil)

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" (translated). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "double-blind" (translated). Insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "double-blind" (translated). Insufficient information on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no statement on missing outcome data; no missing outcome data assumed
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Gupta 2007

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron

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Gupta 2007 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20 (first 6 hours)
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 7.7
- *Weight (mean ± SD, median (IQR), median (range))*: 50.1 ± 5.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg to 2 mg/kg tramadol at induction
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20 (first 6 hours)
- *Age (mean ± SD, median (IQR), median (range))*: 39.5 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 50.6 ± 7.15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg to 2 mg/kg tramadol at induction
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20 (first 6 hours)
- *Age (mean ([range])*: 38.75 ± 7.85
- *Weight (mean ± SD, median (IQR), median (range))*: 52.2 ± 6.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg to 2 mg/kg tramadol at induction

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Gupta 2007 *(Continued)*

- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: female, between 20 and 60 years of age, ASA grade I and II, informed consent

Excluded criteria: history of previous exposure to general anaesthesia, gastrointestinal disease, motion sickness, PONV; pregnancy and menstruation; had taken antiemetic drugs within 24 hours of operation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Granisetron • *Dose*: 3 mg • *Time point of administration*: 10 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Ondansetron • *Dose*: 4 mg • *Time point of administration*: 10 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Metoclopramide • *Dose*: 10 mg • *Time point of administration*: 10 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Renu Wakhloo **Institution:** Department of Anaesthesiology and ICU, Government Medical College, Jammu, J India **Email:** NA **Address:** Department of Anaesthesiology, Govt. Medical College-Jammu, J India **Language:** English **Duration of study:** NA

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Gupta 2007 *(Continued)*

	Trial registry number: NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...using double blind randomization technique..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "using double blind randomization technique, these patients were given either Group A (granisetron 3mg), Group B (ondansetron 4mg) or Group C (metoclopramide 10mg). All the drugs were diluted in 50ml normal saline and given slowly 10 minutes before induction" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "investigator who collected post-operative data was blinded to study drug administered while in the recovery ward"
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: for the outcome "emesis" at the second, third, and fourth time points, patients are missing without reasons stated (> 15%)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the treatment groups were comparable with regards to patient demographics (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Gupta 2011

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Ondansetron (group O1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 34

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Gupta 2011 *(Continued)*

- *Received treatment (n)*: 34
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 0.2
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23.4 ± 0.12
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 56
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100
- *Use of perioperative opioids (if yes, which?)*: 225 µg intraoperative fentanyl
- *Type of surgery*: breast surgery, vaginal hysterectomy, skin grafting surgery, reconstructive limb surgery

Ondansetron (group O4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 34
- *Received treatment (n)*: 34
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 1.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 22.6 ± 2.12
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 56
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 235 µg intraoperative fentanyl
- *Type of surgery*: breast surgery, vaginal hysterectomy, skin grafting surgery, reconstructive limb surgery

Ondansetron (group O8)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 34
- *Received treatment (n)*: 34
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 5.3
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 22.6 ± 2.12
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 48
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 200 µg intraoperative fentanyl
- *Type of surgery*: breast surgery, vaginal hysterectomy, skin grafting surgery, reconstructive limb surgery

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Gupta 2011 *(Continued)*

Placebo (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 34
- *Received treatment (n)*: 34
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 4.3
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 22.4 ± 1.2
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 180 µg intraoperative fentanyl
- *Type of surgery*: breast surgery, vaginal hysterectomy, skin grafting surgery, reconstructive limb surgery

Included criteria: adults of both sexes, ASA I and II, taking no prescription or over-the-counter medication, normal baseline electrocardiograms, posted for breast surgery, vaginal hysterectomy, skin grafting surgery, and reconstructive limb surgery

Excluded criteria: known to have history of gastrointestinal disease; hormonal therapy; evidence of uncontrolled clinically important neurological, renal, hepatic, cardiovascular, metabolic, or endocrine dysfunction or clinically important abnormalities in laboratory screening tests; vomiting during the 24-hour period before surgery; VAS > 4 at extubation if not extubated after 30 minutes following study medication; not responding to verbal commands after extubation; reaction to study drug; nasogastric tube in situ postoperatively; weighing 45 kg or > 90 kg; pregnant or lactating women

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions

Intervention characteristics

Ondansetron (group O1)

- *Dose*: 1 mg
- *Time point of administration*: 30 minutes before extubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ondansetron (group O4)

- *Dose*: 4 mg
- *Time point of administration*: 30 minutes before extubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ondansetron (group O8)

- *Dose*: 8 mg
- *Time point of administration*: 30 minutes before extubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

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Gupta 2011 *(Continued)*

	Placebo (group P) • *Dose*: normal saline • *Time point of administration*: 30 minutes before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** nil **Country:** India **Setting:** single-centre **Author's name:** Ranabir Pal **Institution:** Department of Community Medicine, Sikkim Manipal Institute of Medical Sciences and Central Referral Hospital, Gangtok, Sikkim **Email:** ranabirmon@yahoo.co.in **Address:** Department of Community Medicine, Sikkim Manipal Institute of Medical Sciences and Central Referral Hospital, 5th Mile, Tadong, Gangtok, Sikkim - 737 102, India **Language:** English **Duration of study:** October 2008 to April 2009 **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the participants were randomly allocated into four groups with 34 participants in each group through a computer-generated random number"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the anesthesiologist who administered the study drugs was blinded about the nature of treatment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "intra-operatively all the data were recorded by an independent observer blinded to the study drugs"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Gupta 2011 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "one hundred and thirty-six adult participants of both sexes were comparable in terms of mean age, sex, Body Mass Index (BMI), and duration of anesthesia. There were no significant differences among the groups with respect to type of surgery performed (Chi square 0.5371, df 9, P=1.00) [Table 1]" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Gupta K 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 33.2 ± 10.4 • *Weight (mean ± SD, median (IQR), median (range))*: 60.9 ± 12.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 25/15/0/0 • *Gender (female in %)*: 52.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 112.34 • *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperatively • *Type of surgery*: laparoscopic cholecystectomy Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 34.9 ± 10.6 • *Weight (mean ± SD, median (IQR), median (range))*: 62.14 ± 10.12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 26/14/0/0 • *Gender (female in %)*: 55 • *Non-smoker (%)*: NA

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Gupta K 2014 *(Continued)*

- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 117.32
- *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperatively
- *Type of surgery*: laparoscopic cholecystectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 35 ± 10.6
- *Weight (mean ± SD, median (IQR), median (range))*: 61.8 ± 11.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 28/12/0/0
- *Gender (female in %)*: 57.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 114.67
- *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperatively
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: adults, ASA I and II, 18 to 58 years of age, of either gender, scheduled for elective laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: history of systemic hypertension, endocrine or metabolic disorders, hepatic or renal disease, cardiopulmonary dysfunction; gastrointestinal disorders; psychiatric disease; morbid obesity; pregnant and menstruating females; history of motion sickness; had taken antiemetic drugs within 24 hours before surgical procedures

Pretreatment: baseline characteristics (age, weight, ASA) no. Potential effect modifiers (gender, history of motion sickness, duration of anaesthesia): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics**

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 5 mg IM

Palonosetron

- *Dose*: 0.075 mg
- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 5 mg IM

Granisetron

- *Dose*: 2 mg
- *Time point of administration*: 5 minutes before induction
- *Route of administration*: IV

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Gupta K 2014 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide 5 mg IM
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 12 hours)* • Outcome type: dichotomous outcome *Headache (0 to 12 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 12 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Kumkum Gupta **Institution:** Departments of Anesthesiology and Critical Care, N.S.C.B. Subharti Medical College, Swami Vivekananda Subharti University, Subhartipuram, NH – 58, Meerut, Uttar Pradesh, India **Email:** kumkumprashant75@gmail.com **Address:** 108, Chanakyapuri, Shastri Nagar, Meerut – 250004, Uttar Pradesh, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study drug preparation was done by an assistant who was unaware to the study protocol and was not involved in the study for any further evaluation of patients" Judgement comment: insufficient information on blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperatively, nausea or emetic episode were recorded by the nursing staff without knowledge of which group of anti-emetic drug was given to the patients"

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Gupta K 2014 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the study was successfully conducted on 120 adult consented patients for their postoperative assessment of PONV" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "all the three groups were comparable for their demographic profiles with respect to age, sex, BMI and ASA physical status and duration of laparoscopic cholecystectomy [Table 1]" Judgement comment: baseline characteristics (age, weight, ASA) no. Potential effect modifiers (gender, history of motion sickness, duration of anaesthesia): no; (history of PONV, non-smoke, perioperative opioids): unclear

Gupta Priyanka 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + granisetron (group G) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 35.64 ± 14.1 • *Weight (mean ± SD, median (IQR), median (range))*: 51 ± 10.308 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 52 • *Non-smoker (%)*: 80 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 258 • *Use of perioperative opioids (if yes, which?)*: 249.8 µg intraoperative fentanyl • *Type of surgery*: craniotomy for brain tumour Dexamethasone + ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 36.56 ± 14.54 • *Weight (mean ± SD, median (IQR), median (range))*: 50.2 ± 11.857 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Gupta Priyanka 2014 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 52
- *Non-smoker (%)*: 88
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 239
- *Use of perioperative opioids (if yes, which?)*: 220.4 µg intraoperative fentanyl
- *Type of surgery*: craniotomy for brain tumour

Dexamethasone (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 37.04 ± 12.74
- *Weight (mean ± SD, median (IQR), median (range))*: 53.6 ± 9.41
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 48
- *Non-smoker (%)*: 88
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 246
- *Use of perioperative opioids (if yes, which?)*: 248 µg intraoperative fentanyl
- *Type of surgery*: craniotomy for brain tumour

Included criteria: ASA I to III, adult patients of either sex, scheduled for elective craniotomy for brain tumour

Excluded criteria: Glasgow coma scale 14, not extubated at end of surgery, on preoperative antiemetic therapy, previous history of PONV/motion sickness/gastro-oesophageal reflux disease, history of allergy to 5-HT3 antagonists

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dexamethasone + granisetron (group G) • *Dose*: dexamethasone 8 mg, granisetron 1 mg • *Time point of administration*: dexamethasone at induction, granisetron at the time of dural close • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone + ondansetron (group O) • *Dose*: dexamethasone 8 mg, ondansetron 1 mg • *Time point of administration*: dexamethasone at induction, ondansetron at the time of dural close • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone (group D) • *Dose*: 8 mg

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Gupta Priyanka 2014 *(Continued)*

- *Time point of administration*: dexamethasone at induction, saline at the time of dural close
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 48 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient **Author's name:** Mayank Gupta **Institution:** Department of Anaesthesia and Intensive Care, Vardhaman Mahavir Medical College and Safdarjung Hospital, Saket, New Delhi, India **Email:** drm_gupta@yahoo.co.in **Address:** 14, Himvihar Apartments, I.P. Extension, New Delhi - 110 092, India **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "at the time of dura closure, patients were randomly assigned to one of the three groups using envelope method to receive" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Quote: "using envelope method to receive" Judgement comment: not stated that envelopes were sequentially numbered, opaque, and sealed (SNOSE)
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "...the time of dural closure. Study medications were prepared by an anesthetist not involved in PONV monitoring in identical 2 ml syringes. Neuromuscular blockade was reversed with..."

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Gupta Priyanka 2014 *(Continued)*

All outcomes		Judgement comment: anaesthesiologist was not blinded but only received information about group allocation at dural closure. Impact on anaesthesia unknown
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "anesthetists who were blinded to group allocation recorded each episode of nausea, retching and vomiting"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...the study, 25 in each group. There were no significant differences in demographic profile [Table 1], intra-operational characteristics [Table 2], type and anatomical location of intracranial tumors among the three groups [Table 3]. A complete response (no PONV..." Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Gupta Pushplata 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 50.52 ± 12.1 • *Weight (mean ± SD, median (IQR), median (range))*: 59.48 ± 10.63 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, tramadol (100 mg IV 6-hourly) • *Type of surgery*: modified radical mastectomy Granisetron • *Assessed for eligibility (n)*: -

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Gupta Pushplata 2014 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 44.16 ± 12.03
- *Weight (mean ± SD, median (IQR), median (range))*: 58.2 ± 8.02
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, tramadol (100 mg IV 6-hourly)
- *Type of surgery*: modified radical mastectomy

Granisetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean +/- SD, median (IQR), median (range))*: 49 ± 7.91
- *Weight (mean ± SD, median (IQR), median (range))*: 61.24 ± 11.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, tramadol (100 mg IV 6-hourly)
- *Type of surgery*: modified radical mastectomy

Included criteria: females, ASA I and II, carcinoma breast stages 1 to 3, going for elective modified radical mastectomy with or without chemotherapy

Excluded criteria: history of motion sickness and previous history of PONV; history of smoking; full stomach; gastro-oesophageal disease; pregnant and menstruating women; had taken antiemetic medication within 24 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (duration of anaesthesia, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 32% (metoclopramide 10 mg) Granisetron • *Dose*: 40 µg/kg

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Gupta Pushplata 2014 *(Continued)*

- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 36% (metoclopramide 10 mg)

Granisetron + dexamethasone

- *Dose*: granisetron 40 µg/kg, dexamethasone 8 mg
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 20% (metoclopramide 10 mg)

Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 6 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** nil **Country:** India **Setting:** inpatient, single-centre **Author's name:** Dr. Shilpi Jain **Institution:** MBS Hospital, Nayapura, Kota, Rajasthan, India **Email:** singhalshilpidr@gmail.com **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "in a double-blind manner, patients were randomly divided into three groups (25 patients each), received either..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Gupta Pushplata 2014 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the anesthesiologist who anesthetized the patient and all involved nurses were unaware of the content of the syringe"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...was taken by every patient. Seventy-five female patients of American Society of Anesthesiologists (ASA) Grade 1 and 2 with carcinoma breast Stages 1-3 going for elective MRM with or without chemotherapy were included in the study. Patients with history of motion..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (duration of anaesthesia, perioperative opioids): unclear

Ha 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 31 • *Received treatment (n)*: 31 • *Analysed (n)*: 31 • *Age (mean ± SD, median (IQR), median (range))*: 54 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 22/9/0/0 • *Gender (female in %)*: 70.97 • *Non-smoker (%)*: 90.3 • *History of PONV/motion sickness (%)*: 3.2/22.6 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 231 • *Use of perioperative opioids (if yes, which?)*: 1084 µg intraoperative remifentanil, 50 µg fentanyl during skin closure, tramadol as rescue analgesic • *Type of surgery*: microvascular decompression with retromastoid craniotomy

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Ha 2015 *(Continued)*

	Ramosetron (group R) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 31 • *Received treatment (n)*: 31 • *Analysed (n)*: 31 • *Age (mean ± SD, median (IQR), median (range))*: 53 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/7/0/0 • *Gender (female in %)*: 70.97 • *Non-smoker (%)*: 96.8 • *History of PONV/motion sickness (%)*: 6.5/19.4 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 261 • *Use of perioperative opioids (if yes, which?)*: 1126 µg intraoperative remifentanil, 50 µg fentanyl during skin closure, tramadol as rescue analgesic • *Type of surgery*: microvascular decompression with retromastoid craniotomy **Included criteria:** 20 to 75 years of age, ASA I or II, scheduled for microvascular decompression (MVD) with retromastoid craniotomy (RMC) **Excluded criteria:** pregnancy; having undergone chemotherapy or ventriculoperitoneal shunt insertion; allergy to ondansetron or ramosetron; having undergone antiemetic therapy within 24 hours before the operation; having systemic steroid therapy within 24 hours before the operation or up to 48 hours during the postoperative period; having had an emergency operation; with cardiovascular disease, respiratory disease, renal disease, or hepatic disease; Glasgow Coma Scale Score < 13 points **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): yes
Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 8 mg • *Time point of administration*: at onset of dural closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ramosetron (group R) • *Dose*: 0.3 mg • *Time point of administration*: at onset of dural closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (PACU, 0 to 1 hour)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (PACU, 1 to 6 hours, 6 to 24 hours, 24 to 48 hours)* • Outcome type: dichotomous outcome

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Ha 2015 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Kyeong Tae Min **Institution:** Yonsei University College of Medicine, Anesthesia and Pain Research Institute, Seoul, Korea **Email:** ktmin501@yuhs.ac **Address:** Department of Anesthesiology and Pain Medicine, Yonsei University College of Medicine, Anesthesia and Pain Research Institute, 50, Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated to receive ondansetron (group O) or ramosetron (group R) according to a computer grouping program"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study medication was prepared by one of the investigators (Ha, SH) in identical 5 ml syringes and administered at an equal volume of 4 ml (ramosetron was prepared with 2 ml of normal saline). The other investigators were unaware of which drug was being administered to the patients"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "investigators who were unaware of the patient treatment group evaluated the occurrence and severity of nausea, the occurrence of vomiting, pain intensity levels, and the requirements of rescue antiemetics or analgesics at the PACU at intervals of 1–6 hours, 6–24 hours and 24–48 hours after surgery"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "sixty-two patients (31 patients in each group) among the 64 patients enrolled in the study were analyzed because two patients (1 in group O and 1 in group R) violated the experimental protocol"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "demographic data showed no statistical significance" Quote: "but the anesthetic duration in group R was longer than that in group O (231 ± 41 minutes vs. 261 ± 53 minutes, P = 0.01, Table 1). The overall incidence rates of..."

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Ha 2015 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): yes

Habib 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Droperidol + ondansetron (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 81 ± 19 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 7/22/1/0 • *Gender (female in %)*: 70 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 23.33 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 83 • *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl intraoperative • *Type of surgery*: laparoscopic cholecystectomy Control (group 3) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: 84 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 7/21/2/0 • *Gender (female in %)*: 73.33 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 16.67 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 94 • *Use of perioperative opioids (if yes, which?)*: 187 µg fentanyl intraoperative • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** adults scheduled for laparoscopic cholecystectomy

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Habib 2004 *(Continued)*

	Excluded criteria: ASA IV or V; antiemetic or glucocorticosteroid use within 24 hours of surgery; allergy to ondansetron, droperidol, or propofol; pregnancy; breastfeeding; obesity (BMI > 34 kg/m^2); mental retardation; psychiatric illness. For women of childbearing potential, a negative serum beta-human chorionic gonadotropin test was confirmed before enrolment **Pretreatment:** baseline characteristics (age, weight ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Droperidol + ondansetron (group 1) • *Dose*: droperidol 0.625 mg, ondansetron 4 mg • *Time point of administration*: droperidol at induction of anaesthesia, ondansetron at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg Control (group 3) • *Dose*: none • *Time point of administration*: none • *Route of administration*: none • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 0 to 2 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** NA **Author's name:** Tong J. Gan **Institution:** Departments of Anesthesiology, Duke University Medical Center, Durham, North Carolina, USA **Email:** Gan00001@mc.duke.edu **Address:** Department of Anesthesiology, Box 3094, Duke University Medical Center, Durham, NC 27710, USA **Language:** English **Duration of study:** NA

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Habib 2004 *(Continued)*

	Trial registry number: NA **Study's primary outcome:** incidence of PONV
Notes	Two out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly assigned to one of three treatment groups. Randomization was achieved by using a sealed envelope technique and was prepared by independent personnel not associated with the study"
Allocation concealment (selection bias)	Unclear risk	Quote: "randomization was achieved by using a sealed envelope technique and was prepared by independent personnel not associated with the study" Judgement comment: not stated; "sequentially numbered, opaque" envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no blinding of anaesthesiologist (no sham intervention)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "data were collected by an independent research nurse who was unaware of the patients' randomization"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the three groups were similar with respect to age, weight, height, sex, ASA status, race, history of PONV or motion sickness, duration of surgery, the amount of preoperative midazolam used, and the amount of fentanyl used during surgery and in the PACU (Table 1)" Judgement comment: baseline characteristics (age, weight ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Habib 2011

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Aprepitant + dexamethasone • *Assessed for eligibility (n)*: -

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Habib 2011 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 57
- *Received treatment (n)*: 52
- *Analysed (n)*: 51
- *Age (mean ± SD, median (IQR), median (range))*: 51 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 85 ± 20
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 1/22/28/0
- *Gender (female in %)*: 55
- *Non-smoker (%)*: 92
- *History of PONV/motion sickness (%)*: 33
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 180
- *Use of perioperative opioids (if yes, which?)*: 1630 µg intraoperative remifentanil, 250 µg intraoperative fentanyl, 117 µg postoperative fentanyl
- *Type of surgery*: craniotomy

Ondansetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 58
- *Received treatment (n)*: 55
- *Analysed (n)*: 53
- *Age (mean ± SD, median (IQR), median (range))*: 48 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 87 ± 22
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 1/27/25/0
- *Gender (female in %)*: 57
- *Non-smoker (%)*: 94
- *History of PONV/motion sickness (%)*: 38
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 179
- *Use of perioperative opioids (if yes, which?)*: 1900 µg intraoperative remifentanil, 276 µg intraoperative fentanyl, 100 µg postoperative fentanyl
- *Type of surgery*: craniotomy

Included criteria: English-speaking, adults, ASA I to III, undergoing elective craniotomy under general anaesthesia

Excluded criteria: hypersensitivity to either of the 2 study medications (ondansetron and aprepitant), taking medications with known antiemetic properties preoperatively within 12 hours before the scheduled surgical procedure (with the exception of dexamethasone, which is used routinely in this patient population to reduce cerebral edema), pregnant or lactating, with substance abuse or significant psychiatric disease, with a nausea verbal rating score (VRS) > 3 (scale 0 to 10) in the preoperative holding area before treatment with study medications, expected need for placement of a nasogastric tube for gastric suction

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Aprepitant + dexamethasone • *Dose*: aprepitant 40 mg, dexamethasone 10 mg

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Habib 2011 *(Continued)*

	• *Time point of administration*: aprepitant 1 to 3 hours before induction of anaesthesia, dexamethasone after induction of anaesthesia • *Route of administration*: aprepitant PO, dexamethasone IV • *Rescue antiemetics (if yes, which?)*: 61% (ondansetron 4 mg) Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 10 mg • *Time point of administration*: ondansetron within 30 minutes of end of surgery, dexamethasone after induction of anaesthesia • *Route of administration*: ondansetron IV, dexamethasone IV • *Rescue antiemetics (if yes, which?)*: 57% (ondansetron 4 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (at 24 hours, at 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** funding was provided by Merck Co.; Ashraf S. Habib received honoraria from Merck Co. **Country:** USA **Setting:** single-centre, inpatient **Author's name:** Ashraf S. Habib **Institution:** Duke University Medical Center, Durham, North Carolina, USA **Email:** habib001@mc.duke.edu **Address:** Duke University Medical Center, Box 3094, Durham, NC 27710, USA **Language:** English **Duration of study:** October 2007 to June 2009 **Trial registry number:** NCT00734929 **Study's primary outcome:** cumulative incidence of vomiting from 0 to 48 hours
Notes	None
Risk of bias	

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Habib 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a computer-generated random sequence. The randomization assignment was prepared using NQuery Advisor TM version 6.0. A 1:1 assignment ratio was used for treatments, with 65% and 35% assignment to supratentorial and infratentorial strata, respectively. Assignments were balanced using the randomly mixed block size provided by the software"
Allocation concealment (selection bias)	Low risk	Quote: "after patient consent, study personnel faxed a request form to the investigational drug service with the patient study number and site of craniotomy. The randomization sequence was only held by the statistician and the investigational drug service"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study drugs were prepared by the investigational drug service and supplied in identical blinded form according to a computer-generated random sequence"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an independent research nurse unaware of the patients' randomization collected the data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "two hundred three subjects were screened for eligibility; of those, 126 consented to participate in the study. One hundred four patients completed the study: 51 in the aprepitant group and 53 in the ondansetron group (Fig. 1)" Judgement comment: missing data < 15 % and balanced between arms. Reasons described and unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00734929 (retrospective registration)
Other bias	Low risk	Quote: "there was no difference in patient demographics, risk factors for PONV, duration of surgery, intraoperative opioids, and postoperative analgesic consumption between the 2 groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Hammas 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + ondansetron + droperidol + metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 58

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Hammas 2002 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 63.79
- *Non-smoker (%)*: 77.59
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl: breast surgery: 0.116 (0.050 to 0.225)/abdominal surgery: 0.217 (0.075 to 0.400); morphine: breast surgery: 5.9 (2 to 19)/abdominal surgery: 7.3 (2 to 13); ketobemidone: breast surgery: 4.3 (1 to 10)/abdominal surgery: 4.3 (2 to 7)
- *Type of surgery*: breast surgery (20), abdominal surgery (38)

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 57
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 63.16
- *Non-smoker (%)*: 77.19
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl: breast surgery: 0.136 (0.075 to 0.275)/abdominal surgery: 0.217 (0.100 to 0.400); morphine: breast surgery: 6.8 (2 to 14)/abdominal surgery: 5.5 (5 to 7); ketobemidone: breast surgery: 4.5 (2 to 8)/abdominal surgery: 5.8 (1 to 20)
- *Type of surgery*: breast surgery (19), abdominal surgery (38)

Included criteria: ASA I or II, scheduled for breast surgery or abdominal surgery (cholecystectomies and inguinal hernia repairs)

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear

Interventions

Intervention characteristics

Dexamethasone + ondansetron + droperidol + metoclopramide

- *Dose*: dexamethasone 4 mg, ondansetron 4 mg, droperidol 1.25 mg, metoclopramide 10 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dixyrazine 5 to 10 mg IV

Control

- *Dose*: none
- *Time point of administration*: -
- *Route of administration*: -

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Hammas 2002 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: dixyrazine 5 to 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (5 to 8 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Sweden **Setting:** inpatient and outpatient, single-centre **Author's name:** Magnus Wattwill **Institution:** Department of Anesthesia and Intensive Care, Örebro Medical Center Hospital, Örebro, Sweden **Email:** magnus.wattwil@orebroll.se **Address:** Department of Anesthesia and Intensive Care, Örebro Medical Center Hospital, SE-701 85 Örebro, Sweden **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	Two out of 3 groups relevant (propofol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "through a stratified randomization". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "using random numbers concealed in envelopes". Not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no blinding of anaesthesiologists possible (no placebo treatment)

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Hammas 2002 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "one hundred and eighty patients were scheduled for the study, but eight were excluded due to violation of the study protocol (incorrect premedication, anesthesia or postoperative pain relief)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear

Hanaoka 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: 117 • *Analysed (n)*: 107 • *Age (mean ± SD, median (IQR), median (range))*: 40.1 ± 10.2 • *Weight (mean ± SD, median (IQR), median (range))*: 55.6 ± 8.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 95.33 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/43.93 • *Type of general anaesthesia*: inhalation anaesthesia, alone or in combination with epidural anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 158.3 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: gynaecological surgery (hystero-myoma, ovarian cyst, or other benign gynaecological disease; enucleation of benign tumour; laparoscopic surgery); gynaecological diagnostic laparoscopy; cholecystectomy Granisetron (1 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: 110 • *Analysed (n)*: 104

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Hanaoka 2004 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 39.8 ± 9.1
- *Weight (mean ± SD, median (IQR), median (range))*: 55.7 ± 8.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 95.19
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/41.34
- *Type of general anaesthesia*: inhalation anaesthesia, alone or in combination with epidural anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 148.4
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery (hystero-myoma, ovarian cyst, or other benign gynaecological disease; enucleation of benign tumour; laparoscopic surgery); gynaecological diagnostic laparoscopy; cholecystectomy

Granisetron (3 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 114
- *Analysed (n)*: 104
- *Age (mean ± SD, median (IQR), median (range))*: 40.4 ± 12.2
- *Weight (mean ± SD, median (IQR), median (range))*: 54.1 ± 9.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 96.15
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/41.34
- *Type of general anaesthesia*: inhalation anaesthesia, alone or in combination with epidural anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 163.8
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological surgery (hystero-myoma, ovarian cyst, or other benign gynaecological disease; enucleation of benign tumour; laparoscopic surgery); gynaecological diagnostic laparoscopy; cholecystectomy

Included criteria: between 20 and 65 years of age; scheduled to undergo gynaecological surgery (hystero-myoma, ovarian cyst, or other benign gynaecological disease; enucleation of benign tumour; laparoscopic surgery); gynaecological diagnostic laparoscopy; cholecystectomy under inhalation anaesthesia, alone or in combination with epidural anaesthesia; ASA I to III, preoperative physical status

Excluded criteria: severe hepatic, renal, cardiac, or pulmonary dysfunction or haemopoietic organ disorder; history of drug allergy or anaphylactic symptoms; gastrointestinal transit disorder or active peptic ulcer; brain tumour or epilepsy or receiving a psychotropic agent with an antiemetic effect; had experienced nausea and/or vomiting during the 24 hour period before administration of the study medication; had received another study drug within 3 months of starting the study; were due to use another investigational drug concurrently; had undergone radiotherapy or chemotherapy within the 24 hour period before dosing with the study medication; were due to undergo radiotherapy or chemotherapy during the observation period; were pregnant or nursing; might be, or wished to be, pregnant within 30 days of receiving the study medication

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics**

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Hanaoka 2004 *(Continued)*

	Placebo • *Dose*: saline • *Time point of administration*: immediately before stopping inhalation anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 28% (antiemetic rescue with another antiemetic therapy (except for 5-HT3 receptor antagonists)) Granisetron (1 mg group) • *Dose*: 1 mg • *Time point of administration*: immediately before stopping inhalation anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 14.4% (antiemetic rescue with another antiemetic therapy (except for 5-HT3 receptor antagonists)) Granisetron (3 mg group) • *Dose*: 3 mg • *Time point of administration*: immediately before stopping inhalation anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16.3% (antiemetic rescue with another antiemetic therapy (except for 5-HT3 receptor antagonists))
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, advents occurring within 30 days)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this multicentre trial was sponsored by SmithKline Beecham Seiyaku K.K., Tokyo, Japan **Country:** Japan **Setting:** multi-centre (26), inpatient **Author's name:** Kazuo Hanaoka

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Hanaoka 2004 *(Continued)*

Institution: Department of Anesthesiology, Faculty of Medicine, University of Tokyo, Japan

Email: NA

Address: Department of Anesthesiology, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

Duration of study: NA

Language: English

Study's primary outcome: no vomiting rate (defined as the proportion of patients who did not experience vomiting during the 24 hour period after the end of inhalation anaesthesia)

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "central randomization and minimization" Judgement comment: insufficient information on sequence generation
Allocation concealment (selection bias)	Low risk	Quote: "patients were allocated to intravenous granisetron 3 mg, granisetron 1 mg, or placebo, by central randomization and minimization"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "granisetron was provided as a colorless clear injection, each tube containing 1 mg of granisetron (1.12 mg as granisetron hydrochloride). Placebo injection containing 1 ml of physiological saline appeared identical, to maintain the integrity of the study blinding"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 365 patients who entered the trial, 341 patients received the study medication and were included in population 2: 117 patients in the placebo group, 110 in the granisetron 1-mg group, and 114 in the granisetron 3-mg group. Twenty-six patients were excluded from population 1 due to withdrawal for protocol violations (n 25) or adverse events (n 1; ventricular fibrillation), resulting in a total of 315 patients: 107 patients in the placebo group, 104 in the granisetron 1-mg group, and 104 in the granisetron 3-mg group"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Hechler 2001

Study characteristics

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Hechler 2001 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 669 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 76.08 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 113 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (1 to 2 µg/kg), postoperative piritramide in doses of 3 mg (number of doses/patients not reported) • *Type of surgery*: general surgical, traumatological, gynaecological, or plastic surgery Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 665 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 16 • *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 72.63 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 112 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (1 to 2 µg/kg), postoperative piritramide in doses of 3 mg (number of doses/patients not reported) • *Type of surgery*: general surgical, traumatological, gynaecological, or plastic surgery **Included criteria:** scheduled for elective surgery (general surgery, traumatological, gynaecological, or plastic surgery) requiring general anaesthesia of at least 30 minutes' duration **Excluded criteria:** younger than 18 years or over 75 years of age **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics**

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Hechler 2001 *(Continued)*

	Placebo • *Dose*: NaCl 0.9% • *Time point of administration*: 20 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 3.14% (droperidol 20 µg/kg) Droperidol • *Dose*: 20 µg/kg • *Time point of administration*: 20 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 1.95% (dimenhydrinate 62 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** H. B. Hopf **Institution:** Department of Anaesthesia and Intensive Care Medicine, Kreisklinik Langen, Langen, Germany **Email:** H-B.Hopf@t-online.de **Address:** Abteilung für Anästhesie u. Intensivmedizin, Kreisklinik Langen, Röntgenstrasse 20, 63225 Langen, Germany **Language:** English **Duration of study:** 1 July 1997 to 30 June 1998 **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Hechler 2001 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "patients were randomised (according to a computer generated list in the order of their first appearance in the anaesthesia pre-evaluation ambulance) to one of two groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "received the same volume of normal saline (NaCl 0.9%) 20 min before the end of anaesthesia in a single-blinded manner" Judgement comment: insufficient information on blinding of personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "after discharge to the ward, every patient was visited once or twice within and 24 h after anaesthesia by one of the authors and interviewed personally" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "altogether 1348 patients were randomised. Fourteen patients (12 women, 2 men) were dropped from evaluation: 12 because the operative procedure did not achieve the 30 min minimum duration of anaesthesia, and two because the study drug inadvertently had not been injected. Thus, 1334 patients remained for analysis" Judgement comment: reasons for missing outcome data were described and were unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the demographic data of the two groups were well matched, as shown in Table 1. In addition, distribution of surgical procedures was not different between the groups (PΩ0.664)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Hefni 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 55 ± 9

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Hefni 2014 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 90 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 28/12/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (epidural + inhalational anaesthesia (isoflurane))
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative meperidine
- *Type of surgery*: total abdominal hysterectomy

Dexamethasone (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 56 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 93 ± 4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 27/13/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (epidural + inhalational anaesthesia (isoflurane))
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 125
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative meperidine
- *Type of surgery*: total abdominal hysterectomy

Dexamethasone (6 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 57 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 94 ± 3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 29/11/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (epidural + inhalational anaesthesia (isoflurane))
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative meperidine
- *Type of surgery*: total abdominal hysterectomy

Dexamethasone (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40

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Hefni 2014 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 54 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 92 ± 5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 28/12/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (epidural + inhalational anaesthesia (isoflurane))
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 125
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative meperidine
- *Type of surgery*: total abdominal hysterectomy

Included criteria: females 45 to 60 years of age, ASA II to III, scheduled for total abdominal hysterectomy (TAH) for perimenopausal bleeding

Excluded criteria: history of peptic ulcer disease, contraindication to epidural anaesthesia (back fusion, coagulopathy, local infection) or failure to achieve epidural analgesia, obese, diabetic, had received corticosteroids or immunosuppressive drugs in the last 6 months, had contraindication to corticosteroids

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Control • *Dose*: placebo or no treatment, unclear • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: epidural • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Dexamethasone (4 mg group) • *Dose*: 4 mg • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: epidural • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Dexamethasone (6 mg group) • *Dose*: 6 mg • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: epidural • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Dexamethasone (8 mg group) • *Dose*: 8 mg • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: epidural • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM
Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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Hefni 2014 *(Continued)*

	Postoperative wound infection (0 to 7 days) • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** nil **Country:** Egypt **Setting:** inpatient, single-centre **Author's name:** Amira Fathy Hefni **Institution:** Department of Anesthesia and Intensive Care Medicine, Ain Shams University Hospitals, Cairo, Egypt **Email:** amirafsoliman@hotmail.com **Address:** Department of Anesthesia and Intensive Care Medicine, Ain Shams University Hospitals, Cairo, Egypt **Duration of study:** NA **Language:** English **Study's primary outcome:** pain **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "groups (40 patients per group) using computer-generated random numbers. Patients received a single-shot of..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all study drugs were prepared by the pharmacy and given in equal volumes of 10 ml so that the patient, anesthesiologist and..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all study drugs were prepared by the pharmacy and given in equal volumes of 10 ml so that the patient, anesthesiologist and observers collecting data were blinded to the drug and dose"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...groups and intergroup differences. From 164 patients [who] were enrolled in the study, one patient each in Groups D0 and D4 was lost to follow-up, also epidural procedure cannot be established in one patient each in Groups D6 and D8. So finally 160 patients were involved and divided into four groups, 40 each in Group D0, D4, D6 and D8. Among the 160 patients randomized..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there was a significant reduction of meperidine consumption in the D8 Group (75%), in the D6 Group (50%) and in the D4 (50%) Group during the first 24 h compared with Group D0, with a P < 0.01. All patients of Group D0 re-

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Hefni 2014 *(Continued)*

	quired analgesia, but only 10% in Group D8, 50% in Group D6 and Group D4 were in need [Table 2]" Quote: "...D0, D4, D6 and D8. Among the 160 patients randomized for the study, there were no significant differences between groups in patient characteristics such as age, weight, ASA physical status and duration of surgery [Table 1]. The cumulative intraoperative fentanyl requirements given by the I.V. route were comparable among the four groups [Table 2]. The time to first analgesic..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Hegde 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study, different routes of administration
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 31.5 ± 7.3 • *Weight (mean ± SD, median (IQR), median (range))*: 54.8 ± 10.2 • *BMI (mean ± SD, median (IQR), median (range))*: 22.7 ± 3.8 • *ASA I/II/III/IV (n)*: 39/5/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: TIVA (propofol), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 84.9 • *Use of perioperative opioids (if yes, which?)*: intraoperative, postoperative fentanyl • *Type of surgery*: gynaecological laparoscopic procedures Ondansetron (IV group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 46 • *Received treatment (n)*: 46 • *Analysed (n)*: 43 • *Age (mean ± SD, median (IQR), median (range))*: 32.6 ± 9.1 • *Weight (mean ± SD, median (IQR), median (range))*: 57.3 ± 10.9 • *BMI (mean ± SD, median (IQR), median (range))*: 23.3 ± 4.2 • *ASA I/II/III/IV (n)*: 38/5/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Hegde 2014 *(Continued)*

- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 82.3
- *Use of perioperative opioids (if yes, which?)*: intraoperative, postoperative fentanyl
- *Type of surgery*: gynaecological laparoscopic procedures

Ondansetron (4 mg PO group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 43
- *Received treatment (n)*: 43
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 30.7 ± 7.4
- *Weight (mean ± SD, median (IQR), median (range))*: 57.9 ± 11.8
- *BMI (mean ± SD, median (IQR), median (range))*: 23 ± 3.9
- *ASA I/II/III/IV (n)*: 40/3/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 75.6
- *Use of perioperative opioids (if yes, which?)*: intraoperative, postoperative fentanyl
- *Type of surgery*: gynaecological laparoscopic procedures

Ondansetron (8 mg PO group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 46
- *Received treatment (n)*: 46
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 29.8 ± 6.4
- *Weight (mean ± SD, median (IQR), median (range))*: 55.8 ± 12.4
- *BMI (mean ± SD, median (IQR), median (range))*: 22.7 ± 4.2
- *ASA I/II/III/IV (n)*: 38/5/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77.3
- *Use of perioperative opioids (if yes, which?)*: intraoperative, postoperative fentanyl
- *Type of surgery*: gynaecological laparoscopic procedures

Included criteria: ASA I or II, women 18 to 65 years of age, scheduled for elective gynaecological laparoscopic procedure under general anaesthesia

Excluded criteria: previous history of PONV or motion sickness, had received antiemetic therapy within 24 hours preoperatively, pregnant (except those undergoing medical termination of pregnancy with laparoscopic tubal ligation), receiving opioid and steroid treatment, with body mass index > 30

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics**

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Hegde 2014 *(Continued)*

	Placebo • *Dose*: placebo • *Time point of administration*: ODF placebo preoperative area just before shifting to operating room; saline placebo before induction of general anaesthesia • *Route of administration*: placebo ODF PO; saline placebo IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV Ondansetron (IV group) • *Dose*: 4 mg • *Time point of administration*: ODF placebo preoperative area just before shifting to operating room; ondansetron before induction of general anaesthesia • *Route of administration*: placebo ODF PO; ondansetron IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV Ondansetron (4 mg PO group) • *Dose*: 4 mg • *Time point of administration*: ODF ondansetron preoperative area just before shifting to operating room; saline placebo before induction of general anaesthesia • *Route of administration*: ondansetron ODF PO; saline placebo IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV Ondansetron (8 mg PO group) • *Dose*: 8 mg • *Time point of administration*: ODF ondansetron preoperative area just before shifting to operating room; saline placebo before induction of general anaesthesia • *Route of administration*: ondansetron ODF PO; saline placebo IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 8 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (7 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Delvin Formulations Pvt. Limited, Chennai, India, supplied free placebo ODFs for this study **Country:** India **Setting:** inpatient, single-centre

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Hegde 2014 *(Continued)*

Author's name: Harihar V. Hegde

Institution: Department of Anaesthesiology, SDM College of Medical Sciences and Hospital, Sattur, Dharwad, Karnataka, India

Email: drharryhegde@yahoo.co.in

Address: Department of Anaesthesiology, SDM College of Medical Sciences and Hospital, Dharwad - 580 009, Karnataka, India

Duration of study: March to September 2012

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a block randomisation technique with varying block sizes and serially numbered, sealed envelopes"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...and serially numbered, sealed envelopes. The envelopes were opened in the preoperative area just before administration of the study drug. All the patients were administered two ODFs in the preoperative area by one of the investigators just before shifting to the operating room. Patients in the ODF4 group received one ODF of ondansetron (containing ondansetron 4 mg) plus one placebo ODF, ODF8 group received two ODFs of ondansetron, whereas patients in the placebo and IV groups received two placebo ODFs. The placebo ODFs were formulated by the manufacturer of the ODF of ondansetron to have an identical appearance and flavour. In the operating room, after..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patient to tolerate oral intake. PONV was assessed in two epochs of 0-6 and 7-24 h by an anaesthesiologist who was not involved in administration of the study drugs, intraoperative management, and blinded to the group allocations. An 11-point numerical rating scale..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...was considered as significant. One hundred and eighty women were randomised into four groups. Since there was postoperative protocol violation in six patients and one patient received intraoperative methyl ergometrine, they were withdrawn from the study [Figure 1]. Data of 173 patients were analyzed. The patient characteristics, types of..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...of 173 patients were analyzed. The patient characteristics, types of surgical procedure, duration of surgery, duration of anaesthesia, duration of pneumoperitoneum, intraoperative consumption of fentanyl and airway (ETT/PLMA) usage were similar in all the four groups [Table 1]. Postoperative consumption of morphine, time to oral intake, time to first vomit, patient satisfaction score and the incidence of adverse effects were also comparable between

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Hegde 2014 *(Continued)*

	the groups [Table 2]. One patient each in the IV and ODF4 groups who complained of a headache postoperatively had headache preoperatively as well. All except two patients described ODF as 'pleasant'. One patient described ODF to be excessively sweet and the other described it as sweet to begin with and bitter later on. The incidence of postoperative nausea..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Heidari 2015a

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 37.9 ± 14.6 • *Weight (mean ± SD, median (IQR), median (range))*: 65.6 ± 10.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 19/11/0/0 • *Gender (female in %)*: 80 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 157.5 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, intraoperative morphine • *Type of surgery*: middle ear surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 36.3 ± 14.9 • *Weight (mean ± SD, median (IQR), median (range))*: 66.3 ± 13.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 18/12/0/0 • *Gender (female in %)*: 56.67 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)

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Heidari 2015a *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 139.2
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, intraoperative morphine
- *Type of surgery*: middle ear surgery

Included criteria: ASA I and II, between 18 and 60 years of age, non-pregnant or lactating females, not in menstruation period, without history of addiction or using antivomiting drugs, motion sickness, obesity (body mass index > 30), central nervous system disorders especially cerebellar problems, candidate for middle ear surgery

Excluded criteria: technique of anaesthesia was changed, uncontrolled bleeding during surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of motion sickness, duration of anaesthesia): no; (history of PONV, perioperative opioids, non-smoker): unclear

Interventions	**Intervention characteristics** Granisetron • *Dose*: 3 mg • *Time point of administration*: 2 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: placebo • *Time point of administration*: 2 minutes before induction of anaesthesia • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (8 to 16 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/ drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** source of support was Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Azim Honarmand **Institution:** Department of Anesthesia, Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

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Heidari 2015a *(Continued)*

Email: honarmand@med.mui.ac.ir

Address: Department of Anesthesia, Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Duration of study: November 2008 to November 2010

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	Two out of 3 groups relevant (gabapentin)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer generated randomization method"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "...a computer generated randomization method. Group I received 3 mg iv in a volume of 3 ml 2 minutes before induction of anesthesia; Group II received oral gabapentin 300 mg 1 hour before induction of anesthesia; Group III received placebo. The study drugs were administered by a physician who was not involved in data recording. Data gathering was performed by..." Judgement comment: participants may be aware of group allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...not involved in data recording. Data gathering was performed by a nurse who was not informed from the study group allocation. The standard monitoring included EKG"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the demographic and clinical data including sex, age, BMI, duration of surgery, duration of recovery stay and duration of anesthesia was not significantly different among three groups (P > 0.05) [Table 1]" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of motion sickness, duration of anaesthesia): no; (history of PONV, perioperative opioids, non-smoker): unclear

Heidari 2015b

Study characteristics

Methods	**Study design:** randomized controlled trial

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Heidari 2015b *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Scopalamine (hyoscine) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** 18 to 65 years old, ASA I and II, laparoscopic cholecystectomy **Excluded criteria:** allergy, cardiac disease **Pretreatment:** baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear (no information)
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 0.1 mg/kg • *Time point of administration*: 30 minutes before end of surgery

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Heidari 2015b *(Continued)*

	• *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: metoclopramide Scopalamine (hyoscine) • *Dose*: 0.15 mg/kg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: metoclopramide
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (at recovery)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Gholamreza Khalili **Institution:** Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran **Email:** khalili@med.mui.ac.ir **Address:** NA **Duration of study:** NA **Language:** Persian (translated by Arash Afshari) **Study's primary outcome:** postoperative shivering **Trial registry number:** NA
Notes	Two out of 3 groups relevant (pethidine)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly divided". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement

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Heidari 2015b *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear (no information)

Heinke 1996-1

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 43 • *Received treatment (n)*: NA • *Analysed (n)*: 43 • *Age (mean ± SD, median (IQR), median (range))*: 55.0 ± 17.3 • *Weight (mean ± SD, median (IQR), median (range))*: 74.8 ± 13.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 37.21 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: TIVA (propofol, alfentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 131.0 • *Use of perioperative opioids (if yes, which?)*: induction alfentanil 15 to 25 µg/kg, maintenance alfentanil 30 µg/kg/h • *Type of surgery*: pars plana vitrectomy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 42 • *Received treatment (n)*: NA • *Analysed (n)*: 42 • *Age (mean ± SD, median (IQR), median (range))*: 53.6 ± 16.0

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Heinke 1996-1 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 72.7 ± 13.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 45.24
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: TIVA (propofol, alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 118.9
- *Use of perioperative opioids (if yes, which?)*: induction alfentanil 15 to 25 µg/kg, maintenance alfentanil 30 µg/kg/h
- *Type of surgery*: pars plana vitrectomy

Included criteria: adults, ASA I to III, scheduled for pars plana vitrectomy

Excluded criteria: adipositas per magna, history of PONV

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia,): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: none • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV as second choice Droperidol • *Dose*: 2.5 mg • *Time point of administration*: at beginning of operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV as second choice
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** W. Heinke **Institution:** Klinik und Poliklinik für Anästhesiologie und Intensivtherapie der medizinischen Fakultät der Universität Leipzig **Email:** NA **Address:** Klinik und Poliklinik für Anästhesiologie und Intensivtherapie der medizinischen Fakultät der Universität Leipzig, Liebigstraße 20 a, D-04103 Leipzig **Duration of study:** February 1994 to March 1995

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Heinke 1996-1 *(Continued)*

	Language: German (2 German reviewers) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two sub-studies (TIVA + balanced anaesthesia)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "nach dem Zufallsprinzip" (translated: randomly). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no blinding (different anaesthetic techniques, no placebo intervention in control group)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: outcome assessment was made by physicians and nurses who were unaware of the applied anaesthetic technique
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia,): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Heinke 1996-2

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 39 • *Received treatment (n)*: NA • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 56.2 ± 15.4 • *Weight (mean ± SD, median (IQR), median (range))*: 77.6 ± 12.1

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Heinke 1996-2 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 38.46
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 118.2
- *Use of perioperative opioids (if yes, which?)*: induction alfentanil 15 to 25 µg/kg, maintenance alfentanil 30 µg/kg/h
- *Type of surgery*: pars plana vitrectomy

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 38
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 55.4 ± 15.9
- *Weight (mean ± SD, median (IQR), median (range))*: 78.1 ± 15.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 39.47
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 130.0
- *Use of perioperative opioids (if yes, which?)*: induction alfentanil 15 to 25 µg/kg, maintenance alfentanil 30 µg/kg/h
- *Type of surgery*: pars plana vitrectomy

Included criteria: adults, ASA I to III, scheduled for a pars plana vitrectomy

Excluded criteria: adipositas per magna, history of PONV

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia,): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: none • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV as second choice Droperidol • *Dose*: 2.5 mg • *Time point of administration*: at beginning of operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV as second choice
Outcomes	*PONV (0 to 24 hours)*

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Heinke 1996-2 *(Continued)*

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** W. Heinke **Institution:** Klinik und Poliklinik für Anästhesiologie und Intensivtherapie der medizinischen Fakultät der Universität Leipzig **Email:** NA **Address:** Klinik und Poliklinik für Anästhesiologie und Intensivtherapie der medizinischen Fakultät der Universität Leipzig, Liebigstraße 20 a, D-04103 Leipzig **Duration of study:** February 1994 to March 1995 **Language:** German (2 German reviewers) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two sub-studies (TIVA + balanced anaesthesia)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "nach dem Zufallsprinzip" (translated: randomly). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no blinding (different anaesthetic techniques, no placebo intervention in control group)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: outcome assessment was made by physicians and nurses who were unaware of the applied anaesthetic technique
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia,): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Helmers 1993

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 235 • *Age (mean ± SD, median (IQR), median (range))*: 42.9 ± 8.5 • *Weight (mean ± SD, median (IQR), median (range))*: 65.1 ± 10.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane/isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 91 • *Use of perioperative opioids (if yes, which?)*: 258.4, 37 • *Type of surgery*: abdominal hysterectomy, vaginal hysterectomy, gynaecological laparotomy, other major gynaecological surgery, other surgery Ondansetron (1 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 231 • *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 8.3 • *Weight (mean ± SD, median (IQR), median (range))*: 66.5 ± 10.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane/isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 91 • *Use of perioperative opioids (if yes, which?)*: 262.9, 35.4 • *Type of surgery*: abdominal hysterectomy, vaginal hysterectomy, gynaecological laparotomy, other major gynaecological surgery, other surgery Ondansetron (8 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Helmers 1993 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 228
- *Age (mean ± SD, median (IQR), median (range))*: 42.3 ± 8.4
- *Weight (mean ± SD, median (IQR), median (range))*: 65.7 ± 10.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93
- *Use of perioperative opioids (if yes, which?)*: 256.5, 35.6
- *Type of surgery*: abdominal hysterectomy, vaginal hysterectomy, gynaecological laparotomy, other major gynaecological surgery, other surgery

Ondansetron (16 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 229
- *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 8.8
- *Weight (mean ± SD, median (IQR), median (range))*: 65.4 ± 11.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 262.7 µg intraoperative fentanyl, 39.2 mg postoperative morphine
- *Type of surgery*: abdominal hysterectomy, vaginal hysterectomy, gynaecological laparotomy, other major gynaecological surgery, other surgery

Included criteria: women, ASA I or II; 18 to 65 years of age; scheduled to undergo gynaecological laparotomy, vaginal hysterectomy, or major vaginal surgery under general anaesthesia

Excluded criteria: evidence of uncontrolled clinically important neurological, renal, hepatic, cardiovascular, metabolic, or endocrine dysfunction or clinically important abnormalities in laboratory screening tests; experienced vomiting or had received an antiemetic 24 hours before administration of the study medication; participated in a clinical study with an unregistered compound within a month of taking part in the study; scheduled to have a nasogastric tube in situ postoperatively; weighed < 45 kg or > 90 kg, pregnant or breastfeeding

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics**

Placebo

- *Dose*: isotonic saline with citrate buffer
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV

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Helmers 1993 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: metoclopramide or prochlorperazine

Ondansetron (1 mg group)

- *Dose*: 1 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide or prochlorperazine

Ondansetron (8 mg group)

- *Dose*: 8 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide or prochlorperazine

Ondansetron (16 mg group)

- *Dose*: 16 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide or prochlorperazine

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 7 days)

- Outcome type: dichotomous outcome

Constipation (0 to 7 days)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 0 to 7 days)

- Outcome type: general notes on side effects

Identification

Sponsorship source: this study was supported by Glaxo Group Research Limited, Greenford, Middlesex, United Kingdom

Country: Netherlands, Irland, Sweden, United Kingdom, Republic of South Africa, France

Setting: inpatient, multi-centre

Author's name: Henk Helmers

Institution: Eemland Hospital- De Lichtenberg, Utrechtseweg 160, 3818 ES Amersfoort, The Netherlands

Email: NA

Address: 1 Maria Montessorilaan, 3818 LR Amersfoort, The Netherlands

Language: English

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Helmers 1993 *(Continued)*

	Duration of study: NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: no detailed information on randomization method provided ('randomized')
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no detailed information on blinding provided ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no detailed information on blinding provided ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: 7 out of 923 patients were excluded with reasons: protocol violations, incorrect surgery, a gastric tube, other prophylactic antiemetics
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no information on a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Helmy 1999

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 16

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Helmy 1999 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 23/17/0/0
- *Gender (female in %)*: 77.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 26/14/0/0
- *Gender (female in %)*: 80
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 137
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/16/0/0
- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 146
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA

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Helmy 1999 *(Continued)*

- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 76 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/18/0/0
- *Gender (female in %)*: 85
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 139
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: either sex, ASA I or II, scheduled for laparoscopic cholecystectomy under TIVA

Excluded criteria: history of drug abuse; previous allergic reactions to serotonin antagonists; had vomited or retched or had received any antiemetic therapy within 24 hours before surgery; clinical or laboratory evidence of renal, haematological, hepatic, cardiovascular, pulmonary, neurological, or endocrine disorder

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): unclear

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM

Placebo

- *Dose*: placebo
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (4 to 24 hours)

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Helmy 1999 *(Continued)*

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Egypt **Setting:** inpatient, single-centre **Author's name:** S.A.K. Helmy **Institution:** Department of Anaesthesia, Faculty of Medicine, Cairo University, Cairo, Egypt **Email:** NA **Address:** 2 Abdel-Wahab Saleim St., Maadi, Cairo, Egypt **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated to receive..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the anaesthetists, nurses and surgeons caring for these patients were blinded to the study drugs"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "anaesthetists, nurses and surgeons caring for these patients were blinded to the study drugs"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 160 patients were entered into the study (40 patients in each group). All patients underwent laparoscopic cholecystectomy under TIVA" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Helmy 1999 *(Continued)*

Other bias	Unclear risk	Quote: "there were no significant differences between the four study groups with regard to the demographic data, ASA grade, duration of anaesthesia, recovery time, administration of postoperative analgesic drugs or duration of hospital stay (Table 1). Analysis of pre-operative questioning did not show any significant differences with regard to the history of PONV, motion sickness or the incidence of drug allergies" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): unclear

Hemmati 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 46 • *Received treatment (n)*: NA • *Analysed (n)*: 46 • *Age (mean ± SD, median (IQR), median (range))*: 51.5 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 91.30 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 46 • *Received treatment (n)*: NA • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 47.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 84.09 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Hemmati 2014 *(Continued)*

- *Type of general anaesthesia*: TIVA (propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: undergoing laparoscopic cholecystectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear (no information). Potential effect modifiers (gender): no; (duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear (no information)

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 5 mg • *Time point of administration*: 10 minutes before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide Placebo • *Dose*: saline • *Time point of administration*: 10 minutes before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** R. Ghorbani **Institution:** Research Center for Social Determinants of Health, Department of Community Medicine, Semnan University of Medical Sciences, Semnan, I.R. Iran **Email:** r_ghorbani@semums.ac.ir **Address:** Training Community of Semnan University of Medical Sciences, Damghan, Semnan, I.R. Iran **Duration of study:** NA **Language:** Persian (translated by Amir Farahani) **Study's primary outcome:** NA **Trial registry number:** IRCT2014062118168N1
Notes	None

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Hemmati 2014 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "divided the patients into two groups randomly". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: exclusion of 2 patients in the saline group. Reason for exclusion was severe vomiting and nausea
Selective reporting (reporting bias)	Unclear risk	Judgement comment: IRCT2014062118168N1 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear (no information). Potential effect modifiers (gender): no; (duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear (no information)

Hessami 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 53 • *Received treatment (n)*: 53 • *Analysed (n)*: 53 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 6.1 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26.3 ± 4.4 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 77.36 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Hessami 2012 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 59
- *Use of perioperative opioids (if yes, which?)*: incremental doses of 5 µg sufentanil administered every 15 minutes
- *Type of surgery*: laparoscopic cholecystectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 51
- *Received treatment (n)*: 51
- *Analysed (n)*: 51
- *Age (mean ± SD, median (IQR), median (range))*: 41.2 ± 8.2
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 27.2 ± 5.1
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 72.55
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 63
- *Use of perioperative opioids (if yes, which?)*: incremental doses of 5 µg sufentanil administered every 15 minutes
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, 20 to 60 years or age, laparoscopic cholecystectomy

Excluded criteria: pregnancy, BMI > 30, history of previous abdominal surgery, existence of underlying disease, opium or steroid consumption during the week before the operation

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

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Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: 15 minutes before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 6% (metoclopramide 10 mg)

Granisetron

- *Dose*: 3 mg
- *Time point of administration*: 15 minutes before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 4% (metoclopramide 10 mg)

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

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Hessami 2012 *(Continued)*

	Subjects with any AE (0 to 24 hours) • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** none declared **Country:** Iran **Setting:** NA **Author's name:** Mitra Yari **Institution:** Department of Surgery, Kermanshah University of Medical Sciences, Kermanshah, IR Iran **Email:** myari@kums.ac.ir **Address:** Department of Anaesthesiology, Kermanshah University of Medical Sciences, Imam Reza Hospital, Parastar Blvd, Kermanshah, IR Iran **Language:** English **Duration of study:** NA **Trial registry number:** IRCT138903033939N1 **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: "the patients were allocated, by computer-generated random numbers, into tow groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: "concealed in sealed opaque envelopes until a group was assigned." Not stated as "sequentially numbered" envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: IRCT138903033939N1 (retrospective registration)

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Hessami 2012 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Ho 1990

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 30 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 54 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction • *Type of surgery*: laparoscopy Prochlorperazine (group IV) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 30 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 49 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction • *Type of surgery*: laparoscopy

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Ho 1990 *(Continued)*

Included criteria: female, ASA I or II, between 18 and 50 years of age, 42 to 79 kg in weight, underwent outpatient laparoscopy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Control (group I) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: NA Prochlorperazine (group IV) • *Dose*: 5 mg • *Time point of administration*: immediately after admission to recovery room • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** outpatient, single-centre **Author's name:** R.T. Ho **Institution:** Department of Anesthesiology, Chang Gung Memorial Hospital, 123, Ta-Pei Road, Niao Sung Hsiang, Kaohsiung Hsein, Taiwan, R.O.C. **Email:** NA **Address:** Department of Anesthesiology, Chang Gung Memorial Hospital, 123, Ta-Pei Road, Niao Sung Hsiang, Kaohsiung Hsein, Taiwan, R.O.C. **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 4 groups relevant (electro-acupuncture)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...the end of the procedure. The patients were allocated randomly to one of four groups, each consisting of 25 persons"

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Ho 1990 *(Continued)*

		Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no blinding (different interventions, no treatment in control group)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the age, weight, and duration of anaesthesia did not differ significantly among the groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Honarmand 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Haloperidol (group H) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 38.7 ± 15.8 • *Weight (mean ± SD, median (IQR), median (range))*: 66.8 ± 13.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 13/7/0/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: 75 • *History of PONV/motion sickness (%)*: 15/15 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 214.0

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Honarmand 2012 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 3 µg/kg fentanyl at induction, intraoperative morphine, 0.05 mg meperidine as rescue analgesic
- *Type of surgery*: middle ear surgery (tympanoplasty or mastoidectomy)

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 37.3 ± 14.1
- *Weight (mean ± SD, median (IQR), median (range))*: 61.8 ± 13.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 16/4/0/0
- *Gender (female in %)*: 65
- *Non-smoker (%)*: 95
- *History of PONV/motion sickness (%)*: 15/10
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 221.0
- *Use of perioperative opioids (if yes, which?)*: 3 µg/kg fentanyl at induction, intraoperative morphine, 0.01 mg meperidine as rescue analgesic
- *Type of surgery*: middle ear surgery (tympanoplasty or mastoidectomy)

Included criteria: ASA I or II, 18 to 60 years old, scheduled for middle ear surgery (tympanoplasty or mastoidectomy)

Excluded criteria: gastrointestinal tract disease; diabetes mellitus; difficult airway; psychiatric disorder; seizure disorder; Parkinson's disease; previous intolerance to haloperidol administration; nausea and vomiting; obesity (BMI > 35 kg/m^2); QTc interval > 450 ms; received any antiemetics within 24 hours before surgery; allergy to metoclopramide, meperidine, or haloperidol; history of extrapyramidal syndrome or akathisia; pregnancy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

Interventions	**Intervention characteristics** Haloperidol (group H) • *Dose*: 2 mg • *Time point of administration*: 30 minutes before conclusion of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; 2.5 mg (mean) Placebo (group C) • *Dose*: saline • *Time point of administration*: 30 minutes before conclusion of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; 6.5 mg (mean)
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome

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Honarmand 2012 *(Continued)*

Arrhythmia (0 to 24 hours)

- Outcome type: dichotomous outcome

QT prolongation (0 to 24 hours)

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Mohammadreza Safavi **Institution:** Departments of Anesthesiology and Critical Care, Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran **Email:** safavi@med.mui.ac.ir **Address:** Department of Anesthesiology and Critical Care, Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	Two out of 4 groups relevant (midazolam)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "by using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "...i.v.. A nurse anesthetist prepared identical syringes containing either normal saline or the study medications for each subject" Judgement comment: no information on blinding of anaesthesiologists
Blinding of outcome assessment (detection bias)	Low risk	Quote: "the patients and investigator who collected all data were blinded to the group randomization"

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Honarmand 2012 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "80 patients were enrolled in the study. No patient was excluded from the study due to any problem"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "...study due to any problem. There was no difference in patient characteristics such as sex, ASA, age, weight, types of operation performed, history of PONV, motion sickness, smoking, phase of menstrual cycle, time to tracheal extubation, duration of PACU stay, durations of surgery and anesthesia among the 4 groups [Table 1]" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

Honarmand 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: 35 • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 26.4 ± 13.6 • *Weight (mean ± SD, median (IQR), median (range))*: 70.0 ± 9.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 19/16/0/0 • *Gender (female in %)*: 25.71 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 147.5 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 2 µg/kg, morphine 0.1 mg/kg • *Type of surgery*: mastoidectomy, tympanoplasty Placebo (group S) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: 35 • *Analysed (n)*: 35

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Honarmand 2016 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 25.6 ± 13.5
- *Weight (mean ± SD, median (IQR), median (range))*: 69.4 ± 8.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 20/15/0/0
- *Gender (female in %)*: 17.14
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 144.7 ± 13.4
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 2 µg/kg, morphine 0.1 mg/kg
- *Type of surgery*: mastoidectomy, tympanoplasty

Included criteria: ASA I or II; 18 to 62 years of age; scheduled for elective middle ear surgery, mastoidectomy, or tympanoplasty

Excluded criteria: history of motion sickness, antiemetic therapy within 24 hours preoperatively, receiving opioid treatment, smoking, pregnancy, with anaesthetic technique changed

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness): no; (history of PONV, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: IV metoclopramide 0.15 mg/kg Placebo (group S) • *Dose*: 0.9% • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: IV metoclopramide 0.15 mg/kg
Outcomes	*Vomiting (0 to 2 hours, score 2 + 3)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours, score 2 + 3)* • Outcome type: dichotomous outcome *Headache (time point unknown)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran **Country:** Iran **Setting:** NA

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Honarmand 2016 *(Continued)*

Author's name: Mohammadreza Safavi

Institution: Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences Isfahan, Iran

Email: safavi@med.mui.ac.ir

Address: NA

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: incidence of PONV

Notes	Two out of 4 groups relevant (midazolam)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomization was done by using random allocation software"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study drugs were administered by an anesthesiologist blinded to data collection"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "no patient was excluded"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness): no; (history of PONV, perioperative opioids): unclear

Honkavaara 1996

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics**

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Honkavaara 1996 *(Continued)*

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 42.11
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: middle ear surgery

Ondansetron (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: middle ear surgery

Ondansetron (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA

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Honkavaara 1996 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: middle ear surgery

Included criteria: undergoing middle ear surgery, ASA I or II, 15 to 62 years of age

Excluded criteria: regular or temporary use of antiemetic drugs, vomiting or retching within 24 hours before operation

Pretreatment: baseline characteristics (age, weight, ASA): no (no data provided). Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no (no data provided); (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: placebo • *Time point of administration*: after insertion of an IV cannula, before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 63.16% (droperidol 10 µg/kg IV or IM) Ondansetron (4 mg group) • *Dose*: 4 mg • *Time point of administration*: after insertion of an IV cannula, before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 37.5% (droperidol 10 µg/kg IV or IM) Ondansetron (8 mg group) • *Dose*: 8 mg • *Time point of administration*: after insertion of an IV. cannula, before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 50% (droperidol 10 µg/kg IV or IM)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatient, single-centre **Author's name:** Pekka Honkavaara **Institution:** Department of Anaesthesia, Otolaryngological Hospital, University of Helsinki, Haartmaninkatu, Helsinki, Finland **Email:** NA **Address:** Department of Anaesthesia, Otolaryngological Hospital, University of Helsinki, Haartmaninkatu 4E, FIN-00290 Helsinki, Finland

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Honkavaara 1996 *(Continued)*

	Duration of study: NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "twenty-five patients were allocated randomly to one of three groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "...in a double-blind manner" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a trained nurse, who was unaware of the nature of the study drug, assessed the incidence of nausea, retching and vomiting"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "PONV and ear surgery 317 patients in the placebo and ondansetron groups did not differ significantly in age, weight, sex, phases of the menstrual cycle, details of anaesthesia, duration of anaesthesia or operation, mean concentration of inspired isoflurane, total dose of fentanyl given, dose of lignocaine given topically during surgery or need for oxycodone after operation. There were no side effects" Judgement comment: baseline characteristics (age, weight, ASA): no (no data provided). Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no (no data provided); (history of PONV/motion sickness, non-smoker): unclear

Hu 2017

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis

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Hu 2017 *(Continued)*

Participants

Baseline characteristics

Palonosetron (group P 2.5)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 43
- *Received treatment (n)*: 43
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 40.60 ± 13.08
- *Weight (mean ± SD, median (IQR), median (range))*: 61.96 ± 12.07
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 32.56
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 73.30
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, postoperative tramadol
- *Type of surgery*: eye enucleation, orbital hydroxyapatite implant surgery

Palonosetron (group P 7.5)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 43
- *Received treatment (n)*: 43
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 44.93 ± 14.01
- *Weight (mean ± SD, median (IQR), median (range))*: 64.28 ± 8.70
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 32.56
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 69.12
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, postoperative tramadol
- *Type of surgery*: eye enucleation, orbital hydroxyapatite implant surgery

Palonosetron + droperidol (group P + D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 43
- *Received treatment (n)*: 43
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 42.56 ± 13.48
- *Weight (mean ± SD, median (IQR), median (range))*: 69.12 ± 14.20
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 30.23
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA

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Hu 2017 *(Continued)*

- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77.23
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, postoperative tramadol
- *Type of surgery*: eye enucleation, orbital hydroxyapatite implant surgery

Included criteria: 18 to 70 years of age, ASA I and II, scheduled for elective eye enucleation and orbital hydroxyapatite implant surgery

Excluded criteria: history of gastrointestinal, liver, and kidney disease, allergy to 5-HT3 receptor antagonists and droperidol, intake of antiemetics 24 hours preoperatively

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear

Interventions	**Intervention characteristics** Palonosetron (group P 2.5) • *Dose*: 2.5 µg/kg • *Time point of administration*: between 10 seconds and 5 minutes before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 150 µg/kg IM Palonosetron (group P 7.5) • *Dose*: 7.5 µg/kg • *Time point of administration*: between 10 seconds and 5 minutes before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 150 µg/kg IM Palonosetron + droperidol (group P + D) • *Dose*: palonosetron 2.5 µg/kg, droperidol 15 µg/kg • *Time point of administration*: between 10 seconds and 5 minutes before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 150 µg/kg IM
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *QT prolongation (0 to 72 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 72 hours)* • Outcome type: dichotomous outcome *Headache (0 to 72 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 72 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 72 hours)*

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Hu 2017 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** study authors report no conflicts of interest in this work **Country:** China **Setting:** inpatient, single-centre **Author's name:** Fang Tan **Institution:** Department of Anesthesiology, Eye, Ear, Nose and Throat Hospital of Fudan University, Shanghai Medical College of Fudan University, Shanghai, China **Email:** tanfang@eentanesthesia.com **Address:** Department of Anesthesiology, Eye, Ear, Nose and Throat Hospital of Fudan University, Shanghai Medical College of Fudan University, 83 Fenyang Road, Xuhui, Shanghai, China **Language:** English **Duration of study:** 20 January 2015 to 30 June 2015 **Trial registry number:** ChiCTR-IPR-15005852 **Study's primary outcome:** complete response (CR) rates at 4, 24, 48, and 72 hours after surgery
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number list in a block of three"
Allocation concealment (selection bias)	Unclear risk	Quote: "kept in sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque" envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the current study used a randomized, double-blind, positive-controlled method for patients, researchers, and staff in charge of data collection" Quote: "the envelope was opened by a nurse anaesthetist not involved in the study, who also prepared the palonosetron (Ousai [palonosetron hydrochloride injection]; specification: 5 mL, 0.25 mg; Qilu Pharmaceutical Co., Ltd., Hainan, China) and droperidol treatments (droperidol injection; specification: 2 mL, 5 mg..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the data were assessed by the researchers when they were unaware of treatment allocation" Judgement comment: the study was blinded 'for patients, researchers, and staff in charge of data collection
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 129 patients were enrolled in the study, and all patients completed this clinical trial (Figure 1)"

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Hu 2017 *(Continued)*

		Judgement comment: no missing outcome data
Selective reporting (reporting bias)	High risk	Judgement comment: ChiCTR-IPR-15005852 (prospective registration). One primary outcome (time to treatment failure) was not reported in the final study report and another primary outcome (severity of nausea and vomiting) changed to a secondary endpoint in the final study report. Three prespecified study arms were not reported in the final study report (granisetron, palonosetron 5 µg/kg, palonosetron with dexamethasone)
Other bias	Low risk	Quote: "the baseline characteristics, such as age, height, body weight, anaesthesia time, and Apfel's simplified risk score for PONV (female gender, nonsmoking status, prior history of motion sickness or PONV, postoperative opioids), 14 of the patients were balanced among all the three groups (P.0.05; Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear

Huang 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 32 (27 to 35) • *Weight (mean ± SD, median (IQR), median (range))*: 54 (42 to 72) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 65 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction • *Type of surgery*: laparoscopic tubal ligation Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 38

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Huang 2001 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 34 (31 to 36)
- *Weight (mean ± SD, median (IQR), median (range))*: 56 (46 to 75)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 68
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic tubal ligation

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 35 (30 to 37)
- *Weight (mean ± SD, median (IQR), median (range))*: 56 (45 to 76)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 64
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: laparoscopic tubal ligation

Included criteria: women, ASA I or II, scheduled for outpatient laparoscopic tubal ligation

Excluded criteria: breastfeeding, weighing > 90 kg, history of PONV, motion sickness, had received an antiemetic within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 5 mg • *Time point of administration*: after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10%; ondansetron 4 mg IV Metoclopramide • *Dose*: 10 mg • *Time point of administration*: after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 26%; ondansetron 4 mg IV Placebo

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Huang 2001 *(Continued)*

- *Dose*: saline
- *Time point of administration*: after tracheal intubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 42%; ondansetron 4 mg IV

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours, PACU)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** outpatient, single-centre **Author's name:** Jhi-Joung Wang **Institution:** Department of Medical Research and Anesthesiology, Chi-Mei Medical Center, Tainan; and the Department of Anesthesiology, Kaohsiung Medical University, Kaohsiung, Taiwan **Email:** 400003@mail.chimei.org.tw **Address:** Department of Anesthesiology, Chi-Mei Medical Center, Tainan, Taiwan. Phone: 886-6-2517844; Fax: 886-6-2832639 **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer generated random number table"

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Huang 2001 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications totaled 2 mL, were prepared by one of the investigators and were administered in a double-blind fashion"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...protection. The patients and the investigator who collected the data were blinded to the patient's group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 120 patients enrolled in this study, three patients who did not complete the surgical procedure (laparoscopic tubal ligation) due to intra-abdominal adhesions and two patients who could not be contacted by telephone after hospital discharge were eliminated from the study. The data obtained from the remaining 115 patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the patients' characteristics (e.g., age, weight, and height), interval since the last menstrual period and the durations of anesthesia and surgery were similar among the groups (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Huang 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 21 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 39.7 ± 5.5 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 22.7 ± 1.2 • *ASA I/II/III/IV (n)*: 13/7/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 52.4

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Huang 2016 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 1 patient with postoperative sufentanil 5 μg
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron + dexamethasone (group 3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 22
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 38.6 ± 8.9
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 22.5 ± 2.0
- *ASA I/II/III/IV (n)*: 15/5/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 54.3
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 2 patients with postoperative sufentanil 5 μg
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, had undergone laparoscopic cholecystectomy

Excluded criteria: systemic cardiovascular or endocrine disease, coagulopathy, needle puncture site infection, BMI > 30, history of chronic pain, hypersensitive or allergic to any medicine

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (gender, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group 2) • *Dose*: 0.1 mg/kg • *Time point of administration*: end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron + dexamethasone (group 3) • *Dose*: ondansetron 0.1 mg/kg, dexamethasone 10 mg • *Time point of administration*: ondansetron end of surgery, dexamethasone after intubation • *Route of administration*: ondansetron IV, dexamethasone perineural • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)*

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Huang 2016 *(Continued)*

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** none **Country:** China **Setting:** inpatient, single-centre **Author's name:** Shuan-Ke Wang **Institution:** Department of Anesthesiology and Department of Orthopedics, Second Hospital of Lanzhou University, Lanzhou 730030, China **Email:** wsk2zzy@126.com **Address:** Department of Orthopedics, Second Hospital of Lanzhou University, Lanzhou 730030, China **Duration of study:** November 2013 to April 2014 **Language:** English **Study's primary outcome:** effect of intervention on time of first request for additional analgesics **Trial registry number:** NA
Notes	Two out of 3 groups relevant (without TAP block)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly divided" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "patients and postoperative assessors were blinded to the intervention protocol, while members of anesthesia and operation groups were not blinded"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperative assessors were blinded to the intervention protocol"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...was considered statistically significant. In 65 patients initially enrolled, 5 were excluded: 2 patients in group I and 1 patient in group III were converted to open cholecystectomy"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the patients in all groups were comparable in age, BMI and operative time (Table 1)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (gender, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Huseyinoglu 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 28 • *Received treatment (n)*: 28 • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 30.46 ± 3.25 • *Weight (mean ± SD, median (IQR), median (range))*: 79.08 ± 11.27 • *BMI (mean ± SD, median (IQR), median (range))*: 29.41 ± 4.05 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 42.50 • *Use of perioperative opioids (if yes, which?)*: 50 µg intraoperative fentanyl, 50 mg meperidine at end of surgery • *Type of surgery*: elective caesarean birth Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 28 • *Received treatment (n)*: 28 • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 30.78 ± 3.96 • *Weight (mean ± SD, median (IQR), median (range))*: 77.39 ± 10.69 • *BMI (mean ± SD, median (IQR), median (range))*: 28.58 ± 3.32 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 40.07 • *Use of perioperative opioids (if yes, which?)*: 50 µg intraoperative fentanyl, 50 mg meperidine at end of surgery • *Type of surgery*: elective caesarean birth Dimenhydrinate • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 28

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Huseyinoglu 2016 *(Continued)*

- *Received treatment (n)*: 28
- *Analysed (n)*: 28
- *Age (mean ± SD, median (IQR), median (range))*: 29.50 ± 6.27
- *Weight (mean ± SD, median (IQR), median (range))*: 78.09 ± 11.39
- *BMI (mean ± SD, median (IQR), median (range))*: 29.63 ± 4.13
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 40.50
- *Use of perioperative opioids (if yes, which?)*: 50 µg intraoperative fentanyl, 50 mg meperidine at end of surgery
- *Type of surgery*: elective caesarean birth

Included criteria: pregnant women scheduled for elective caesarean births, singleton pregnancies at 39 or more gestational weeks

Excluded criteria: women with rupture of membranes, placental insertion anomalies, active labor; history of nausea and vomiting; maternal (hypertensive pregnancy disorder, gestational or pre-gestational diabetes, maternal vascular disease, urinary tract infection, any known chronic illness) or foetal (rupture of membranes, congenital malformations, intrauterine growth restriction, abnormal non-stress test or biophysics profile) complications

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV, duration of anaesthesia, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: NaCl • *Time point of administration*: 1 hour before anticipated procedure • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: 50%; ondansetron hydrochloride 4 mg Metoclopramide • *Dose*: 10 mg • *Time point of administration*: 1 hour before anticipated procedure • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: 7%; metoclopramide Dimenhydrinate • *Dose*: 50 mg • *Time point of administration*: 1 hour before anticipated procedure • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: 11%; dimenhydrinate
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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Huseyinoglu 2016 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Kahraman Ülker **Institution:** Istanbul Memorial Hospital **Email:** kahramanulker@hotmail.com **Address:** Istanbul Memorial Hospital, Okmeydanı, S¸is¸li, 3483 Istanbul, Turkey **Duration of study:** December 2010 to June 2011 **Language:** English **Study's primary outcome:** PONV rate **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated randomization table"
Allocation concealment (selection bias)	Unclear risk	Quote: "on the morning of the surgery, the women were admitted to the obstetrics and gynecology department and assigned into one of the groups by the nurse responsible for the follow-up. In case where a woman changed her mind to participate or receive regional anesthesia, the next woman was assigned into the same group in the same order and received the same protocol number" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "patients were blinded to the medication they received" Judgement comment: no further information on blinding of anaesthesiologists
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 95 women invited to participate, 11 did not participate in the study. Three of them did not want to participate in the study and eight of them changed their mind in the operative theatre and received regional anesthesia"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic data including maternal age, height, weight, body mass index, gravidity, parity, miscarriage, induced abortion, the number of offspring, and the medical history did not show significant differences among the three groups (p [0.05). Table 1 summarizes the comparison of the demographic data of the groups"

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Huseyinoglu 2016 *(Continued)*

	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV, duration of anaesthesia, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Hval 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 53 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 8.7 • *BMI (mean ± SD, median (IQR), median [range])*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 84 • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg was given 10 minutes before the end of surgery and rescue analgesia with fentanyl 0.5 µg/kg IV upon request • *Type of surgery*: breast surgery Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 52 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 70 • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg was given 10 minutes before the end of surgery and rescue analgesia with fentanyl 0.5 µg/kg IV upon request

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Hval 2007 *(Continued)*

- *Type of surgery*: breast surgery

Included criteria: females, admitted for ambulatory breast cancer surgery expected to last 1 to 2 hours, between 18 and 60 years of age, ASA I or II

Excluded criteria: psychiatric, neurological, or liver disease; diabetes; used regular medication with known or suspected sedative or analgesic effects; excessive alcohol drinkers or drug abusers; any contraindication to NSAIDs, glucocorticoids, or other drugs planned for anaesthesia; intake of any sedatives or analgesics for the last 24 hours

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids -> no difference in risk factors reported): unclear

Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 16 mg • *Time point of administration*: shortly after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 20 mg IV Placebo (group P) • *Dose*: NA • *Time point of administration*: shortly after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 20 mg IV
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Intramural Departmental Funding **Country:** Norway **Setting:** outpatient **Author's name:** Johan Raeder **Institution:** Departments of Anaesthesia and Surgery, Ullevaal University Hospital, Oslo, Norway **Email:** johan.rader@medisin.uio.no **Address:** Department of Anaesthesia, Ullevaal University Hospital, N-0407 Oslo, Norway **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** pain (VAS > 0 on a 0 to 10 scale) during first 24 hours after discharge

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Hval 2007 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated list of random numbers"
Allocation concealment (selection bias)	Unclear risk	Quote: "the syringes were drawn up by a nurse not participating in any other aspect of the study, and labeled with the patient number" Judgement comment: insufficient information to judge whether the investigator could have foreseen allocation of participants to groups
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the syringes were drawn up by a nurse not participating in any other aspect of the study, and labeled with the patient number" Judgement comment: because the nurse who prepared the medication was not participating in any other aspect of the study, we assume blinding of participants and anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "there were no drop-outs"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the groups in preoperative risk factors for nausea (i.e., nonsmoking status, previous travel sickness or post- operative nausea and vomiting) or pain (i.e., preoperative pain, pain or analgesics last week), or in pre- or perioperative medication (data not shown)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids -> no difference in risk factors reported): unclear

Ibrahim 2013

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Ibrahim 2013 *(Continued)*

- *Randomized (n)*: 21
- *Received treatment (n)*: NA
- *Analysed (n)*: 21
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25 ± 5
- *ASA I/II/III/IV (n)*: 12/9/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 80.95
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 107
- *Use of perioperative opioids (if yes, which?)*: 1.8 µg/kg intraoperative fentanyl
- *Type of surgery*: breast surgery (mastectomy, tumour biopsy, reductive mastoplasty, other plastic surgery)

Olanzapine (5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 21
- *Received treatment (n)*: NA
- *Analysed (n)*: 21
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 4
- *ASA I/II/III/IV (n)*: 10/11/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 76.19
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 103
- *Use of perioperative opioids (if yes, which?)*: 2.0 µg/kg intraoperative fentanyl
- *Type of surgery*: breast surgery (mastectomy, tumour biopsy, reductive mastoplasty, other plastic surgery)

Olanzapine (10 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 27 ± 4
- *ASA I/II/III/IV (n)*: 12/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 75
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 110
- *Use of perioperative opioids (if yes, which?)*: 2.1 µg/kg intraoperative fentanyl

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Ibrahim 2013 *(Continued)*

- *Type of surgery*: breast surgery (mastectomy, tumour biopsy, reductive mastoplasty, other plastic surgery)

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 5
- *ASA I/II/III/IV (n)*: 11/9/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 85
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105
- *Use of perioperative opioids (if yes, which?)*: 1.9 µg/kg intraoperative fentanyl
- *Type of surgery*: breast surgery (mastectomy, tumour biopsy, reductive mastoplasty, other plastic surgery)

Included criteria: females scheduled for breast surgery (mastectomy, tumour biopsy, reductive mastoplasty, other plastic surgery), ASA I or II

Excluded criteria: pre-existing nausea, vomiting, or motion sickness; receiving opioids or drugs with known antiemetic properties in the 24 hours before surgery; history of oesophageal reflux or opioid or alcohol abuse; serum creatinine > 2.0 mg/dL; serum alanine aminotransferase (ALT) or aspartate transaminase (AST) > 2 times the upper limit of normal; body weight twice the ideal body weight

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness): no; (history of PONV): unclear

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Interventions

Intervention characteristics

Placebo

- *Dose*: sugar pills
- *Time point of administration*: 4 hours and 1 hour before induction
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: NA

Olanzapine (5 mg group)

- *Dose*: 5 mg
- *Time point of administration*: 4 hours before induction of anaesthesia, placebo 1 hour before induction
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: NA

Olanzapine (10 mg group)

- *Dose*: 10 mg
- *Time point of administration*: 4 hours before induction of anaesthesia, placebo 1 hour before induction
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron

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Ibrahim 2013 *(Continued)*

- *Dose*: 16 mg
- *Time point of administration*: 1 hour before induction of anaesthesia, placebo 4 hours before induction
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Arrhythmia (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Egypt **Setting:** inpatient, single-centre **Author's name:** Mohamed Ibrahim **Institution:** Department of Anaesthesia, Zagazig University, Egypt **Email:** mibrahim72@windowslive.com **Address:** Palestine Madina Road, P.O. Box 7692, Jeddah 21472, Saudi Arabia **Duration of study:** NA **Language:** English **Study's primary outcome:** emetic episodes and occurrence of nausea **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated to one of four groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "after a patient was assigned to a treatment group, the assignment was recorded and placed in a sealed envelope by a person not involved in the study. A pharmacist, who was also not involved in the study, prepared the study medications and sealed it in an envelope"

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Ibrahim 2013 *(Continued)*

		Judgement comment: it is unclear how the allocation was done
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "to ensure blindness, placebo drug was given in OL5 and OL10 groups 1 h before induction and 4 h before induction in ON16. Placebo group of patients received sugar pills 4 and 1 h before induction" Quote: "a nurse or a physician, who was blinded to the patient treatment groups, gave the study drugs and recorded preoperative and postoperative data" Quote: "a pharmacist, who was also not involved in the study, prepared the study medication and sealed it in an envelope" Quote: "the trial arms in the study were blinded in spite of different olanzapine and ondansetron pharmacokinetics that affect time of drug administration"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a nurse or a physician, who was blinded to the patient treatment groups, gave the study drugs and recorded preoperative and postoperative data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "eighty-two patients were included in the study" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences in patients' characteristics between treatment groups, including relation of surgery time with stage of menstrual cycle. The mean duration of anesthesia and duration of operation were not different. Also, no significant differences were noted among groups with respect to surgery type (Table 1)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness): no; (history of PONV): unclear

Ionescu 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 50 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Ionescu 2007 *(Continued)*

- *ASA I/II/III/IV (n)*: 16/14/0/0
- *Gender (female in %)*: 30
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (fentanyl, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 50
- *Use of perioperative opioids (if yes, which?)*: 0.007 mg/kg intraoperative fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 51 ± 16
- *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 13/17/0/0
- *Gender (female in %)*: 23
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (fentanyl, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 52
- *Use of perioperative opioids (if yes, which?)*: 0.006 mg/kg intraoperative fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: laparoscopic cholecystectomy under general anaesthesia, ASA I or II

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 4 mg • *Time point of administration*: before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.0162 mg/kg (NA) Ondansetron • *Dose*: 4 mg • *Time point of administration*: before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.00261 mg/kg (NA)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)*

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Ionescu 2007 *(Continued)*

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** Russia **Setting:** inpatient, single-centre **Author's name:** D. Ionesku **Institution:** NA **Email:** NA **Address:** NA **Duration of study:** NA **Language:** Russian (translated by Alena Rudenko) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "sealed envelope method" (Translation). Insufficient information on allocation concealment. Not stated SNOSE
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "a nurse not involved in the study prepared and applied the study drugs in identical syringes" (translation)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

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Ionescu 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 23 • *Received treatment (n)*: NA • *Analysed (n)*: 22 • *Age (mean ± SD, median (IQR), median (range))*: 54.9 ± 13.5 • *Weight (mean ± SD, median (IQR), median (range))*: 75.5 ± 14.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 10/12/0/0 • *Gender (female in %)*: 63.64 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 41.6 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 0.78 mg/kg postoperative pethidine • *Type of surgery*: laparoscopic cholecystectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 23 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 50.8 ± 13.9 • *Weight (mean ± SD, median (IQR), median (range))*: 80.3 ± 7.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 10/10/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 44.9 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 1.01 mg/kg postoperative pethidine • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** ASA I or II, scheduled for laparoscopic cholecystectomy under general anaesthesia **Excluded criteria:** immune system disorders, known inflammatory disease (including acute cholecystitis), abnormal white cell count, asthma, obesity (BMI ≥ 30 kg/m^2), diabetes, gastric ulcer, allergies, history of PONV, current steroid or anti-inflammatory medication

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Ionescu 2014 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV, duration of anaesthesia): no; (history of motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg, ondansetron 4 mg Placebo • *Dose*: saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg, ondansetron 4 mg
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** the study was supported by research grant no. 41025 funded by the National Centre for the Management of Projects (CNMP), Romania **Country:** Romania **Setting:** inpatient, single-centre **Author's name:** Daniela C. Ionescu **Institution:** Department of Anesthesia and Intensive Care, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Email:** daniela_ionescu@umfcluj.ro **Address:** DEAA, Sectia ATI, Clinica Chirurgie III, Str. Croitorilor, nr 19 - 21, 400162 Cluj-Napoca, Romania **Duration of study:** January 2008 and August 2009 **Language:** English **Study's primary outcome:** IL-6 concentration **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Ionescu 2014 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated sequence"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "before induction of anaesthesia, dexamethasone 4 mg (1 ml clear solution) was given to patients in the dexamethasone group, and isotonic saline 1 ml was administered to patients in the control group" Judgement comment: no statement on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the interleukin assays were performed in one laboratory by the same team for all patients; the laboratory staff were not aware of the study group and were not involved in the patients' anaesthesia" Judgement comment: no information about PONV assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 46 enrolled patients, 42 completed the study. One patient was excluded from the dexamethasone group because of acute inflammation of the gall bladder discovered intraoperatively despite meeting the inclusion criteria, and three patients were excluded" Judgement comment: "...from the control group due to technical problems. We present the data from the remaining 42 patients who completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic and clinical data were similar in both groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV, duration of anaesthesia): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Isik 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 41.03 ± 12.6 • *Weight (mean ± SD, median (IQR), median (range))*: 70.7 ± 11.95 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 26/4/0/0

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Isik 2006 *(Continued)*

- *Gender (female in %)*: 46.67
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 224.25
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: middle ear surgery

Dexamethasone (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 36.2 ± 11.2
- *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 17.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/6/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 213.33
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: middle ear surgery

Included criteria: 25 to 55 years of age, undergoing mastoidectomy under general anaesthesia, ASA I or II

Excluded criteria: used any antiemetic drugs in the last 24 hours, history of vertigo in motor vehicles, smokers

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of motion sickness): no; (history of PONV): unclear

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: after surgical skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10%; not defined Dexamethasone (group D) • *Dose*: 5 mg • *Time point of administration*: immediately after anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 36.7%; not defined
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 12 hours)*

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Isik 2006 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Mustafa Arslan **Institution:** Department of Anesthesiology and Reanimation, Faculty of Medicine, Gazi University, Bsevler, Ankara, Turkey **Email:** marslan36@yahoo.com, marslan36@hotmail.com **Address:** 48. Sokak, Seda Apartmanı, 24/17, Yenimahalle-Kirikkale, Turkey **Duration of study:** January to December 2004 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized into 2 groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the administration of the drugs previously labeled was carried out by an investigator other than the one who collected the data and the patients were not informed of the group they belonged to in order to meet the criteria of a double blind study" Judgement comment: no information on blinding of anaesthesiologists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the one who collected the data and the patients were not informed of the group they belonged to in order to meet the criteria of a double blind study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Isik 2006 *(Continued)*

Other bias	Unclear risk	Quote: "in the statistical comparison between groups in terms of age, body weight, length, ASA group, gender, duration of operation and anesthesia (Table 2) and the MABP and HR values (Figure 1) during operation, no statistically significant difference" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of motion sickness): no; (history of PONV): unclear

Iwamoto 1978

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (male group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: NA • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 49 (16 to 78) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 0 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 183 • *Use of perioperative opioids (if yes, which?)*: morphine sulfate or meperidine hydrochloride • *Type of surgery*: ocular surgery, retinal detachment, cataract extraction, corneal transplant, strabismus, enucleation Control (female group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 46 • *Received treatment (n)*: NA • *Analysed (n)*: 46 • *Age (mean ± SD, median (IQR), median (range))*: 57 (18 to 87) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)

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Iwamoto 1978 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 159
- *Use of perioperative opioids (if yes, which?)*: morphine sulfate or meperidine hydrochloride
- *Type of surgery*: ocular surgery, retinal detachment, cataract extraction, corneal transplant, strabismus, enucleation

Droperidol (male group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 37
- *Received treatment (n)*: NA
- *Analysed (n)*: 37
- *Age (mean ± SD, median (IQR), median (range))*: 45 (18 to 77)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 0
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 168
- *Use of perioperative opioids (if yes, which?)*: morphine sulfate or meperidine hydrochloride
- *Type of surgery*: ocular surgery, retinal detachment, cataract extraction, corneal transplant, strabismus, enucleation

Droperidol (female group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 41
- *Received treatment (n)*: NA
- *Analysed (n)*: 41
- *Age (mean ± SD, median (IQR), median (range))*: 48 (15 to 75)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 161
- *Use of perioperative opioids (if yes, which?)*: morphine sulfate or meperidine hydrochloride
- *Type of surgery*: ocular surgery, retinal detachment, cataract extraction, corneal transplant, strabismus, enucleation

Included criteria: ASA I to III, 15 to 87 years of age

Excluded criteria: NA

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control (male group)

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Iwamoto 1978 *(Continued)*

- *Dose*: no treatment
- *Time point of administration*: no treatment
- *Route of administration*: no treatment
- *Rescue antiemetics (if yes, which?)*: NA

Control (female group)

- *Dose*: no treatment
- *Time point of administration*: no treatment
- *Route of administration*: no treatment
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (male group)

- *Dose*: 5 mg
- *Time point of administration*: in recovery room before mental alertness was evident
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (female group)

- *Dose*: 5 mg
- *Time point of administration*: in recovery room before mental alertness was evident
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Kumiko Iwamoto **Institution:** Department of Anesthesiology and the Jules Stein Eye Institute, UCLA School of Medicine, Los Angeles, CA, USA **Email:** NA **Address:** UCLA School of Medicine, Los Angeles, CA 90024, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Four groups with same gender pooled into 2 groups for analysis
Risk of bias	

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Iwamoto 1978 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly assigned". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no placebo treatment in the control group. Anaesthesiologists were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were observed for 24 hours postoperatively by nurses who had not been informed of the study groups, and nausea, retching, or emesis was noted"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Jakobsson 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 34 • *Received treatment (n)*: NA • *Analysed (n)*: 34 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 57 • *Use of perioperative opioids (if yes, which?)*: 2.6 µg intraoperative fentanyl, postoperative morphine

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Jakobsson 1999 *(Continued)*

- *Type of surgery*: gynaecological laparoscopic surgery

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 34
- *Received treatment (n)*: NA
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 35 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 61
- *Use of perioperative opioids (if yes, which?)*: 2.9 µg intraoperative fentanyl, postoperative morphine
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: ASA I or II, women aged 18 to 50 years scheduled for laparoscopic surgery for elective sterilization, cyst resection, or diagnostic procedures for infertility or pain

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Tropisetron • *Dose*: 5 mg • *Time point of administration*: 10 to 20 minutes before induction • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: droperidol 1 mg IV control • *Dose*: no treatment • *Time point of administration*: NA • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: droperidol 1 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (PACU discharge to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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Jakobsson 1999 *(Continued)*

	Complete response (no PONV) in 24 hours • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Sweden **Setting:** inpatient, single-centre **Author's name:** Jan Jakobsson **Institution:** Department of Anaesthesia, Sabbatsberg Närsjukhuset, Stockholm, Sweden **Email:** NA **Address:** Department of Anaesthesia, Sabbatsberg Närsjukhuset, M M Medical Inc., Olivercronas väg 1, 11324 Stockholm, Sweden **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	Secondary publication.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no placebo intervention in the control group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the two groups of patients—tropisetron and control group—were comparable with respect to age and weight, duration of anesthesia/surgery, and surgical procedures. Demographic data and perioperative observations are presented in Table 1"

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Jakobsson 1999 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Jalali 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron (generic) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 51 • *Received treatment (n)*: NA • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range))*: 54.18 ± 20.41 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 45.10 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 32.55 • *Use of perioperative opioids (if yes, which?)*: postoperative pentazocine • *Type of surgery*: eye surgery Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 54.02 ± 19.02 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 31.60 • *Use of perioperative opioids (if yes, which?)*: postoperative pentazocine • *Type of surgery*: eye surgery Granisetron (brand name Kytril)

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Jalali 2014 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 53.61 ± 21.62
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 43.67
- *Use of perioperative opioids (if yes, which?)*: postoperative pentazocine
- *Type of surgery*: eye surgery

Included criteria: male or female, 15 to 87 years of age, undergoing eye surgery under general anaesthesia

Excluded criteria: pregnant or breastfeeding, at risk of QT prolongation, history of motion sickness or other movement disorders, previous postoperative vomiting, gastrointestinal disorders, received an antiemetic within 24 hours before surgery

Pretreatment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Granisetron (generic) • *Dose*: 40 µg/kg • *Time point of administration*: 2 to 5 minutes after induction of anaesthesia (before the start of surgery) • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 0.2 mg/kg • *Time point of administration*: 2 to 5 minutes after induction of anaesthesia (before the start of surgery) • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Granisetron (brand-name Kytril) • *Dose*: 40 µg/kg • *Time point of administration*: 2 to 5 minutes after induction of anaesthesia (before the start of surgery) • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome

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Jalali 2014 *(Continued)*

Headache (0 to 6 hours and 6 to 24 hours)

- Outcome type: dichotomous outcome

Constipation (0 to 6 hours and 6 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 0 to 24 hours)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this study was conducted with financial support that was provided by the Clinical Trial Research Center, Tehran, Iran **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Yunes Panahi **Institution:** Chemical Injuries Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran **Email:** yunespanahi@yahoo.com **Address:** Chemical Injuries Research Center, Baqiyatallah University of Medical Sciences, Molla-Sadra Ave., Vanak Sq., Tehran 19945/581, Iran **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "subjects were randomly (using random number table) allocated to receive generic granisetron (n = 51; 40 µg/kg), kytril (n = 50; 40 µg/kg) or metoclopramide (n = 50; 0.2 mg/kg), intravenously 2-5 min after induction of anaesthesia (prior to the start of surgery)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no information on blinding of outcome assessors
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Jalali 2014 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "patients' demographic profile is summarized in Table 1. There was no statistically significant difference between the groups regarding most of their baseline characteristics in the study. The mean age of all patients in this study was 53.93 ± 20.24 years. Of the 151 patients who entered the study, 68 (45%) were male and 83 (55%) were female. The mean duration of anaesthesia in the kytril group was significantly higher than those of biogeneric granisetron and metoclopramide groups (p<0.01)" Judgement comment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear; (duration of anaesthesia): yes

Jamil 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 19.6 ± 0.625 • *Weight (mean ± SD, median (IQR), median (range))*: 56.26 ± 1.295 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 50/0/0/0 • *Gender (female in %)*: 58 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/24 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 39.54 • *Use of perioperative opioids (if yes, which?)*: 0.05 mg/kg morphine at induction • *Type of surgery*: tonsillectomy Prochlorperazine (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 18.14 ± 0.479

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Jamil 2005 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 55.46 ± 1.074
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 50/0/0/0
- *Gender (female in %)*: 64
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/20
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 39.75
- *Use of perioperative opioids (if yes, which?)*: 0.05 mg/kg morphine at induction
- *Type of surgery*: tonsillectomy

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 18.88 ± 0.539
- *Weight (mean ± SD, median (IQR), median (range))*: 54.34 ± 0.977
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 50/0/0/0
- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/30
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 45.18
- *Use of perioperative opioids (if yes, which?)*: 0.05 mg/kg morphine at induction
- *Type of surgery*: tonsillectomy

Included criteria: 16 to 30 years of age, ASA I, both sexes

Excluded criteria: with preoperative emesis; taking anxiolytics or sedatives; history of drug allergy, clotting disorders, vertigo, or ear disease; airway difficulty or pregnancy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide (group A) • *Dose*: 0.1 to 0.2 mg/kg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8%; metoclopramide 0.1 to 0.2 mg/kg IV Prochlorperazine (group B) • *Dose*: 0.1 to 0.2 mg/kg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2%; metoclopramide 0.1 to 0.2 mg/kg IV Placebo (group C)

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Jamil 2005 *(Continued)*

	• *Dose*: 5% dextrose in normal saline • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 12%; metoclopramide 0.1 to 0.2 mg/kg IV
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Pakistan **Setting:** single-centre **Author's name:** Muhammad Jamil **Institution:** Department of Anaesthesiology, Ayub Medical College Teaching Hospital, Abbottabad **Email:** NA **Address:** Department of Anaesthesia, Ayub Medical College Teaching Hospital, Abbottabad **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients randomly received in a double blind fashion either..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind fashion either..." Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a trained nurse unaware of the nature of the study drugs observed and nursed the patients in the recovery room and wards"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Jamil 2005 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients in all the three groups were similar with no statistically significant difference regarding age (P=0.192), weight (P=0.4803). There was also similarity amongst the groups with respect to ASA physical status, the history of previous anaesthetic exposure, history of motion sickness, type and duration of surgical procedure. (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Jamwal 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondanstron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 38.32 ± 10.59 • *Weight (mean ± SD, median (IQR), median (range))*: 58.94 ± 5.09 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 65.20 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Ramosetron (group R) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 38.46 ± 9.15 • *Weight (mean ± SD, median (IQR), median (range))*: 59.04 ± 4.81 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Jamwal 2016 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 71.22
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Palonosetron (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 38.94 ± 9.99
- *Weight (mean ± SD, median (IQR), median (range))*: 58.08 ± 5.84
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 69.50
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: female, 25 to 55 years of age, ASA I and II, undergoing laparoscopic cholecystectomy

Excluded criteria: received antiemetic 24 hours before surgery, concomitant administration of steroids and psychotropic drugs, pregnant or lactating, known prolonged QTc interval or bundle branch block, chemotherapy and allergy to the drugs used in the study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Ondanstron (group O)

- *Dose*: 4 mg
- *Time point of administration*: 3 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ramosetron (group R)

- *Dose*: 0.3 mg
- *Time point of administration*: 3 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Palonosetron (group P)

- *Dose*: 0.075 mg
- *Time point of administration*: 3 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

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Jamwal 2016 *(Continued)*

Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome *QT prolongation (0 to 2 hours, 2 to 6 hours, 6 to 12 hours, 12 to 24 hours, 24 to 48 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 48 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** single-centre **Author's name:** Anju Jamwal **Institution:** Department of Anaesthesia, Govt Medical College Jammu J India 180001 **Email:** NA **Address:** Department of Anaesthesia, Govt. Medical College Jammu J India 180001 **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...were randomly divided into 3 groups with 50 patients each" Judgement comment: no statement on the randomization method
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement

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Jamwal 2016 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no statistically significant difference in all three groups with respect to age, weight and duration of surgery" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Janicki 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + dolasetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 75 • *Age (mean ± SD, median (IQR), median (range))*: 45.5 ± 12.3 • *Weight (mean ± SD, median (IQR), median (range))*: 84.5 ± 26.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 11/54/10/0 • *Gender (female in %)*: 84 • *Non-smoker (%)*: 56 • *History of PONV/motion sickness (%)*: NA (no imbalance in preoperative Apfel score) • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane or sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (no imbalance in preoperative Apfel score) • *Use of perioperative opioids (if yes, which?)*: 227 µg intraoperative fentanyl, 6.08 mg intraoperative morphine • *Type of surgery*: head and neck, orthopaedic, laparoscopic, open abdominal, mastectomy Dexamethasone + granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 75 • *Age (mean ± SD, median (IQR), median (range))*: 47 ± 12.5 • *Weight (mean ± SD, median (IQR), median (range))*: 97.1 ± 30.8

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Janicki 2006 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 15/49/9/0
- *Gender (female in %)*: 84
- *Non-smoker (%)*: 59
- *History of PONV/motion sickness (%)*: NA (no imbalance in preoperative Apfel score)
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane or sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (no imbalance in preoperative Apfel score)
- *Use of perioperative opioids (if yes, which?)*: 261 µg intraoperative fentanyl, 6.04 mg intraoperative morphine
- *Type of surgery*: head and neck, orthopaedic, laparoscopic, open abdominal, mastectomy

Included criteria: adults, ASA I to III, moderate to high risk for PONV (Apfel PONV score ≥ 2), scheduled for elective surgery under general anaesthesia

Excluded criteria: pregnancy or breastfeeding, use of propofol for maintenance of anaesthesia, allergy to study medication, neuroaxial anaesthesia, history of vomiting within 24 hours before anaesthesia, history of cardiac arrhythmia and/or history of antiarrhythmic therapy, history of vomiting from any organic aetiology

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness -> no imbalance in preoperative Apfel score): unclear

Interventions	**Intervention characteristics** Dexamethasone + dolasetron • *Dose*: dexamethasone 4 mg, dolasetron 12.5 mg • *Time point of administration*: dexamethasone before anaesthesia induction, dolasetron 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: promethazine (12.5 to 25 mg, PO, every 4 to 6 hours as needed) Dexamethasone + granisetron • *Dose*: dexamethasone 4 mg, granisetron 1 mg • *Time point of administration*: dexamethasone before anaesthesia induction, granisetron 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: promethazine (12.5 to 25 mg, PO, every 4 to 6 hours as needed)
Outcomes	*Vomiting (in the PACU)* • Outcome type: dichotomous outcome *Vomiting (PACU to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by an Independent Investigator Grant for PKJ from Roche Pharmaceuticals

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Janicki 2006 *(Continued)*

Country: USA

Setting: single-centre

Author's name: Piotr K. Janicki

Institution: Department of Anesthesiology, Pennsylvania State University College of Medicine, Milton S. Hershey Medical Center, Hershey, PA, USA

Email: pjanicki@psu.edu

Address: Department of Anesthesiology, Hershey Medical Center, H 187, 500 University Drive, Hershey, PA 17033-0850, USA

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: incidence of complete response to PONV prophylaxis between 2 study groups

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to computer-generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "all other study personnel and subjects were blinded to treatment assignment" Judgement comment: anaesthetists were aware of the study drug
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the blinded investigator made the assessments at 30 min intervals after the end of anesthesia until the time of discharge. Patients were contacted again at 24 hours after the operation by an investigator who was unaware of the treatment group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 159 subjects signed the informed consent. Nine patients who were enrolled were not included in the analysis: three patients who were lost to follow-up for the data collection, one patient enrolled despite the presence of exclusion criteria, one patient withdrawn because of change in anesthetic plan, and four patients withdrawn because of protocol violations in the treatment" Judgement comment: reasons for missing outcome data were described and were unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no information on study protocol or trial registry number reported
Other bias	Low risk	Quote: "the demographic characteristics of the remaining 150 patients are shown in Table 1. There were no statistical differences in any of the demographic characteristics. Likewise, there were no differences between groups in relation to the use and dosage of intraoperative analgesics (e.g., fentanyl, mor-

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Janicki 2006 *(Continued)*

phine, and ketorolac) or neuromuscular reversal drugs. During the course of the study, no adverse effects were recorded in any of the study subjects"

Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness -> no imbalance in preoperative Apfel score): unclear

Jee 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 37.1 ± 3.3 • *Weight (mean ± SD, median (IQR), median (range))*: 60.2 ± 8.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 47/3/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 96 • *History of PONV/motion sickness (%)*: 24 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 110.5 • *Use of perioperative opioids (if yes, which?)*: fentanyl PCA • *Type of surgery*: gynaecological operation (laparoscopy/laparotomy) Dexamethasone + metoclopramide (group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 38.7 ± 3.2 • *Weight (mean ± SD, median (IQR), median (range))*: 61.6 ± 6.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 48/2/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 94 • *History of PONV/motion sickness (%)*: 26 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 118.3 • *Use of perioperative opioids (if yes, which?)*: fentanyl PCA

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Jee 2010 *(Continued)*

- *Type of surgery*: gynaecological operation (laparoscopy/laparotomy)

Included criteria: female, adult, ASA I and II, undergoing gynaecological operation with IV-PCA

Excluded criteria: hypersensitivity to metoclopramide, ondansetron or dexamethasone, use of antiemetic drugs, presence of extrapyramidal motor disease, current steroid medication, liver or renal disease, peptic ulcer

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Dexamethasone + ondansetron (group O) • *Dose*: dexamethasone 5 mg, ondansetron 4 mg • *Time point of administration*: dexamethasone after tracheal intubation, ondansetron at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg IV Dexamethasone + metoclopramide (group M) • *Dose*: dexamethasone 5 mg, metoclopramide 20 mg • *Time point of administration*: dexamethasone after tracheal intubation, metoclopramide at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg IV
Outcomes	*Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Arrhythmia (0 to 36 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 36 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** single-centre, inpatient **Author's name:** Hea-Jo Yoon **Institution:** Department of Anesthesiology and Pain Medicine, Cheil General Hospital and Women Healthcare Center, Kwandong University College of Medicine, Seoul, Korea **Email:** heajo7890@hanmail.net **Address:** Cheil General Hospital and Women Healthcare Center, Kwandong University College of Medicine, 1-19, Mukjeong-dong, Jung-gu, Seoul 100-380, Korea **Duration of study:** NA **Language:** English

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Jee 2010 *(Continued)*

	Study's primary outcome: NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using computer generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences in age, body weight, height, ASA, or PONV risk factors between groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Jellish 1995

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 34 • *Received treatment (n)*: NA • *Analysed (n)*: 34 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 2.5

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Jellish 1995 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 74.4 ± 2.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 53
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 157.9
- *Use of perioperative opioids (if yes, which?)*: postoperative fentanyl at 0.25 µg/kg IV, if severe pain
- *Type of surgery*: middle ear procedures

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 34
- *Received treatment (n)*: NA
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 44 ± 2.7
- *Weight (mean ± SD, median (IQR), median (range))*: 77.2 ± 3.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 53
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 162.9
- *Use of perioperative opioids (if yes, which?)*: postoperative fentanyl at 0.25 µg/kg IV, if severe pain
- *Type of surgery*: middle ear procedures

Included criteria: 18 to 65 years of age, scheduled for elective middle ear procedures: tympanoplasty, stapedectomy, and/or ossiculoplasty

Excluded criteria: delayed gastric emptying secondary to diabetes, chronic cholecystitis, neuropathy, neuromuscular disorders, obesity (i.e. weighed > 150% of ideal body weight)

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: metoclopramide 5 mg IV Droperidol • *Dose*: 25 µg/kg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 5 mg IV
Outcomes	*Vomiting (0 to 24 hours)*

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Jellish 1995 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (PACU)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** W. Scott Jellish **Institution:** Department of Anesthesiology, Loyola University Medical Center, Maywood, IL, USA **Email:** NA **Address:** 2160 South First Avenue, Maywood, IL 60153, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (propofol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized study". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: quote: "open (non blinded) study design"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "all recovery characteristics were assessed by a research nurse, who was blinded to the anesthetic"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry reported

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Jellish 1995 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Jellish 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 47 ± 2 • *Weight (mean ± SD, median (IQR), median (range))*: 80 ± 2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 35 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 124 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction • *Type of surgery*: middle ear procedures Droperidol (group 3) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 2 • *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 57 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 132 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction • *Type of surgery*: middle ear procedures Placebo (group 1)

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Jellish 1997 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 2
- *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 62
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 137
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: middle ear procedures

Included criteria: healthy, ASA I and II, scheduled for elective middle ear procedures (tympanoplasty, stapedectomy, ossiculoplasty, or mastoidectomy)

Excluded criteria: delayed gastric emptying secondary to diabetes, chronic cholecystitis, neuropathy, neuromuscular disorders, pregnancy, obesity (> 150% of ideal body weight)

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (perioperative opioids, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (gender): yes

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Interventions

Intervention characteristics

Ondansetron (group 2)

- *Dose*: 4 mg
- *Time point of administration*: 10 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 20%; metoclopramide 10 mg IV, trimethobenzamide (Tigan) 200 mg suppository

Droperidol (group 3)

- *Dose*: 25 µg/kg
- *Time point of administration*: 10 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 18%; metoclopramide 10 mg IV, trimethobenzamide (Tigan) 200 mg suppository

Placebo (group 1)

- *Dose*: 0.9% saline solution
- *Time point of administration*: 10 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 23%; metoclopramide 10 mg IV, trimethobenzamide (Tigan) 200 mg suppository

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Outcomes

Vomiting (PACU)

- Outcome type: dichotomous outcome

Vomiting (PACU to 24 hours after PACU)

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Jellish 1997 *(Continued)*

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** supported in part by a grant from Glaxo Wellcome, Inc., Research Triangle Park, NC, USA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** W. Scott Jellish **Institution:** Department of Anesthesiology, Loyola University Medical Center, Maywood, IL, USA **Email:** NA **Address:** Department of Anesthesiology, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Secondary publication.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "they were then randomly assigned by a computer generated lottery"
Allocation concealment (selection bias)	Unclear risk	Quote: "given droperidol 25 mcg/kg IV. All study medications were diluted in equal volumes (2 ml) and placed in a numbered envelope to which the attending anesthesiologist..." Judgement comment: not stated: "sequentially numbered, opaque, and sealed envelope" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "to which the attending anesthesiologist and the trained individual who was collecting recovery data in the post-anesthesia care unit (PACU) were blinded"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "trained individual who was collecting recovery data in the post-anesthesia care unit (PACU) were blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "demographically, all three groups were similar except for gender ratio"

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Jellish 1997 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (perioperative opioids, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (gender): yes

Jeon 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 44.9 ± 13.3 • *Weight (mean ± SD, median (IQR), median (range))*: 53.6 ± 3.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 43/17/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 168.5 • *Use of perioperative opioids (if yes, which?)*: no • *Type of surgery*: thyroidectomy Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 45.4 ± 12.1 • *Weight (mean ± SD, median (IQR), median (range))*: 52.7 ± 3.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 42/18/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 165.0 • *Use of perioperative opioids (if yes, which?)*: no • *Type of surgery*: thyroidectomy Ramosetron + dexamethasone

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Jeon 2010 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: 60
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 49.1 ± 12.1
- *Weight (mean ± SD, median (IQR), median (range))*: 53.3 ± 3.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 46/14/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 169.1
- *Use of perioperative opioids (if yes, which?)*: no
- *Type of surgery*: thyroidectomy

Included criteria: adult, female, ASA I and II, scheduled to undergo thyroidectomy under general anaesthesia

Excluded criteria: known hypersensitivity or contraindication to study medication; use of antiemetics within 24 hours before surgery; presence of gastrointestinal, renal, or liver disease; smoking; history of motion sickness and/or previous postoperative emesis; pregnancy; breastfeeding

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: immediately after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 7% (metoclopramide 10 mg) Dexamethasone • *Dose*: 8 mg • *Time point of administration*: immediately after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 27% (metoclopramide 10 mg) Ramosetron + dexamethasone • *Dose*: ramosetron 0.3 mg, dexamethasone 8 mg • *Time point of administration*: immediately after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 5% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)*

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Jeon 2010 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Kyung-Hwa Kwak **Institution:** Department of Anesthesiology and Pain Medicine, Kyungpook National University Hospital, Jung gu, Daegu, Korea **Email:** kwakkh@knu.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Kyungpook National University Hospital, 200 Dongduk-ro, Jung gu, Daegu 700-721, Korea **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV in 24 hours
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "the group assignment was prepared by the enrolling anesthesiologist in sealed opaque envelopes" Judgement comment: not mentioned that envelopes were sequentially numbered (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the enrolling anesthesiologist was not the same person as the treating anesthesiologist. A total of 180 sealed envelopes containing the names of the groups (60 for each) were prepared before initiation of the study. The envelopes were opened before induction of anesthesia, and the drugs were prepared by an independent nurse who was not participating in any other part of the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients, the anesthesiologist present during surgery, and the anesthesiologist who collected the postoperative data were all blinded with respect to the randomization process and the identity of the study drugs"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Jeon 2010 *(Continued)*

Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Jespersen 1989

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Scopolamine (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 43.1 ± 8.5 • *Weight (mean ± SD, median (IQR), median (range))*: 66.3 ± 15.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (pethidine, alfentanil, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 19 • *Use of perioperative opioids (if yes, which?)*: pethidine/alfentanil • *Type of surgery*: outpatient abrasion or abortion Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 52 • *Age (mean ± SD, median (IQR), median (range))*: 41.3 ± 9.6 • *Weight (mean ± SD, median (IQR), median (range))*: 65.2 ± 10.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (pethidine, alfentanil, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 17 • *Use of perioperative opioids (if yes, which?)*: pethidine/alfentanil • *Type of surgery*: outpatient abrasion or abortion **Included criteria:** female outpatients, undergoing abrasion/abortion

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Jespersen 1989 *(Continued)*

	Excluded criteria: not understanding oral or written information, hypersensitivity to scopolamine, intake of antidepressive or neuroleptic drugs, breastfeeding, intake of steroids, glaucoma, denying participation **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Scopolamine (group A) • *Dose*: 0.5 mg over 72 hours • *Time point of administration*: evening before surgery • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: NA Placebo (group P) • *Dose*: NA • *Time point of administration*: NA • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (on awakening)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Denmark **Setting:** outpatient, single-centre **Author's name:** Torben Worsoe Jespersen **Institution:** NA **Email:** NA **Address:** Johannes Ewaldsvej 88, DK - 8230, Åbyhøj **Duration of study:** NA **Language:** Danish (translated by Ottar Gadeholt) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None
Risk of bias	

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Jespersen 1989 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" (translated). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no information on blinding provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no information on blinding provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: missing outcome data < 15%. Reasons described and unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Jin 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 45.5 ± 9.4 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 22.5 ± 3.5 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 55.0 • *Use of perioperative opioids (if yes, which?)*: 450.0 µg fentanyl intraoperatively

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Jin 2013 *(Continued)*

- *Type of surgery*: thyroid tumour surgery

Droperidol (IV group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 46.0 ± 9.8
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23.6 ± 2.5
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 60.0
- *Use of perioperative opioids (if yes, which?)*: 500.0 µg fentanyl intraoperatively
- *Type of surgery*: thyroid tumour surgery

Droperidol (acupoint injection)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 44.2 ± 12.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 21.9 ± 2.2
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 57.5
- *Use of perioperative opioids (if yes, which?)*: 400.0 µg fentanyl intraoperatively
- *Type of surgery*: thyroid tumour surgery

Included criteria: thyroid cancer operation, ASA I to II, female, 20 to 25 years of age, operation duration 120 minutes, no previous smoking, syncope history, signed operation agreement

Excluded criteria: BMI > 25 kg/m^2, pregnancy or breastfeeding, previous PONV, cervical nerve disease, gastritis or ulcus history

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV): no; (history of motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 2 mL NaCl • *Time point of administration*: 30 minutes before anaesthesia • *Route of administration*: IV

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Jin 2013 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide Droperidol (IV group) • *Dose*: 2.5 mg • *Time point of administration*: 30 minutes before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide Droperidol (acupoint injection) • *Dose*: 2.5 mg • *Time point of administration*: 30 minutes before anaesthesia • *Route of administration*: acupoint injection • *Rescue antiemetics (if yes, which?)*: metoclopramide
Outcomes	*Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Jun-lu Wang **Institution:** Department of Anesthesiology, First Affiliated Hospital of Wenzhou Medical College, Zhejiang, China **Email:** wangjunlu973@163.com **Address:** Department of Anesthesiology, First Affiliated Hospital of Wenzhou Medical College, Zhejiang (325000), China **Duration of study:** NA **Language:** Chinese (translated by Chiung-Wen Chang) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Three out of 4 groups relevant (acupoint stimulation)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "...randomly assigned to the control group,...". No further information on sequence generation provided

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Jin 2013 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: quote: "...single-blinded..."; "...the procedure was conducted by personnel not knowing the experiment" (translated). Participants were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "...single-blinded..."; "...the procedure was conducted by personnel not knowing the experiment" (translated). Participants were not blinded Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV): no; (history of motion sickness, perioperative opioids): unclear

Jo 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ramosetron (group R) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 0 • *History of PONV/motion sickness (%)*: 2.5/12.5 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 67 • *Use of perioperative opioids (if yes, which?)*: remifentanil intraoperative, 1 µg/kg fentanyl postoperative • *Type of surgery*: laparoscopic cholecystectomy Dexamethasone (group D) • *Assessed for eligibility (n)*: -

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Jo 2012 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 44 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 0
- *History of PONV/motion sickness (%)*: 0/10
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 69
- *Use of perioperative opioids (if yes, which?)*: remifentanil intraoperative, 1 µg/kg fentanyl postoperative
- *Type of surgery*: laparoscopic cholecystectomy

Ramosetron + dexamethasone (group RD)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 44 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 0
- *History of PONV/motion sickness (%)*: 0/5
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 71
- *Use of perioperative opioids (if yes, which?)*: remifentanil intraoperative, 1 µg/kg fentanyl postoperative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: female, scheduled for elective laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: ASA III or IV; smoking status; antiemetic medication within 24 hours before surgery; administration of steroids within 24 hours before surgery or during the 24 hours after surgery; gastrointestinal, renal, or hepatic disease; insulin-dependent diabetes mellitus; obesity (body mass index > 35 kg/m^2); conversion to open cholecystectomy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Ramosetron (group R) • *Dose*: 0.3 mg • *Time point of administration*: placebo before induction of anaesthesia, ramosetron approximately 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

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Jo 2012 *(Continued)*

	Dexamethasone (group D) • *Dose*: 8 mg • *Time point of administration*: dexamethasone before induction of anaesthesia, placebo approximately 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ramosetron + dexamethasone (group RD) • *Dose*: ramosetron 0.3 mg, dexamethasone 8 mg • *Time point of administration*: dexamethasone before induction of anaesthesia, ramosetron approximately 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Republic of Korea **Setting:** inpatient, single-centre **Author's name:** Yong Seon Choi **Institution:** Department of Anesthesiology and Pain Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea **Email:** yschoi@yuhs.ac **Address:** Department of Anesthesiology and Pain Medicine, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response during 24 hours **Trial registry number:** NA
Notes	None
Risk of bias	

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Jo 2012 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated randomization list"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not stated: "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the envelopes were opened before anesthetic induction by a physician not involved in the study. The physician then prepared the appropriate study medication"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "total of 146 patients were assessed for eligibility; 120 of these patients were enrolled in the study and completed surgical procedures (Fig. 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients' characteristics and operative data were all similar among the three groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Joe 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 52 • *Age (mean ± SD, median (IQR), median (range))*: 42.1 ± 10.2 • *Weight (mean ± SD, median (IQR), median (range))*: 63.2 ± 19.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 80.77 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 9.6/30.8

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Joe 2009 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 134.9
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Control (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 42.6 ± 9.1
- *Weight (mean ± SD, median (IQR), median (range))*: 58.6 ± 9.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 88
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 10.0/40
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 160.4
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Dolasetron (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 39.7 ± 9.9
- *Weight (mean ± SD, median (IQR), median (range))*: 62.6 ± 11.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 81.63
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 10.2/40.8
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 152.8
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Dolasetron (group D+P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 52
- *Age (mean ± SD, median (IQR), median (range))*: 41.1 ± 10.6
- *Weight (mean ± SD, median (IQR), median (range))*: 59.2 ± 9.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0

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Joe 2009 *(Continued)*

- *Gender (female in %)*: 90.38
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 3.8/32.7
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 161.1
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Included criteria: healthy, ASA I or II, 20 to 60 years of age, underwent thyroidectomy under general anaesthesia at Ajou University Hospital

Excluded criteria: history of drug addiction; pregnancy; postoperative PCA; history of drug addiction; respiratory, endocrine, neurological disorders; > 20% of normal body weight

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Control (group C) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: (11.8%) 10 mg metoclopramide IV Control (group P) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: (14.0%) 10 mg metoclopramide IV Dolasetron (group D) • *Dose*: 210 µg/kg • *Time point of administration*: dolasetron: after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (4.1%) 10 mg metoclopramide IV Dolasetron (group D+P) • *Dose*: 210 µg/kg • *Time point of administration*: dolasetron: after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (5.8%) 10 mg metoclopramide IV
Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA

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Joe 2009 *(Continued)*

Country: Korea

Setting: inpatient, single-centre

Author's name: Sook Young Lee

Institution: Department of Anesthesiology and Pain Medicine, School of Medicine

Email: anesylee@ajou.ac.kr

Address: Ajou University, San 5,Woncheondong, Yeongtong-gu, Suwon 443-721, Korea

Duration of study: NA

Language: Korean (Google Translator)

Study's primary outcome: NA

Trial registry number: NA

Notes	Group C and P, group D, D + P pooled for analysis Group C + D with thiopental for induction Group P, D + P with propofol for induction

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly allocated". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no placebo treatment in control groups. Anaesthesiologists were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "nurses who did not know the patient's group" (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Jokela 1999

Study characteristics

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Jokela 1999 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 49 (20 to 78) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27 (18 to 39) • *ASA I/II/III/IV (n)*: 25/27/8/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 82 • *History of PONV/motion sickness (%)*: 32/42 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 112 • *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl, 27 mg oxycodone • *Type of surgery*: laparoscopic cholecystectomy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 48 (19 to 74) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26 (19 to 38) • *ASA I/II/III/IV (n)*: 33/24/3/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 72 • *History of PONV/motion sickness (%)*: 42/27 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 106 • *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl, 27 mg oxycodone • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** female inpatients scheduled to undergo elective laparoscopic cholecystectomy, over 18 years of age, ASA I to III **Excluded criteria:** pregnant or breastfeeding, evidence of metabolic disorders, Parkinson's disease, taking medication with antiemetic activity **Pretreatment:** baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Tropisetron

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Jokela 1999 *(Continued)*

- *Dose*: 5 mg
- *Time point of administration*: at the beginning of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 42% (metoclopramide 10 mg IV)

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: at the beginning of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 50% (metoclopramide 10 mg IV)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (after 2 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatient, multi-centre (2) **Author's name:** Ritva Jokela **Institution:** Department of Anaesthesiology, Lapland Central Hospital, Rovaniemi, Finland **Email:** NA **Address:** Department of Anaesthesiology, Lapland Central Hospital, PB 8041, FIN-96101 Rovaniemi, Finland **Duration of study:** October 1997 to May 1998 **Language:** English **Study's primary outcome:** incidence of nausea or vomiting

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Jokela 1999 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the study patients were randomly assigned, at an equal ratio" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Low risk	Quote: "the treatment allocation codes were contained in sealed opaque envelopes, and for each consecutive enrolled patient the assisting nurses opened the next envelope in order and prepared the study drug as outlined, but did not participate in the postoperative assessment"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the treatment allocation codes were contained in sealed opaque envelopes, and for each consecutive enrolled patient the assisting nurses opened the next envelope in order and prepared the study drug as outlined, but did not participate in the postoperative assessment"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "all patients were interviewed on the ward by the authors on the first postoperative day up to 24 hours after surgery" Quote: "the treatment allocation codes were contained in sealed opaque envelopes, and for each consecutive enrolled patient the assisting nurses opened the next envelope in order and prepared the study drug as outlined, but did not participate in the postoperative assessment" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 120 patients participated in the study: 60 patients received tropisetron 5 mg and 60 received droperidol 1.25 mg. One hundred and fifteen patients underwent scheduled laparoscopic cholecystectomy. Five laparoscopies (4%) were finally converted into laparotomy because of technical difficulties (two in the tropisetron group and three in the droperidol group); however, all these patients were included in the analysis. Forty-six patients were studied in Lapland Central Hospital and 74 patients in Oulu University Hospital"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "there were no significant differences between the groups in the demographic data (Table 1). The duration of anaesthesia and surgery were also similar, as well as the doses of intraoperative fentanyl administered" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Jokela 2000

Study characteristics

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Jokela 2000 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: NA • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 51 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27 ± 6 • *ASA I/II/III/IV (n)*: 24/29/7/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 83 • *History of PONV/motion sickness (%)*: 42/33 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 105 • *Use of perioperative opioids (if yes, which?)*: fentanyl 4.2 µg/kg, oxycodone 0.05 mg/kg IV in PACU, 0.1 mg/kg IM on the ward • *Type of surgery*: mastectomy, tumour biopsy, reductive mastoplastic or other plastic surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: NA • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 52 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27 ± 5 • *ASA I/II/III/IV (n)*: 28/29/3/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 82 • *History of PONV/motion sickness (%)*: 42/20 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 117 • *Use of perioperative opioids (if yes, which?)*: fentanyl 4.2 µg/kg, oxycodone 0.05 mg/kg IV in PACU, 0.1 mg/kg IM on the ward • *Type of surgery*: mastectomy, tumour biopsy, reductive mastoplastic or other plastic surgery **Included criteria:** adult, female, ASA I to III, scheduled for breast surgery **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Control

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Jokela 2000 *(Continued)*

- *Dose*: no treatment
- *Time point of administration*: -
- *Route of administration*: -
- *Rescue antiemetics (if yes, which?)*: 48% (droperidol 0.75 mg IV)

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 8% (droperidol 0.75 mg IV)

Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatient, multi-centre (2) **Author's name:** Ritva Jokela **Institution:** Department of Anesthesia and Intensive Care,Women's Hospital, University of Helsinki, Helsinki **Email:** Ritva.M.Jokela@hus.fi **Address:** Department of Anesthesia and Intensive Care, Women's Hospital, University of Helsinki, PO Box 140 (Haartmaninkatu 2), FIN-00029 HUS, Finland **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of nausea
Notes	Two out of 3 groups relevant (propofol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned to one of three anesthetic treatment groups" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Jokela 2000 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no statement on blinding. Due to study design, blinding of anaesthesiologists impossible
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "after 2 hours and 24 hours, the patients were interviewed by a nurse or one of the authors, who were blinded as to the method of anesthesia used"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "the treatment groups were also similar demographically" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Jokela 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline Characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 51 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 5 • *ASA I/II/III/IV (n)*: 45/48/7/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 80 • *History of PONV/motion sickness (%)*: 71.6/33.3 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 123 • *Use of perioperative opioids (if yes, which?)*: 6.0 µg/kg fentanyl intraoperative, 0.33 mg/kg oxycodone postoperative • *Type of surgery*: thyroid or parathyroid surgery Tropisetron • *Assessed for eligibility (n)*: -

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Jokela 2002 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 49 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 5
- *ASA I/II/III/IV (n)*: 52/38/10/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 66.6
- *History of PONV/motion sickness (%)*: 76.6/30
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 108
- *Use of perioperative opioids (if yes, which?)*: 5.3 µg/kg fentanyl intraoperative, 0.35 mg/kg oxycodone postoperative
- *Type of surgery*: thyroid or parathyroid surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 59
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 5
- *ASA I/II/III/IV (n)*: 64/31/5/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 84.7
- *History of PONV/motion sickness (%)*: 71.1/49.1
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 111
- *Use of perioperative opioids (if yes, which?)*: 5.9 µg/kg fentanyl intraoperative, 0.34 mg/kg oxycodone postoperative
- *Type of surgery*: thyroid or parathyroid surgery

Included criteria: adult, ASA I to III, female, scheduled for thyroid or parathyroid surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 16 mg
- *Time point of administration*: 1 hour before the operation
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: (64%) droperidol 0.75 mg IV

Tropisetron

- *Dose*: 5 mg

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Jokela 2002 *(Continued)*

- *Time point of administration*: 1 hour before the operation
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: (50%) droperidol 0.75 mg IV

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: 1 hour before the operation
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: (71%) droperidol 0.75 mg IV

Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatient, multi-centre (3) **Author's name:** Ritva Jokela **Institution:** Department of Anaesthesia and Intensive Care, Helsinki University **Email:** ritva.m.jokela@hus.fi **Address:** Department of Anaesthesia and Intensive Care, Helsinki University, PB 140 (Haartmaninkatu 2), FIN-00029 HUCH, Finland **Duration of study:** NA **Language:** English **Study's primary outcome:** PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly assigned (sealed envelope technique)" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: stated: "sequentially numbered, opaque, and sealed envelopes" (SNOSE)

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Jokela 2002 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "a study nurse or one of the investigators interviewed the patients after 2 hours in the PACU and after 24 hours on the ward" Judgement comment: no statement on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "we enrolled 200 patients in the study. Six patients were excluded as a result of a reoperation during the study period and 15 patients because of protocol violations. In the final analysis we had 179 patients: 60 in the ondansetron (Group O) and tropisetron (Group T) groups, and 59 in the metoclopramide (Group M) group. One hundred and sixteen patients were studied at Oulu University Hospital, 37 at Lapland Central Hospital, and 26 at Kuopio University Hospital"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Jones 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: 74 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 82.14 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (inhalation agent of choice, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: NA Scopolamine + ondansetron

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Jones 2006 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 28
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: 77
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 85.71
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (inhalation agent of choice, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: NA

Included criteria: ASA I and II, 18 years of age or older, reported at least 3 of the 5 risk factors

Excluded criteria: recent upper respiratory tract infection; recent use of serotonin antagonists, scopolamine, antiemetic drugs, or psychoactive drugs; hypersensitivity to serotonin antagonists or scopolamine; pregnant

Pretreatment: baseline characteristics (weight): no; (age, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids no imbalance in risk factors reported): unclear. "No difference was noted in gender, age, weight, height, ethnic background, or number of risk factors present between groups (Table 1)"

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: placebo at least 2 hours before induction, ondansetron 30 minutes before emergence
- *Route of administration*: placebo transdermal patch, ondansetron IV
- *Rescue antiemetics (if yes, which?)*: 68%

Scopolamine + ondansetron

- *Dose*: scopolamine 1.5 mg over 72 hours, ondansetron 4 mg
- *Time point of administration*: scopolamine at least 2 hours before induction, ondansetron 30 minutes before emergence
- *Route of administration*: scopolamine transdermal patch, ondansetron IV
- *Rescue antiemetics (if yes, which?)*: 29%

Outcomes

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 72 hours)

- Outcome type: dichotomous outcome

Headache (0 to 72 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 72 hours' observation)

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Jones 2006 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** Chief, Bureau of Medicine and Surgery, Navy Department, Washington, DC, USA. Clinical Investigation Program sponsored this report # S-02-099, as required by NSHSBETHINST 6000.41A **Country:** USA **Setting:** inpatient and outpatient **Author's name:** Shari Jones **Institution:** Naval Medical Center San Diego, California, USA **Email:** NA **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "via a computer-generated randomization process"
Allocation concealment (selection bias)	Low risk	Quote: "they were identical in appearance to the TD scopolamine patches that were purchased for this study and were not in the hospital formulary. The scopolamine patches were designed to deliver 1.5 mg of scopolamine in a time-release manner during 72 hours. The pharmacy generated a random number table and placed the patches in dark plastic bags numbered 1 to 60. All of the patches then were maintained in a secure location by the investigators until subjects were consented and enrolled in the study. The patches were numbered individually before being placed on subjects by the investigators" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "subjects and investigators were unaware of which patch was being placed until the completion of data collection"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "neither the investigators nor the subjects were informed of group assignment until the conclusion of data collection"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "we enrolled 60 subjects in this double-blind, randomized, placebo-controlled study. A total of 4 subjects were disenrolled, 1 for inadvertent removal of the patch, 1 for incomplete data collection, and 2 for intentional removal of patches secondary to headaches (ondansetron only group). This left a total of 56 subjects with data for analysis (28 in each group)"

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Jones 2006 *(Continued)*

		Judgement comment: exclusion of 2 patients after occurrence of headache (headache as outcome of interest)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "no difference was noted in gender, age, weight, height, ethnic background, or number of risk factors present between groups (Table 1). No significant differences in preoperative, intraoperative, or postoperative analgesic or anxiolytic requirements; volatile agent requirements; or need for reversal from neuromuscular blockade were noted between groups" Judgement comment: baseline characteristics (weight): no; (age, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids no imbalance in risk factors reported): unclear

Joo 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 40 (20 to 60) • *Weight (mean ± SD, median (IQR), median (range))*: 56.9 ± 5.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 40/10/0/0 • *Gender (female in %)*: 100% • *Non-smoker (%)*: 100% • *History of PONV/motion sickness (%)*: 52% • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 150.3 • *Use of perioperative opioids (if yes, which?)*: 104.7 µg remifentanil, 470.1 µg fentanyl via PCA • *Type of surgery*: gynaecological laparoscopic surgery Haloperidol 1 mg + dexamethasone • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 39 (20 to 60) • *Weight (mean ± SD, median (IQR), median (range))*: 55.0 ± 7.9

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Joo 2015 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 41/8/0/0
- *Gender (female in %)*: 100%
- *Non-smoker (%)*: 100%
- *History of PONV/motion sickness (%)*: 57%
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 157.9
- *Use of perioperative opioids (if yes, which?)*: 97.2 µg remifentanil, 465.6 µg fentanyl via PCA
- *Type of surgery*: gynaecological laparoscopic surgery

Haloperidol 2 mg + dexamethasone

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 41 (21 to 58)
- *Weight (mean ± SD, median (IQR), median (range))*: 54.4 ± 5.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 39/11/0/0
- *Gender (female in %)*: 100%
- *Non-smoker (%)*: 100%
- *History of PONV/motion sickness (%)*: 56%
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 156.4
- *Use of perioperative opioids (if yes, which?)*: 92.5 µg remifentanil, 467.8 µg fentanyl via PCA
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: ASA I or II, female, 20 to 65 years of age, scheduled for gynaecologic laparoscopic surgery and intravenous (IV) PCA for postoperative pain control. Based on Apfel's simplified risk score, patients in this study had the following 3 standard PONV risk factors: female, non-smoker, and use of opioid analgesics after surgery

Excluded criteria: known allergy or intolerance to study drug; history of cardiac arrhythmia; psychiatric illness; long-term treatment with a dopamine antagonist; use of opioids or steroids within 1 week of surgery; use of antiemetic in the 24 hours before the study; inability to use the PCA device; gastrointestinal, renal, or hepatic disease; insulin-dependent diabetes or obesity, body mass index > 35 kg/m^2

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 5 mg • *Time point of administration*: dexamethasone at induction, placebo 30 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 30% (ondansetron 4 mg) Haloperidol 1 mg + dexamethasone • *Dose*: dexamethasone 5 mg, haloperidol 1 mg • *Time point of administration*: dexamethasone at induction, haloperidol 30 minutes before end of anaesthesia

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Joo 2015 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 11% (ondansetron 4 mg) Haloperidol 2 mg + dexamethasone • *Dose*: dexamethasone 5 mg, haloperidol 2 mg • *Time point of administration*: dexamethasone at induction, haloperidol 30 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (ondansetron 4 mg)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Arrhythmia (PACU)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** departmental resources only. No sponsor involvement **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Young Eun Moon **Institution:** Department of Anesthesiology and Pain Medicine, Seoul St.Mary´s Hospital, College of Medicine, The Catholic University of Korea **Email:** anemoon@naver.com **Address:** 222 Banpo-daero, Seocho-gu, Seoul 137-701, Republic of Korea **Language:** English **Duration of study:** NA **Trial registry number:** NCT01639599 **Study's primary outcome:** incidence of PONV in 24 hours
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated codes"

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Joo 2015 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "using computer-generated codes placed in sequentially numbered, opaque envelopes, the enrolled patients were assigned randomly to one of three groups" Judgement comment: not stated; "sealed" envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "a nurse anesthetist not involved in the treatment opened the envelopes and prepared the study drugs in identical syringes with a total volume of 2 mL (diluted with saline). The patients and attending anesthesiologists were blinded to the group assignments"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "staff who remained blind to the group assignment made the postoperative evaluations"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 150 patients registered for the study, one was excluded due to an intra-operative conversion to laparotomy (Fig. 1). The remaining 149 patients, consisting of 50, 49, and 50 patients in groups H0, H1, and H2, respectively, completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01639599 (retrospective registration)
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Joo 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline Characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: 35 • *Analysed (n)*: 31 • *Age (mean ± SD, median (IQR), median (range))*: 34.10 ± 15.14 • *Weight (mean ± SD, median (IQR), median (range))*: 61.38 ± 9.50 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 54.84 • *Non-smoker (%)*: 64.52 • *History of PONV/motion sickness (%)*: 6.45/38.71 • *Type of general anaesthesia*: combined anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 35.24 • *Use of perioperative opioids (if yes, which?)*: 0.05 µg/kg/min to 0.1 µg/kg/min remifentanil intraoperative

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Joo 2016 *(Continued)*

- *Type of surgery*: strabismus surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: 35
- *Analysed (n)*: 26
- *Age (mean ± SD, median (IQR), median (range))*: 35.69 ± 17.13
- *Weight (mean ± SD, median (IQR), median (range))*: 65.32 ± 10.63
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 46.15
- *Non-smoker (%)*: 65.38
- *History of PONV/motion sickness (%)*: 7.69/38.46
- *Type of general anaesthesia*: combined anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 35.95
- *Use of perioperative opioids (if yes, which?)*: 0.05 µg/kg/min to 0.1 µg/kg/min remifentanil intraoperative
- *Type of surgery*: strabismus surgery

Ramosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: 35
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 34.13 ± 13.66
- *Weight (mean ± SD, median (IQR), median (range))*: 59.64 ± 10.39
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 59.38
- *Non-smoker (%)*: 65.63
- *History of PONV/motion sickness (%)*: 6.25/40.63
- *Type of general anaesthesia*: combined anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 36.64
- *Use of perioperative opioids (if yes, which?)*: 0.05 µg/kg/min to 0.1 µg/kg/min remifentanil intraoperative
- *Type of surgery*: strabismus surgery

Included criteria: between 18 and 60 years of age, ASA I and II, scheduled for strabismus surgery under general anaesthesia

Excluded criteria: had taken any analgesics, steroids, or antiemetics 24 hours before surgery; had gastrointestinal disease

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics**

Placebo

- *Dose*: saline
- *Time point of administration*: at end of surgery

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Joo 2016 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (45.2%) metoclopramide 10 mg IV Ondansetron • *Dose*: 4 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (34.6%) metoclopramide 10 mg IV Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (9.4%) metoclopramide 10 mg IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (at 2 hours, 24 hours, and 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (at 2 hours, 24 hours, and 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** none **Country:** Korea **Setting:** outpatient, single-centre **Author's name:** Jin Joo **Institution:** Department of Ophthalmology, Seoul St. Mary's Hospital, College of Medicine **Email:** eyeshin@catholic.ac.kr **Address:** Seoul St. Mary's Hospital,College of Medicine, The Catholic University of Korea, Seoul, Korea **Duration of study:** April 2011 to April 2012 **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** KCT0000688
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a computerized randomization list was generated, and identical syringes..."

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Joo 2016 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "by personnel not involved in the study, according to the list"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "every episode of nausea or vomiting was recorded during the first 2 hours after surgery, and the presence of nausea at 2 hours after surgery was asked by a member of the nursing staff who was blinded to the study drug used"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "among 120 patients recruited, 12 patients were excluded because they did not meet inclusion criteria; they showed ASA physical status >2. Another three patients were excluded because they did not agree to participate. Hence, 105 were randomly allocated to three groups. Among 16 follow-up loss patients, three patients and 13 patients did not respond to 24 hours and 48 hours telephone call, respectively (Fig. 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: KCT0000688 (retrospective registration)
Other bias	Low risk	Quote: "there were no significant differences in patients' characteristics, Apfel's four risk factors for PONV (female gender, nonsmoking, prior history of motion sickness or PONV, and the use of intraoperative opioids) [14], and the duration of surgery and anesthesia among the groups (Table 1)..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Joris 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (30% oxygen group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 84 • *Non-smoker (%)*: 70 • *History of PONV/motion sickness (%)*: 0

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Joris 2003 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 116
- *Use of perioperative opioids (if yes, which?)*: tramadol 2 mg/kg at end of surgery, mean piritramide in PACU (4 ± 3 mg; 29 patients)
- *Type of surgery*: total or partial thyroidectomy

Control (80% oxygen, group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 86
- *Non-smoker (%)*: 68
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 111
- *Use of perioperative opioids (if yes, which?)*: tramadol 2 mg/kg at end of surgery, mean piritramide in PACU (4 ± 2 mg; 24 patients)
- *Type of surgery*: total or partial thyroidectomy

Droperidol (30% oxygen)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 82
- *Non-smoker (%)*: 62
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 122
- *Use of perioperative opioids (if yes, which?)*: tramadol 2 mg/kg at end of surgery, mean piritramide in PACU (3 ± 4 mg; 19 patients)
- *Type of surgery*: total or partial thyroidectomy

Included criteria: scheduled for elective thyroid surgery, 19 to 70 years of age, ASA I to III

Excluded criteria: obesity (> 150% ideal body weight), gastro-oesophageal reflux, history of motion sickness, previous PONV, preoperative vomiting, antiemetic therapy, any pulmonary disease

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics**

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Joris 2003 *(Continued)*

	Control (30% oxygen group) • *Dose*: no treatment • *Time point of administration*: NA • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: alizapride 50 mg; tropisetron 2 mg, if PONV > 30 minutes Control (80% oxygen group) • *Dose*: no treatment • *Time point of administration*: NA • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: alizapride 50 mg; tropisetron 2 mg, if PONV > 30 minutes Droperidol (30% oxygen) • *Dose*: droperidol 0.625 mg • *Time point of administration*: droperidol immediately after induction of anaesthesia • *Route of administration*: droperidol IV • *Rescue antiemetics (if yes, which?)*: alizapride 50 mg; tropisetron 2 mg, if PONV > 30 minutes
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** supported in part by NIH Grants GM 58273 and GM 061655 (Bethesda, MD) and the Commonwealth of Kentucky Research Challenge Trust Fund (Louisville, KY). None of the authors has any personal financial interest related to this research **Country:** Belgium **Setting:** NA **Author's name:** Jean L. Joris **Institution:** Department of Anaesthesia and Intensive Care Medicine, Belgium **Email:** Jean.Joris@chu.ulg.ac.be **Address:** Department of Anaesthesia and Intensive Care Medicine, CHU de Liège, Domaine du Sart-Tilman, B-4000 Liège, Belgium **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	Two control groups without antiemetic pooled for analysis (different oxygen concentration)

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Joris 2003 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "after induction of anaesthesia, patients were randomly assigned to the following three groups" Judgement comment: no information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "patients and surgeons were blinded as to group assignment" Judgement comment: anaesthetists were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "blinded observers recorded the incidence and the severity of nausea and vomiting"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "morphometric and demographic characteristics of the participating patients were recorded. Details of anaesthetic and surgical management were similarly recorded. Postoperative pain scores were evaluated" Quote: "morphometric and demographic characteristics of the patients in all groups were similar except for age; the patients in the 30% O_2 group were younger than those in the other groups" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Joshi 2014

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50

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Joshi 2014 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 36.62 ± 14.35
- *Weight (mean ± SD, median (IQR), median (range))*: 53.22 ± 12.63
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79.66
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic procedures such as appendicectomy, diagnostic laparoscopy, cholecystectomy, hernioplasty

Palonosetron (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 36.67 ± 12.0
- *Weight (mean ± SD, median (IQR), median (range))*: 52.90 ± 13.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 81.66
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic procedures such as appendicectomy, diagnostic laparoscopy, cholecystectomy, hernioplasty

Included criteria: either sex, 18 to 60 years of age, ASA I and II, undergoing general anaesthesia for various laparoscopic surgical procedures

Excluded criteria: history of motion sickness, history of PONV, pregnant and menstruating women, received any anaesthetic in past 24 hours, body mass index > 35

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: 5 minutes after induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (metoclopramide 10 mg IV) Palonosetron (group P) • *Dose*: 0.075 mg • *Time point of administration*: 5 minutes after induction • *Route of administration*: IV

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Joshi 2014 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: 4% (metoclopramide 10 mg IV)
Outcomes	*Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Harshil Joshi **Institution:** BJ Medical College, Civil Hospital, Ahmedabad, Gujarat, India **Email:** NA **Address:** Civil Hospital, Haripura, Asarwa, Haripura, Asarwa, Ahmedabad, Gujarat 380016, Indien **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly divided into two groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "randomized double blinded study" Judgement comment: insufficient information on blinding provided ("double-blinded")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blinded")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Joshi 2014 *(Continued)*

Other bias	Unclear risk	Quote: "our study, both the groups were comparable with regards to age, sex, weight, duration of anesthesia and type of surgery" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Judkins 1982

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Haloperidol (10 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 12 • *Age (mean ± SD, median (IQR), median (range))*: 47.5 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl (up to 0.2 mg), pethidine via Cardiff Palliator: 529.8 mg (180 to 1080) • *Type of surgery*: cholecystectomy, biliary bypass surgery, surgery for duodenal ulcer Haloperidol (5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 11 • *Age (mean ± SD, median (IQR), median (range))*: 57.0 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA

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Judkins 1982 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: fentanyl (up to 0.2 mg), pethidine via Cardiff Palliator: 602.7 mg (300 to 1140)
- *Type of surgery*: cholecystectomy, biliary bypass surgery, surgery for duodenal ulcer

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 11
- *Age (mean ± SD, median (IQR), median (range))*: 47.0
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl (up to 0.2 mg), pethidine via Cardiff Palliator: 478.3 mg (210 to 1410)
- *Type of surgery*: cholecystectomy, biliary bypass surgery, surgery for duodenal ulcer

Included criteria: between 18 and 70 years of age, scheduled for elective major upper abdominal surgery but otherwise fit

Excluded criteria: NA

Pretreatment: baseline characteristics (ASA, weight): unclear; (age): yes. Potential effect modifiers (perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear; (gender): yes

Interventions	**Intervention characteristics** Haloperidol (10 mg group) • *Dose*: 10 mg • *Time point of administration*: as premedication • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: 17% NA Haloperidol (5 mg group) • *Dose*: 5 mg • *Time point of administration*: as premedication • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: 18% NA Placebo • *Dose*: NA • *Time point of administration*: as premedication • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: 73% NA
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)*

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Judkins 1982 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** the study authors would like to thank G.D. Searle and Co., for supplies of haloperidol and placebo and for financial and technical support **Country:** UK **Setting:** NA **Author's name:** K.C. Judkins **Institution:** Royal Gwent Hospital, Newport. Gwent NPT 2UB **Email:** NA **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomised". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind study")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind study")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "...and surgery for duodenal ulcer. More females were recruited to the placebo and to the 10 mg haloperidol study groups than to the 5 mg haloperidol group. This latter group tended to be older with a median age of 57.0 years as compared with 47.0 and 47.5 years respectively for the placebo. Weights ranged from 47.5 to 87.0 kg. Dosage of pethidine (mean and range) taken by patients is given in Table 1 and graphically presented in Fig. 1. It can be seen firstly that there was wide individual variation in dosage required; secondly that the dose of analgesic needed was greatest in the first 6 postoperative

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Judkins 1982 *(Continued)*

hours and thereafter fell dramatically; and finally that differences in analgesic requirements between treatment groups were not statistically significant"

Judgement comment: baseline characteristics (ASA, weight): unclear; (age): yes. Potential effect modifiers (perioperative opioids): no; (history of PONV/ motion sickness, duration of anaesthesia, non-smoker): unclear; (gender): yes

Jung 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Aprepitant (A80 group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 5 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 38 • *History of PONV/motion sickness (%)*: 1/3 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 123 • *Use of perioperative opioids (if yes, which?)*: 5 patients received ketorolac 30 mg IV; 2 patients received fentanyl 50 µg IV • *Type of surgery*: laparoscopic total hysterectomy Aprepitant (A125 group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 5 • *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 38 • *History of PONV/motion sickness (%)*: 1/4 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 122

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Jung 2013 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 4 patients received ketorolac 30 mg IV; 3 patients received fentanyl 50 µg IV
- *Type of surgery*: laparoscopic total hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 37
- *History of PONV/motion sickness (%)*: 0/2
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 126
- *Use of perioperative opioids (if yes, which?)*: 4 patients received ketorolac 30 mg IV; 2 patients received fentanyl 50 µg IV
- *Type of surgery*: laparoscopic total hysterectomy

Included criteria: ASA I or II, 21 to 60 years of age, scheduled for elective laparoscopic total hysterectomy

Excluded criteria: liver, neurological, and active pulmonary disease; cardiac arrhythmia; allergy to any perioperative medication used in this study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Aprepitant (A80 group) • *Dose*: 80 mg • *Time point of administration*: 2 hours before induction • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 8% (dexamethasone 5 mg, metoclopramide 10 mg) Aprepitant (A125 group) • *Dose*: 125 mg • *Time point of administration*: 2 hours before induction • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 10% (dexamethasone 5 mg, metoclopramide 10 mg) Placebo • *Dose*: 10 mL saline • *Time point of administration*: 2 hours before induction • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 20% (dexamethasone 5 mg, metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 2 hours)*

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Jung 2013 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (2 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 48 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Hong Seuk Yang **Institution:** Department of Anesthesiology and Pain Medicine, Asan Medical Center, College of Medicine University of Ulsan, South Korea **Email:** hsyang@amc.seoul.kr **Address:** Department of Anesthesiology and Pain Medicine, Asan Medical Center, College of Medicine University of Ulsan, 388-1 Pungnap-dong Songpa-gu, Seoul 138-736, South Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NCT01440673
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a randomization list was generated using Microsoft Excel's random function"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "to achieve blinding, an independent researcher prepared the study solutions, which consisted of a drinking cup wrapped in foil containing 10 ml saline in the control group and a cup containing dissolved aprepitant tablets in the treatment groups"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "recorded throughout the hospital stay by specially trained personnel blinded to all patient treatments"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Jung 2013 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01440673 (retrospective registration)
Other bias	Low risk	Quote: "the three groups of patients did not differ in characteristics, surgery or anesthesia duration, or and Apfel's simplified risk score (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Kaja 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ramosetron (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 43.2 • *Weight (mean ± SD, median (IQR), median (range))*: 48.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: balanced anaesthesia (N_2O, inhalational agents, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 88.67 • *Use of perioperative opioids (if yes, which?)*: anaesthesia with fentanyl (2 µg/kg); 7 patients received tramadol for postoperative pain • *Type of surgery*: major abdominal surgeries (most common surgeries were laparotomy, cholecystectomy, and abdominal hysterectomy) Ondansetron (group II) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 42.7 • *Weight (mean ± SD, median (IQR), median (range))*: 48.67 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA

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Kaja 2014 *(Continued)*

- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, inhalational agents, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 87.67
- *Use of perioperative opioids (if yes, which?)*: anaesthesia with fentanyl (2 µg/kg); 6 patients received tramadol for postoperative pain
- *Type of surgery*: major abdominal surgeries (most common surgeries were laparotomy, cholecystectomy, and abdominal hysterectomy)

Included criteria: ASA I and II, hospitalized, 18 to 60 years of age; scheduled for major abdominal surgery under general anaesthesia

Excluded criteria: gastrointestinal (GI) disease, such as hiatus hernia, gastro-oesophageal regurgitation disorder, peptic ulcer disease, and autonomic dysfunction disorder, pregnant and lactating women; renal, hepatic, or neurological impairment; any antiemetic medication within 24 hours before surgery; history of motion sickness, PONV in previous surgery or vomiting; Ryle's tube in situ in the last 24 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (gender, non-smoker): unclear

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Interventions

Intervention characteristics

Ramosetron (group I)

- *Dose*: 0.3 mg
- *Time point of administration*: before extubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ramosetron 0.3 mg IV

Ondansetron (group II)

- *Dose*: 4 mg
- *Time point of administration*: before extubation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ramosetron 0.3 mg IV

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (2 to 6 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Subjects with any SAE (0 to 24 hours)

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (0 to 1 hour, 1 to 2 hours, 2 to 6 hours, 6 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 1 hour, 1 to 2 hours, 2 to 6 hours, 6 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 1 hour, 1 to 2 hours, 2 to 6 hours, 6 to 24 hours)

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Kaja 2014 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Dr. Mukarram Iqbal **Institution:** Department of Anesthesia, Mahadevappa Rampure Medical College, Gulbarga, Karnataka, India **Email:** mdmukarramiqbal@yahoo.com **Address:** H-No: 11, MIG II phase, KHB Vakkalgera Colony, Gulbarga – 585 104, Karnataka, India **Duration of study:** January 2011 to June 2012. **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomized to the two groups by using random number tables"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind study")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind study")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (gender, non-smoker): unclear

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Kaki 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 41.4 ± 10.3 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 17/8/0/0 • *Gender (female in %)*: 72 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg/h to 2 µg/kg/h intraoperative, postoperative morphine • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide (group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 43.4 ± 10.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 19/6/0/0 • *Gender (female in %)*: 64 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg/h to 2 µg/kg/h intraoperative, postoperative morphine • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Kaki 2008 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 43.4 ± 9.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 20/5/0/0
- *Gender (female in %)*: 76
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg/h to 2 µg/kg/h intraoperative, postoperative morphine
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: adults, ASA I or II, 18 to 50 years old

Excluded criteria: ASA III and IV, emergency surgery, pregnancy, morbid obesity, susceptibility to vomiting or retching, allergy to study medicine, ongoing antiemetic or psychotropic medications use, mental retardation, psychiatric illness

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo (group P) • *Dose*: 1 mL saline • *Time point of administration*: 10 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Metoclopramide (group M) • *Dose*: 10 mg • *Time point of administration*: 10 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: 10 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Saudi Arabia

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Kaki 2008 *(Continued)*

Setting: single-centre, inpatient

Author's name: Abdullah M. Kaki

Institution: Department of Anesthesia, Faculty of Medicine, King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia

Email: amkaki@yahoo.com

Address: Department of Anesthesia, King Abdulaziz University Hospital, PO Box 2907, Jeddah 21461, Kingdom of Saudi Arabia

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomization was achieved by using a sealed envelope technique prepared by an independent personnel" Judgement comment: insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Quote: "ten minutes prior to the end of anesthesia, randomization was achieved by using a sealed envelope technique prepared by an independent personnel" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the anesthesia was performed by an anesthesiologist not involved in the before or after operation patient care" Judgement comment: anaesthesiologist was not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an independent research assistant who was unaware of the patients' randomization collected all data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 78 patients were enrolled in the study. Three patients were excluded from the study, one patient in group M, after the laparoscopic approach was changed to laparotomy for surgical reasons, and 2 patients; one in placebo group for after surgery complications (surgical), and one in group O, due to improper selection"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no significant intergroup difference in the patient demographic data, ASA classification, or surgical time"

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Kaki 2008 *(Continued)*

Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Kakuta 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 38 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 53 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 21/9/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 86.67 • *History of PONV/motion sickness (%)*: 46.67 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane + remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 180 ± 59 • *Use of perioperative opioids (if yes, which?)*: 3.1 ± 2.0 mg remifentanil, 7.0 ± 8.1 mg postoperative pentazocine • *Type of surgery*: laparoscopic gynaecological surgery Aprepitant • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/6/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 80 • *History of PONV/motion sickness (%)*: 43.33 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane + remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 173 ± 45 • *Use of perioperative opioids (if yes, which?)*: 2.6 ± 1.1 mg remifentanil, 3.0 ± 6.1 mg postoperative pentazocine • *Type of surgery*: laparoscopic gynaecological surgery

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Kakuta 2011 *(Continued)*

	Included criteria: female, 20 to 70 years of age, ASA I or II, undergoing elective laparoscopic gynaecological surgical procedures with general anaesthesia **Excluded criteria:** obesity (BMI > 33), pregnancy, steroid use, abnormal liver or renal function, neuronal disease **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes
Interventions	**Intervention characteristics** Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: metoclopramide Aprepitant • *Dose*: 80 mg • *Time point of administration*: 180 minutes before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: metoclopramide
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Grant-in-Aid for Young Scientists from Japan Society for the Promotion of Science, Tokyo **Country:** Japan **Setting:** single-centre **Author's name:** Yasuo M. Tsutsumi **Institution:** Department of Anesthesiology, Institute of Health Bioscience, University of Tokushima Graduate School, Tokushima, Japan **Email:** NA **Address:** Department of Anesthesiology, Institute of Health Bioscience, University of Tokushima Graduate School, 3-18-15 Kuramoto, Tokushima 770-8503, Japan, Fax: +81-88-633-7182 **Language:** English **Duration of study:** NA **Trial registry number:** JPRN-UMIN000003850 (not referenced in the study report) **Study's primary outcome:** NA
Notes	None

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Kakuta 2011 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized into two groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: control group without placebo treatment. Anaesthesiologists and participants were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "sixty four total patients were enrolled, but only 60 patients participated in the study. Four patients withdrew due to either changes in the surgical procedure from laparoscopic to laparotomy, changes in anaesthesia to propofol, and one patient decided not to receive aprepitant after enrolling"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: JPRN-UMIN000003850 (prospective registration). Frequency of PONV was prespecified as primary outcome in the protocol. The definition of primary and secondary outcomes in the final study report remained unclear
Other bias	High risk	Quote: "to receive aprepitant after enrolling. Thirty patients were in each group and the mean ages for the control group and NK1 group were insignificant at 38 and 35 years, respectively. There were no significance between patient height or weight and both groups had relatively similar ASA physical states and risk factors for PONV (Table 1). Furthermore, patients in both groups had similar menstrual cycle phases. All patients tolerated aprepitant without any adverse effects. Surgical/anesthetic values throughout the procedure also remained insignificant between control and NK1 groups (Table 2). Duration of anesthesia, length of procedure, patient blood loss, and infused fluid volume were all similar. Additionally, similar doses of remifentanil and rocuronium were used in both groups. PONV incidence at acute phase" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Kakuta 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics**

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Kakuta 2015 *(Continued)*

Fosaprepitant (NK1 group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 21
- *Received treatment (n)*: 21
- *Analysed (n)*: 19
- *Age (mean ± SD, median (IQR), median (range))*: 61 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 6/13/0/0
- *Gender (female in %)*: 57.8
- *Non-smoker (%)*: 89.47
- *History of PONV/motion sickness (%)*: 5.26
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane or desflurane, remifentanil, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 242
- *Use of perioperative opioids (if yes, which?)*: 2.5 mg remifentanil intraoperatively, 74 µg fentanyl intraoperatively, 721 µg fentanyl postoperatively
- *Type of surgery*: lower limb surgery

Ondansetron (ONS group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 22
- *Received treatment (n)*: 21
- *Analysed (n)*: 19
- *Age (mean ± SD, median (IQR), median (range))*: 56 ± 16
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 5/14/0/0
- *Gender (female in %)*: 68.4
- *Non-smoker (%)*: 89.47
- *History of PONV/motion sickness (%)*: 10.53
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane or desflurane, remifentanil, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 264
- *Use of perioperative opioids (if yes, which?)*: 3.0 mg remifentanil intraoperatively, 79 µg fentanyl intraoperatively, 726 µg fentanyl postoperatively
- *Type of surgery*: lower limb surgery

Included criteria: ASA I and II, scheduled to undergo lower limb surgery (total hip arthroplasty, total knee arthroplasty, rotational acetabular osteotomy) under general anaesthesia

Excluded criteria: ASA III or IV, abnormal liver and/or renal function, use of other antiemetics

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Fosaprepitant (NK1 group)

- *Dose*: 150 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

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Kakuta 2015 *(Continued)*

	Ondansetron (ONS group) • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was supported entirely by JSPS KAKENHI (Grant Number 24791598) **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Yasuo M. Tsutsumi **Institution:** Department of Anesthesiology, Tokushima University, Kuramoto, Tokushima, Japan **Email:** tsutsumi@tokushima-u.ac.jp **Address:** Department of Anesthesiology, Tokushima University, 3-18-15 Kuramoto, Tokushima770-8503, Japan **Duration of study:** 31 January 2014 to 8 May 2015 **Language:** English **Study's primary outcome:** incidence of vomiting (power analysis) **Trial registry number:** UMIN000012999
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "the patients were subjected to randomized, computer-generated allocation (QuickCalcs, GraphPad Inc., La Jolla, CA, USA)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Kakuta 2015 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, anaesthesiologists, and observers were all 'blinded' to the study medication"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients, anaesthesiologists, and observers were all 'blinded' to the study medication"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of 48 patients considered eligible for the study, 5 refused and 43 agreed to participate. One patient in ONS group was excluded due to the operation being called off, and 2 patients in each group were converted to intravenous patient-controlled analgesia for pain relief because of dislodgement or occlusion of the epidural catheter"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: UMIN000012999 (prospective registration). Frequency of PONV without any time specification was prespecified as a primary outcome in the protocol. The definition of primary and secondary outcomes in the final study report remained unclear. A power analysis was performed for incidence of vomiting
Other bias	Low risk	Quote: "there were no significant differences in patient demographics, risk factors for PONV, duration of surgery and anaesthesia, intraoperative and postoperative opioid use, and postoperative analgesic intake between the 2 groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Kanakoudis 1985

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 42.9 ± 11.6 • *Weight (mean ± SD, median (IQR), median (range))*: 59.9 ± 6.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 15/15/NA • *Gender (female in %)*: 0 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 76.8

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Kanakoudis 1985 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg pethidine preoperative, fentanyl intraoperative
- *Type of surgery*: breast, thyroid, neck, or upper and lower limb surgery

Domperidone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 44.3 ± 9.9
- *Weight (mean ± SD, median (IQR), median (range))*: 62.1 ± 7.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 15/15/NA
- *Gender (female in %)*: 0
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88.3
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg pethidine preoperative, fentanyl intraoperative
- *Type of surgery*: breast, thyroid, neck, or upper and lower limb surgery

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 44.4 ± 12.5
- *Weight (mean ± SD, median (IQR), median (range))*: 61.2 ± 5.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 16/14/NA
- *Gender (female in %)*: 0
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 98.7
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg pethidine preoperative, fentanyl intraoperative
- *Type of surgery*: breast, thyroid, neck, or upper and lower limb surgery

Included criteria: male; ASA I or II; scheduled for breast, thyroid, neck, or upper and lower limb surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear; (duration of anaesthesia): yes

Interventions	**Intervention characteristics**

Placebo

- *Dose*: NaCl 0.9%
- *Time point of administration*: 30 minutes before end of anaesthesia
- *Route of administration*: IV

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Kanakoudis 1985 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: NA

Domperidone

- *Dose*: 20 mg
- *Time point of administration*: 30 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol

- *Dose*: 2.5 mg
- *Time point of administration*: 30 minutes before end of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Greece **Setting:** NA **Author's name:** Ph. Kanakoudis **Institution:** NA **Email:** NA **Address:** NA **Duration of study:** NA **Language:** Greek (translated by Argyro Fassoulaki) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly" (translated). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "double blind fashion" (translated). Insufficient information on blinding provided
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement comment: quote: "double blind fashion" (translated). Insufficient information on blinding provided

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Kanakoudis 1985 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear; (duration of anaesthesia): yes

Karabayirli 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group K) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 37 ± 3 • *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 73.33 • *Non-smoker (%)*: 80 • *History of PONV/motion sickness (%)*: 6.67 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 188 • *Use of perioperative opioids (if yes, which?)*: premedication with pethidine 25 mg IV, induction with fentanyl 1 µg/kg • *Type of surgery*: middle ear surgery Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 34 ± 3 • *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 4 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Karabayirli 2003 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: 56.25
- *History of PONV/motion sickness (%)*: 18.75
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 198
- *Use of perioperative opioids (if yes, which?)*: premedication with pethidine 25 mg IV, induction with fentanyl 1 µg/kg
- *Type of surgery*: middle ear surgery

Dexamethasone (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 3
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: 86.67
- *History of PONV/motion sickness (%)*: 13.33
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 148
- *Use of perioperative opioids (if yes, which?)*: premedication with pethidine 25 mg IV, induction with fentanyl 1 µg/kg
- *Type of surgery*: middle ear surgery

Included criteria: ASA I or II, 18 to 60 years of age, elective middle ear surgery

Excluded criteria: history of gastrointestinal disease, renal disease, liver disease, cerebral disease, vestibular apparatus, insufficiency of the vertebra-basilar flow area, intake of antiemetics

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (perioperative opioids): unclear; (duration of anaesthesia): yes

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Interventions

Intervention characteristics

Control (group K)

- *Dose*: NA
- *Time point of administration*: NA
- *Route of administration*: NA
- *Rescue antiemetics (if yes, which?)*: (53%) metoclopramide 10 mg IV

Ondansetron (group O)

- *Dose*: 8 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: (18.8%) metoclopramide 10 mg IV

Dexamethasone (group D)

- *Dose*: 5 mg

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Karabayirli 2003 *(Continued)*

- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: (20%) metoclopramide 10 mg IV

Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** NA **Author's name:** Sallnaz Karabayirli **Institution:** Ankara Univcrsitesi Tip Fakiiltesi ibn-t Sina Hastanesi Anestcziyoloji ve Reaniroasyon Anabilim Dali **Email:** drsarinaz@yahou.com **Address:** Samanpazan-Aiikara, Turkey **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Three out of 4 groups relevant (supplemental oxygen)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly assigned". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Karabayirli 2003 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (perioperative opioids): unclear; (duration of anaesthesia): yes

Kaul 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 80 • *Age (mean ± SD, median (IQR), median (range))*: 37.73 ± 13.58 • *Weight (mean ± SD, median (IQR), median (range))*: 56.68 ± 10.98 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 60/20/0/0 • *Gender (female in %)*: 51.25 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (N_2O, halothane, opioid) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 117.2 • *Use of perioperative opioids (if yes, which?)*: 52.87 ± 19.88 mg pethidine intraoperative, 7.26 ± 1.38 mg morphine postoperative • *Type of surgery*: gall bladder, gynaecological, orthopaedic, ophthalmological, ENT, miscellaneous Ondansetron (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 81 • *Age (mean ± SD, median (IQR), median (range))*: 37.58 ± 12.98 • *Weight (mean ± SD, median (IQR), median (range))*: 57.96 ± 9.00 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 64/17/0/0 • *Gender (female in %)*: 55.56 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (N_2O, halothane, opioid) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 116.6

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Kaul 1996 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 52.22 ± 14.41 mg pethidine intraoperative, 7.12 ± 1.75 mg morphine postoperative
- *Type of surgery*: gall bladder, gynaecological, orthopaedic, ophthalmological, ENT, miscellaneous

Metoclopramide (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: 40.82 ± 13.80
- *Weight (mean ± SD, median (IQR), median (range))*: 57.48 ± 12.01
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 66/14/0/0
- *Gender (female in %)*: 58.75
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, halothane, opioid)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 114.6
- *Use of perioperative opioids (if yes, which?)*: 56.12 ± 17.21 mg pethidine intraoperative, 7.35 ± 1.34 mg morphine postoperative
- *Type of surgery*: gall bladder, gynaecological, orthopaedic, ophthalmological, ENT, miscellaneous

Included criteria: ASA I or II, adults younger than 65 years of age, undergoing an elective surgical procedure under general anaesthesia

Excluded criteria: liver disease, renal impairment, pregnancy or lactation, known allergy to test drugs, neurological or endocrine abnormalities, history of emesis in the last 24 hours, requiring a nasogastric tube in the postoperative period

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo (group A) • *Dose*: NA • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: at discretion of attending physician Ondansetron (group B) • *Dose*: 8 mg • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: at discretion of attending physician Metoclopramide (group C) • *Dose*: 10 mg • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: at discretion of attending physician
Outcomes	*Nausea (0 to 24 hours)*

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Kaul 1996 *(Continued)*

- Outcome type: dichotomous outcome

PONV (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NATCO Pharma Laboratories supplied the drugs (ondansetron, metoclopramide, and placebo) for the study and help in conduct of the study **Country:** India **Setting:** NA **Author's name:** H.L. Kaul **Institution:** Department of Anaestesiology, India Institute of Medical Sciences, New Delhi **Email:** NA **Address:** Department of Anaesthesiology, all India Institute of Medical Sciences, New Delhi 110029 **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "the drugs were enclosed in sealed identical envelopes marked A, B or C and administered to the patient by a nurse (who was not aware of the identity of the tablet) one hour before induction of anaesthesia" Not stated: "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no information on blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no information on blinding of outcome assessors

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Kaul 1996 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Kawano 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 67.7 ± 10.9 • *Weight (mean ± SD, median (IQR), median (range))*: 58.8 ± 9.5 • *BMI (mean ± SD, median (IQR), median (range))*: 25.7 ± 3.2 • *ASA I/II/III/IV (n)*: 9/21/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 16.67 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 174.8 • *Use of perioperative opioids (if yes, which?)*: 1.91 mg remifentanil intraoperative, 0.8 mg pentazocine postoperative as rescue analgesic • *Type of surgery*: knee osteoarthritis surgery (high tibial osteotomy or total knee arthroplasty) Aprepitant + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 68.0 ± 8.7 • *Weight (mean ± SD, median (IQR), median (range))*: 59.3 ± 8.7 • *BMI (mean ± SD, median (IQR), median (range))*: 26.0 ± 3.4 • *ASA I/II/III/IV (n)*: 9/21/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100

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Kawano 2015 *(Continued)*

- *History of PONV/motion sickness (%)*: 30
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 183.1
- *Use of perioperative opioids (if yes, which?)*: 2.087 mg remifentanil intraoperative, 0.5 mg pentazocine postoperative as rescue analgesic
- *Type of surgery*: knee osteoarthritis surgery (high tibial osteotomy or total knee arthroplasty)

Included criteria: non-smoking adult females scheduled for elective knee osteoarthritis surgery (high tibial osteotomy or total knee arthroplasty) under general anaesthesia plus epidural anaesthesia with ASA I or II

Excluded criteria: obesity (BMI > 33 kg/m^2); neurological, renal, or liver disease; allergy to one of the study drugs; current use of drugs with antiemetic properties, including corticosteroids

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: intravenous metoclopramide (10 mg) 0 to 24 hours: 23%

Aprepitant + dexamethasone

- *Dose*: aprepitant 80 mg, dexamethasone 8 mg
- *Time point of administration*: aprepitant 2 hours before induction of anaesthesia, dexamethasone immediately before induction of anaesthesia
- *Route of administration*: aprepitant PO, dexamethasone IV
- *Rescue antiemetics (if yes, which?)*: intravenous metoclopramide (10 mg) 0 to 24 hours: 27%

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (0 to 2 hours)

- Outcome type: dichotomous outcome

Vomiting (2 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Japan

Setting: inpatient, single-centre

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Kawano 2015 *(Continued)*

Author's name: H. Kawano

Institution: Department of Anesthesiology and Clinical Research, National Hospital Organization Zentsuji Hospital, Zentsuji, Japan; Department of Anesthesiology, Tokushima Prefectural Central Hospital, Tokushima, Japan

Email: hir.kawano@gmail.com

Address: Department of Anesthesiology, Tokushima Prefectural Central Hospital, 1-10-3 Kuramoto, Tokushima 770-8539, Japan

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "using the sealed envelope method" Quote: "patients were randomly assigned to either the aprepitant + dexamethasone group or dexamethasone group" Judgement comment: insufficient information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "using the sealed envelope method" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "aprepitant 80 mg was orally administered 2 hours before the induction of anesthesia. In both groups, intravenous dexamethasone 8 mg was administered immediately before the induction of anesthesia" Judgement comment: no placebo treatment in the control group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the incidence and severity of PONV were assessed by observers blinded to group assignment at 2 and 24 hours after surgery"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...was set at P<0.05. All patients completed the study (30 in the aprepitant + dexamethasone group and 30 in the dexamethasone group). There were no significant..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "differences in mean age, height, weight, BMI, ASA physical status, history of motion sickness and/or PONV, and menstrual cycle phase between treatment groups (Table I), although more patients in the aprepitant + dexamethasone group had a history of motion sickness and/or PONV. Similarly, there were no significant differences in intraoperative variables, including duration of anesthesia and surgery; total doses of remifentanil, rocuronium, and

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Kawano 2015 *(Continued)*

	0.375% ropivacaine; surgery type, body temperature, mean blood loss, and mean intravascular fluid volume (Table II)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Kaya 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide (group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 44.3 ± 6.1 • *Weight (mean ± SD, median (IQR), median (range))*: 76.0 ± 11.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 69.3 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl • *Type of surgery*: NA Placebo (group S) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 12.8 • *Weight (mean ± SD, median (IQR), median (range))*: 70.1 ± 9.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 66.3 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl • *Type of surgery*: NA

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Kaya 2000 *(Continued)*

	Included criteria: ASA I and II, 18 to 65 years or age, presenting for elective surgery **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Metoclopramide (group M) • *Dose*: 20 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo (group S) • *Dose*: saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (in recovery room)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (time point unknown)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, PACU)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** F. Nur Kaya **Institution:** Uludag Univ. Tip Tak. Anestieziyoloji Anabilim Dali **Email:** NA **Address:** NA **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 10 groups relevant (e.g. different opioids, local anaesthetics).

Risk of bias

Bias	Authors' judgement	Support for judgement

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Kaya 2000 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Khafagy 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 21/9/0/0 • *Gender (female in %)*: 40 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (epidural + inhalational anaesthesia (isoflurane)) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 100 • *Use of perioperative opioids (if yes, which?)*: 91 µg fentanyl, 30 mg meperidine • *Type of surgery*: bladder stone, varicocelectomy, orchiectomy, herniorrhaphy

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Khafagy 2010 *(Continued)*

	Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 18/12/0/0 • *Gender (female in %)*: 40 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (epidural + inhalational anaesthesia (isoflurane)) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 100 • *Use of perioperative opioids (if yes, which?)*: 102 µg fentanyl, 80 mg meperidine • *Type of surgery*: bladder stone, varicocelectomy, orchiectomy, herniorrhaphy **Included criteria:** 25 to 65 years of age, either sex, ASA I or II, scheduled for various lower abdominal/urological surgeries (e.g. bladder stone, varicocelectomy, orchiectomy, herniorrhaphy) **Excluded criteria:** history of peptic ulcer disease, contraindication to epidural anaesthesia (back fusion, coagulopathy, local infection), failure to achieve epidural analgesia, obese, diabetic, had received corticosteroids or immunosuppressive drugs in the last 6 months, contraindication to corticosteroids **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 4 mg • *Time point of administration*: right before induction of general anaesthesia • *Route of administration*: epidural • *Rescue antiemetics (if yes, which?)*: diphenhydramine 25 mg and metoclopramide 10 mg IM Placebo • *Dose*: 5 mL normal saline • *Time point of administration*: right before induction of general anaesthesia • *Route of administration*: epidural • *Rescue antiemetics (if yes, which?)*: diphenhydramine 25 mg and metoclopramide 10 mg IM
Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA

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Khafagy 2010 *(Continued)*

Country: Egypt

Setting: inpatient, single-centre

Author's name: H.F. Khafagy

Institution: Department of Anesthesiology, Theodor Bilharz Research Institute, Ministry of High Education and Scientific Research, Egypt

Email: hananfkhafagy993@hotmail.com

Address: Warak El-Hadar, Kornish El-Nile, P.O. Box 30 Imbaba, Giza 12411, Egypt

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: meperidine consumption

Notes	Two out of 3 groups relevant (fentanyl)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using computer-generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the patient, anesthesiologist, and observers collecting data were blinded to the patient's study group allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patient, anesthesiologist, and observers collecting data were blinded to the patient's study group allocation"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "two patients were excluded from the study after randomization because of epidural analgesia failure" Judgement comment: 2 patients were excluded after randomization according to study authors, but data for all patients (n = 90) are reported
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Khalil 1994

Study characteristics

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Khalil 1994 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 152 • *Received treatment (n)*: NA • *Analysed (n)*: 143 • *Age (mean ± SD, median (IQR), median (range))*: 33.7 ± 0.8 • *Weight (mean ± SD, median (IQR), median (range))*: 67.0 ± 1.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 30/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 61.5 • *Use of perioperative opioids (if yes, which?)*: alfentanil or fentanyl during anaesthesia • *Type of surgery*: gynaecological, orthopaedic, peripheral, ear/nose/throat/oral, eye, abdominal Ondansetron (1 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 145 • *Received treatment (n)*: NA • *Analysed (n)*: 131 • *Age (mean ± SD, median (IQR), median (range))*: 32.2 ± 0.7 • *Weight (mean ± SD, median (IQR), median (range))*: 67.5 ± 1.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 26/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 60 • *Use of perioperative opioids (if yes, which?)*: alfentanil or fentanyl during anaesthesia • *Type of surgery*: gynaecological, orthopaedic, peripheral, ear/nose/throat/oral, eye, abdominal Ondansetron (4 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 148 • *Received treatment (n)*: NA • *Analysed (n)*: 136 • *Age (mean ± SD, median (IQR), median (range))*: 32.6 ± 1.2 • *Weight (mean ± SD, median (IQR), median (range))*: 66.7 ± 1.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0

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Khalil 1994 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 28/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 59.9
- *Use of perioperative opioids (if yes, which?)*: alfentanil or fentanyl during anaesthesia
- *Type of surgery*: gynaecological, orthopaedic, peripheral, ear/nose/throat/oral, eye, abdominal

Ondansetron (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 144
- *Received treatment (n)*: NA
- *Analysed (n)*: 129
- *Age (mean ± SD, median (IQR), median (range))*: 32.5 ± 0.7
- *Weight (mean ± SD, median (IQR), median (range))*: 65.5 ± 1.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 28/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 60.5
- *Use of perioperative opioids (if yes, which?)*: alfentanil or fentanyl during anaesthesia
- *Type of surgery*: gynaecological, orthopaedic, peripheral, ear/nose/throat/oral, eye, abdominal

Included criteria: healthy women, 18 to 70 years or age, ASA I or II, scheduled for elective outpatient surgical procedure

Excluded criteria: pregnant; more than 100% over ideal body weight; had received a tricyclic antidepressant, phenothiazine, antiemetic, H2 antagonist, or corticosteroid within 24 hours of the study; pre-study serum alanine aminotransferase (ALT) concentrations greater than twice the upper limit of normal, serum creatinine concentration > 2.0 mg/mL; scheduled for liver surgery or biopsy; required gastric suction via intragastric tube intraoperatively or postoperatively; history of emesis or retching within 24 hours before receiving the study drug

Pretreatment: potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Placebo

- *Dose*: 0.9% NaCl
- *Time point of administration*: before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: the choice of antiemetic was left to the physician

Ondansetron (1 mg group)

- *Dose*: 1 mg
- *Time point of administration*: before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: the choice of antiemetic was left to the physician

Ondansetron (4 mg group)

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Khalil 1994 *(Continued)*

	• *Dose*: 4 mg • *Time point of administration*: before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: the choice of antiemetic was left to the physician Ondansetron (8 mg group) • *Dose*: 8 mg • *Time point of administration*: before anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: the choice of antiemetic was left to the physician
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was supported by a grant from Glaxo Research Institute (Research Triangle Park, NC, USA) **Country:** USA **Setting:** outpatient, multi-centre (10) **Author's name:** Samia N. Khalil **Institution:** University of Texas Medical School, Houston, Texas, USA **Email:** NA **Address:** Anesthesia Department, University of Texas Medical School, 6431 Fannin MSMB 5.020, Houston,TX 77030, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** primary efficacy variable was the number of emetic episodes
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement

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Khalil 1994 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "patients were randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "all ondansetron doses were diluted with placebo to a volume of 8 ml and then further diluted with normal saline (0.9% NaCl) to a total volume of 20 ml to maintain the blinded design of the study"; "the study drug was then administered IV in a double-blind fashion"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "in the PACU an independent blinded observer recorded..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "a total of 589 patients were enrolled in the trial. An efficacy subgroup was created by excluding patients with protocol violations which may have affected efficacy results. Forty patients were excluded from the efficacy analysis of the initial 2-h study period, and an additional 10 patients were dropped from the 24-h analysis"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: quote: "there was no difference between treatment groups in ethnic origin, weight, age, height, days since last menstrual period, or previous anaesthetic experience" Baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Khan 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 25.4 ± 5 • *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Khan 2005 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 35
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: diagnostic gynaecological laparoscopy

Ondansetron (group II)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 27.7 ± 11.8
- *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 32
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: diagnostic gynaecological laparoscopy

Control (group VI)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 25.2 ± 4.3
- *Weight (mean ± SD, median (IQR), median (range))*: 67.2 ± 4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 39
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: diagnostic gynaecological laparoscopy

Included criteria: adult, non-pregnant females, 18 to 40 years of age, ASA I or II, scheduled for diagnostic gynaecological laparoscopy

Excluded criteria: severe systemic or endocrine disease with predisposing factors for delayed gastric emptying, such as diabetes; chronic cholecystitis; neuromuscular disorders; history of postoperative nausea and vomiting (PONV) or had received an antiemetic drug or narcotic medication within the last 24 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics**

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Khan 2005 *(Continued)*

	Granisetron (group I) • *Dose*: 40 µg/kg • *Time point of administration*: 3 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (group II) • *Dose*: 40 to 60 µg/kg • *Time point of administration*: 3 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Control (group VI) • *Dose*: 0.9% normal saline • *Time point of administration*: NA • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 4 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 12 hours)* • Outcome type: dichotomous outcome *Headache (0 to 12 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 12 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Saudi Arabia **Setting:** NA, multi-centre (2) **Author's name:** Parhaizgar Khan **Institution:** Department of Anaesthesia Alquwayiyah General Hospital, Saudi Arabia **Email:** NA **Address:** Department of Anaesthesia, Khyber Teaching Hospital, Peshawar **Language:** English **Duration of study:** January 2004 to June 2004 **Trial registry number:** NA **Study's primary outcome:** NA

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Khan 2005 *(Continued)*

Notes	Three out of 6 groups relevant (propofol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "will be randomly allocated to receive" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: anaesthesiologist was not blinded (different treatments for groups)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no significant differences between significant difference in the 4 groups (III, IV, V, the groups regarding age, weight, and duration of VI). Table (3), Fig (4)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Khan 2006

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 37.94 ± 8.59 • *Weight (mean ± SD, median (IQR), median (range))*: 56.32 ± 6.92

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Khan 2006 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: a standardized protocol for general anaesthesia was followed for all patients
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105.0
- *Use of perioperative opioids (if yes, which?)*: tramadol for postoperative pain
- *Type of surgery*: laparoscopic cholecystectomy

Granisetron (group G)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: 60
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 38.0 ± 9.96
- *Weight (mean ± SD, median (IQR), median (range))*: 55.68 ± 7.12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: a standardized protocol for general anaesthesia was followed for all patients
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 107.0
- *Use of perioperative opioids (if yes, which?)*: tramadol for postoperative pain
- *Type of surgery*: laparoscopic cholecystectomy

Granisetron + dexamethasone (group G + D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: 60
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 38.84 ± 9.84
- *Weight (mean ± SD, median (IQR), median (range))*: 56.28 ± 6.63
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: a standardized protocol for general anaesthesia was followed for all patients
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 103.3
- *Use of perioperative opioids (if yes, which?)*: tramadol for postoperative pain
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: both sexes, 20 to 65 years of age, ASA I or II, scheduled for laparoscopic cholecystectomy

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Khan 2006 *(Continued)*

	Excluded criteria: gastrointestinal disease, history of motion sickness, history of PONV, smoker, had received antiemetic or steroid preparations within 24 hours of surgery, pregnant or menstruating **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (gender, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo (group P) • *Dose*: 5 mL normal saline • *Time point of administration*: just before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Granisetron (group G) • *Dose*: 40 µg/kg • *Time point of administration*: just before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Granisetron + dexamethasone (group G + D) • *Dose*: granisetron 40 µg/kg, dexamethasone 8 mg • *Time point of administration*: just before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Authors name:** Mohd. Parvez Khan **Institution:** Department of Anaesthesiology, King George's Medical University, India

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Khan 2006 *(Continued)*

Email: NA

Address: Department of Anaesthesiology, King George's Medical University, Lucknow-226003 U.P. India

Duration of study: NA

Language: English

Study's primary outcome: complete response in 24 hours

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "in this clinical study, the treatment groups were similar with respect to patient's age, sex, weight, duration of anaesthesia, surgical procedure, carbon dioxide insufflation, premedication and drugs given for general anaesthesia and postoperative analgesia" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (gender, perioperative opioids): unclear

Khan 2008

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, combination prophylaxis
Participants	**Baseline characteristics**

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Khan 2008 *(Continued)*

Placebo (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 35.94 ± 10.12
- *Weight (mean ± SD, median (IQR), median (range))*: 55.18 ± 7.52
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 80
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 108.10
- *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg before induction and 1 µg/kg to 2 µg/kg during anaesthesia
- *Type of surgery*: laparoscopic abdominal surgery

Granisetron + droperidol (group GDr)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 36.50 ± 9.4
- *Weight (mean ± SD, median (IQR), median (range))*: 56.32 ± 9.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 75
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 106.25 ± 10.68
- *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg before induction and 1 µg/kg to 2 µg/kg during anaesthesia
- *Type of surgery*: laparoscopic abdominal surgery

Granisetron + dexamethasone (group GDx)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 38.48 ± 10.12
- *Weight (mean ± SD, median (IQR), median (range))*: 54.42 ± 10.25
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 77.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0

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Khan 2008 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 108.90 ± 9.18
- *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg before induction and 1 µg/kg to 2 µg/kg during anaesthesia
- *Type of surgery*: laparoscopic abdominal surgery

Dexamethasone + droperidol (group DxDr)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 28.9 ± 10.22
- *Weight (mean ± SD, median (IQR), median (range))*: 55.34 ± 8.92
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 80
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 107.10 ± 8.12
- *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg before induction and 1 µg/kg to 2 µg/kg during anaesthesia
- *Type of surgery*: laparoscopic abdominal surgery

Included criteria: either sex, ASA I or II, 20 to 60 years of age, scheduled for laparoscopic abdominal surgery

Excluded criteria: gastrointestinal disease; history of postoperative nausea and vomiting (PONV); history of motion sickness; had received opioids, antiemetics, steroids, or NSAIDs; had hypersensitivity to any of the 3 drugs

Pretreatment: baseline characteristics (weight, ASA): no; (age): yes. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Interventions

Intervention characteristics

Placebo (group P)

- *Dose*: 5 mL saline
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 40% (ondansetron 4 mg)

Granisetron + droperidol (group GDr)

- *Dose*: granisetron 3 mg, droperidol 1.25 mg
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 0% (ondansetron 4 mg)

Granisetron + dexamethasone (group GDx)

- *Dose*: granisetron 3 mg, dexamethasone 8 mg
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV

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Khan 2008 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: 0% (ondansetron 4 mg)

Dexamethasone + droperidol (group DxDr)

- *Dose*: dexamethasone 8 mg, droperidol 1.25 mg
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 7.5% (ondansetron 4 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** NA **Author's name:** M. Khan **Institution:** Department of Anesthesiology, CSM Medical University **Email:** NA **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Khan 2008 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "orally on the night before surgery. Patients were randomly allocated to one of the four groups using a computer generated table of random numbers. Group P: Patients received 5ml"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "combination with droperidol 1.25 mg. The study medications were prepared by the technician in identical syringes and in equal volume to make the study double blind. Neither the patient nor the observer was aware of the medication received by the patient. A standard protocol for general anesthesia" Judgement comment: anaesthetists were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "neither the patient nor the observer was aware of the medication received by the patient"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the treatment groups were comparable with regards to patient demographics and types of operation. A complete response was observed" Judgement comment: baseline characteristics (weight, ASA): no; (age): yes. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Khanna 1965

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 200 • *Received treatment (n)*: NA • *Analysed (n)*: 200 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 19 • *Non-smoker (%)*: NA

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Khanna 1965 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: all surgery except intracranial and open heart surgery

Thiethylperazine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 200
- *Received treatment (n)*: NA
- *Analysed (n)*: 200
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 23
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: all surgery except intracranial and open heart surgery

Included criteria: NA

Excluded criteria: younger than 5 years, undergoing intracranial and open heart surgery, operations under local or spinal anaesthesia, given any drugs that have an antiemetic action

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: placebo • *Time point of administration*: immediately on arrival to the postoperative recovery room • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA Thiethylperazine • *Dose*: 10 mg • *Time point of administration*: immediately on arrival to the postoperative recovery room • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Sandoz Pharmaceticals (India) Limited for furnishing Torecan brand thiethylperazine used in the present trial **Country:** India

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Khanna 1965 *(Continued)*

Setting: inpatient, single-centre

Author's name: S.K. Khanna

Institution: Institute of Postgraduate Medical Education Research, Chandigarh

Email: NA

Address: NA

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "made by randomisation". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "ampoules which were coded A and B"; "the codes were not broken till completion of the study" Insufficient information on allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: stated as "double-blind". Neither the individual administering the drug nor the observer knew what agent had been given
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: stated as "double-blind". Neither the individual administering the drug nor the observer knew what agent had been given
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Kil 1999

Study characteristics

Methods	**Study design:** randomized controlled trial

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Kil 1999 *(Continued)*

Study grouping: 4 groups, monoprophylaxis and combination prophylaxis

Participants	**Baseline characteristics**

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 40.8 ± 11.3
- *Weight (mean ± SD, median (IQR), median (range))*: 62.2 ± 10.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 90
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 35/55
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 196.8
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: thyroidectomy surgery

Ondansetron (group O)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 19
- *Received treatment (n)*: 19
- *Analysed (n)*: 19
- *Age (mean ± SD, median (IQR), median (range))*: 37.2 ± 14.8
- *Weight (mean ± SD, median (IQR), median (range))*: 59.2 ± 8.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 89.47
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31.58/21.05
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 186.1
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: thyroidectomy surgery

Droperidol (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 18
- *Received treatment (n)*: 18
- *Analysed (n)*: 18
- *Age (mean ± SD, median (IQR), median (range))*: 35.9 ± 8.8
- *Weight (mean ± SD, median (IQR), median (range))*: 57.6 ± 7.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 88.89

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Kil 1999 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 33.33/ 33.33
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 183.9
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: thyroidectomy surgery

Ondansetron + droperidol (group O+D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 19
- *Received treatment (n)*: 19
- *Analysed (n)*: 19
- *Age (mean ± SD, median (IQR), median (range))*: 41.2 ± 13.2
- *Weight (mean ± SD, median (IQR), median (range))*: 57.7 ± 9.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 84.21
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 5.26/ 42.10
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 157.8
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: thyroidectomy surgery

Included criteria: thyroidectomy, 18 to 65 years of age, ASA I or II

Excluded criteria: more than 50% of standard weight, received antiemetic therapy within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of motion sickness): no; (non-smoker, perioperative opioids): unclear; (history of PONV, duration of anaesthesia): yes

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Interventions

Intervention characteristics

Placebo (group C)

- *Dose*: NaCl 2 mL
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: yes (no details provided)

Ondansetron (group O)

- *Dose*: 70 µg/kg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: yes (no details provided)

Droperidol (group D)

- *Dose*: 10 µg/kg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: yes (no details provided)

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Kil 1999 *(Continued)*

	Ondansetron + droperidol (group O+D) • *Dose*: ondansetron 70 µg/kg, droperidol 10 µg/kg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: yes (no details provided)
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Korea, R.O.C. **Setting:** inpatient, single-centre **Author's name:** Sook Young Lee **Institution:** Ajou University School of Medicine, Suwon, Korea **Email:** NA **Address:** 206 Woldeukeom-ro, Woncheon-dong, Yeongtong-gu,Suwon, Gyeonggi-do, Korea **Duration of study:** June 1998 to October 1998 **Language:** Korean (translated by Woocheol Sim) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement

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Kil 1999 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of motion sickness): no; (non-smoker, perioperative opioids): unclear; (history of PONV, duration of anaesthesia): yes

Kim 1992

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 30.8 ± 4.0 • *Weight (mean ± SD, median (IQR), median (range))*: 53.6 ± 6.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 26/2/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 32.1 • *Use of perioperative opioids (if yes, which?)*: meperidine 1 mg/kg • *Type of surgery*: outpatient laparoscopy Scopolamine (TDS Group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 30.1 ± 2.8 • *Weight (mean ± SD, median (IQR), median (range))*: 52.6 ± 6.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 25/2/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA

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Kim 1992 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 30.7
- *Use of perioperative opioids (if yes, which?)*: meperidine 1 mg/kg
- *Type of surgery*: outpatient laparoscopy

Included criteria: exploratory laparoscopy, 25 to 43 years of age, ASA I and II

Excluded criteria: glaucoma, intestinal obstruction, renal obstruction

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (gender, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: no placebo patch (atropine 0.5 mg) • *Time point of administration*: atropine 0.5 mg right before surgery • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: no rescue medication given Scopolamine (TDS Group) • *Dose*: 1.5 mg scopolamine • *Time point of administration*: at least 8 hours before surgery • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: no rescue medication given
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea, R.O.C. **Setting:** outpatient, single-centre **Author's name:** Jong Hak Kim **Institution:** Department of Anaesthesia, College of Medicine, Ewha Womans University **Email:** NA **Address:** 52 Ewhayeodae-gil, Sinchon-dong, Seodaemun-gu, Seoul, South Korea

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Kim 1992 *(Continued)*

	Duration of study: NA **Language:** Korean **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: participants were randomly divided into 2 groups without any details on sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no placebo patch in the control group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (duration of anaesthesia): no; (gender, history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Kim 1999

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20

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Kim 1999 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 44.1 ± 10.9
- *Weight (mean ± SD, median (IQR), median (range))*: 54.9 ± 7.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 130.3
- *Use of perioperative opioids (if yes, which?)*: 758.1 µg fentanyl postoperative
- *Type of surgery*: hysterectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 44.0 ± 9.7
- *Weight (mean ± SD, median (IQR), median (range))*: 60.0 ± 9.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 122.8
- *Use of perioperative opioids (if yes, which?)*: 847.1 µg fentanyl postoperative
- *Type of surgery*: hysterectomy

Included criteria: ASA I or II, receiving postoperative PCA for pain, written consent

Excluded criteria: renal disease, cardiovascular disease, liver disease, nausea or vomiting within 24 hours before surgery or receiving antiemetic drugs, obesity

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: NaCl 2 mL • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg IV Ondansetron • *Dose*: 4 mg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg IV
Outcomes	*Vomiting (0 to 24 hours)*

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Kim 1999 *(Continued)*

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (at 6 hours, at 24 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** Korea, R.O.C **Setting:** inpatient, single-centre **Author's name:** Soon Im Kim **Institution:** Department of Anaesthesiology, Soonchunhyang University Hospital, Seoul, Korea **Email:** soonnim@hosp.sch.ac.kr **Address:** 59 Daesagwan-ro, Hannam-dong, Yongsan-gu, Seoul, South Korea **Duration of study:** NA **Language:** Korean (translated by Woocheol Sim) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: an investigator blinded to group assignment observed participants at 6 and 24 hours after surgery for PONV, sedation, and adverse events
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Kim 1999 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Kim 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 33.3/NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 105 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: breast surgery Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 21 • *Received treatment (n)*: 21 • *Analysed (n)*: 21 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 28.57/NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 95

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Kim 2000 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: breast surgery

Ondansetron (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 19
- *Received treatment (n)*: 19
- *Analysed (n)*: 19
- *Age (mean ± SD, median (IQR), median (range))*: 48 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31.58/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 89
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: breast surgery

Ondansetron (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 20/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 110
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: breast surgery

Included criteria: fibroadenoma, undergoing breast resection, ASA I or II

Excluded criteria: receiving tranquilizing/sedative or antiemetic drugs within 24 hours before surgery; respiratory disease; hepatologic disease; pregnancy; need or demand PCA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 20 mL • *Time point of administration*: within 5 minutes before anaesthesia

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Kim 2000 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: within 5 minutes before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron (4 mg group)

- *Dose*: 4 mg
- *Time point of administration*: within 5 minutes before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron (8 mg group)

- *Dose*: 8 mg
- *Time point of administration*: within 5 minutes before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea, R.O.C. **Setting:** inpatient, single-centre **Author's name:** Chong Soo Kim **Institution:** Department of Anaesthesiology, College of Medicine, Seoul, National University **Email:** NA **Address:** SMG-SNU Boramae Medical Center. 39, Boramae-Gil, Dongjak-gu, Seoul 156-707, Korea **Duration of study:** NA

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Kim 2000 *(Continued)*

	Language: Korean (translated by Woocheol Sim) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly divided". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Kim 2001

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding and different time points of administration
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 49.1 ± 1.8 • *Weight (mean ± SD, median (IQR), median (range))*: 54.9 ± 1.6

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Kim 2001 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 160.3
- *Use of perioperative opioids (if yes, which?)*: 4.2
- *Type of surgery*: total abdominal hysterectomy

Ondansetron (2 x 2 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 48.3 ± 2.0
- *Weight (mean ± SD, median (IQR), median (range))*: 55.9 ± 1.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 169.2
- *Use of perioperative opioids (if yes, which?)*: 4.7
- *Type of surgery*: total abdominal hysterectomy

Ondansetron (4 mg pre group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 47.5 ± 1.9
- *Weight (mean ± SD, median (IQR), median (range))*: 56.3 ± 1.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 160.3
- *Use of perioperative opioids (if yes, which?)*: 4.8
- *Type of surgery*: total abdominal hysterectomy

Ondansetron (4 mg post group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA

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Kim 2001 *(Continued)*

- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 48.7 ± 1.8
- *Weight (mean ± SD, median (IQR), median (range))*: 58.2 ± 2.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 164.3
- *Use of perioperative opioids (if yes, which?)*: 4.5 mg butorphanol via PCA
- *Type of surgery*: total abdominal hysterectomy

Included criteria: ASA I or II, 30 to 60 years of age, undergoing total abdominal hysterectomy (TAH) under general anaesthesia

Excluded criteria: drug abuse, gigantic or hypersensitive response to drugs

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: before induction of anaesthesia and after surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Ondansetron (2 × 2 mg group)

- *Dose*: 2 × 2 mg
- *Time point of administration*: before induction of anaesthesia and after surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Ondansetron (4 mg pre group)

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Ondansetron (4 mg post group)

- *Dose*: 4 mg
- *Time point of administration*: after surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Outcomes

Headache (0 to 48 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 48 hours)

- Outcome type: dichotomous outcome

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Kim 2001 *(Continued)*

	Adverse events (general notes in the publication, 24 hours' observation) • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Dong Hee Kim **Institution:** Departments of Anesthesiology, Obstetrics, and Gynecology, College of Medicine, Dankook University, Cheonan, Korea **Email:** ybs 90@unitel.co.kr **Address:** 16-5, Anseong-dong, Cheonan, Chungcheongnam-do, Department of Anesthesiology, Dankook University Hospital, Postal Code: 330-715 **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote (translated): "the same observer, who did not know the patient's group observed pain, nausea, vomiting, sedation, and other adverse events immediately after the patient's awakening and at 1, 2, 6, 12, 24, 36 and 48 hours after awakening"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

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Kim 2005a

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 57.0 ± 10.8 • *Weight (mean ± SD, median (IQR), median (range))*: 61.3 ± 11.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 38 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, sevoflurane, isoflurane), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 280.8 • *Use of perioperative opioids (if yes, which?)*: epidural morphine • *Type of surgery*: abdominal surgery Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 55.7 ± 11.0 • *Weight (mean ± SD, median (IQR), median (range))*: 62.0 ± 10.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 36 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, sevoflurane, isoflurane), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 296.2 • *Use of perioperative opioids (if yes, which?)*: epidural morphine • *Type of surgery*: abdominal surgery **Included criteria:** healthy adults, ASA I or II, underwent abdominal surgery under general anaesthesia **Excluded criteria:** history of PONV, frequent experiences of motion sickness, had taken antiemetics within 48 hours before surgery **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Kim 2005a *(Continued)*

Interventions	**Intervention characteristics** Placebo (group C) • *Dose*: saline • *Time point of administration*: after bolus epidural morphine injected to all patients 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron (group O) • *Dose*: 8 mg • *Time point of administration*: after bolus epidural morphine injected to all patients 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Kim Cheon Sook **Institution:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Cheonan Hospital **Email:** kchsook@msn.com **Address:** 23-20 Bongyeong-dong, Cheonan, Chungnam

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Kim 2005a *(Continued)*

	Duration of study: November 2002 to August 2003 **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly divided" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "anesthesiologists who did not have information about the experimental drug visited the patient 6 hours and 24hours after the operation" (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Kim 2005b

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 38 • *Received treatment (n)*: 38

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Kim 2005b *(Continued)*

- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 13.7
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 10.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 2.7/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 101
- *Use of perioperative opioids (if yes, which?)*: none besides fentanyl for induction
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 39
- *Received treatment (n)*: 39
- *Analysed (n)*: 39
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 13.8
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 9.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 5.1/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88
- *Use of perioperative opioids (if yes, which?)*: none besides fentanyl for induction
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: healthy women undergoing laparoscopic cholecystectomy under general anaesthesia, ASA corresponding to body class I to II

Excluded criteria: respiratory, cardiovascular, brain disease; renal or liver abnormalities; vomiting or hepatotoxicity within the liver; obstetric and severe obesity patients

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 2 mL saline • *Time point of administration*: before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (8%) metoclopramide 10 mg IV Ondansetron • *Dose*: 4 mg • *Time point of administration*: before end of surgery • *Route of administration*: IV

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Kim 2005b *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: (0%) metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient**,** single-centre **Author's name:** Soon Im Kim **Institution:** Department of Anesthesiology, Soonchunhyang University Hospital **Email:** soonnim@hosp.sch.ac.kr **Address:** 657 Hannam-dong, Yongsan-gu, Seoul, Postal Code: 140-743 **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "in this prospective, randomized, double-blind, placebo-controlled study" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")

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Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "a designated anesthesiologist who does not know the patient's group visited and interviewed the patient..." (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Kim 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 44.5 ± 1.9 • *Weight (mean ± SD, median (IQR), median (range))*: 54.6 ± 0.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 169.2 • *Use of perioperative opioids (if yes, which?)*: none • *Type of surgery*: thyroidectomy Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 45.8 ± 1.7 • *Weight (mean ± SD, median (IQR), median (range))*: 52.7 ± 0.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Kim 2007 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 164.4
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Ramosetron (group R)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 44.5 ± 1.9
- *Weight (mean ± SD, median (IQR), median (range))*: 53.6 ± 0.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 169.2
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Included criteria: female, ASA I or II, underwent thyroidectomy under general anaesthesia

Excluded criteria: body mass index > 30; pregnancy; gastrointestinal disorders such as heart disease, respiratory disease, brain disease, kidney or liver abnormality, gastritis, gastric ulcer; history of PONV; smoking history; received antiemetics within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Placebo (group C) • *Dose*: saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (52%) metoclopramide 10 mg IV Dexamethasone (group D) • *Dose*: 0.15 mg/kg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (24%) metoclopramide 10 mg IV Ramosetron (group R) • *Dose*: 6 µg/kg • *Time point of administration*: after induction of anaesthesia

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Kim 2007 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (4%) metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Kyung Hwa Kwak **Institution:** Department of Anesthesiology and Pain Medicine, Kyungpook National University **Email:** hwakkh@hotmail.com **Address:** 50, Samdeok-dong, Jung-gu, Daegu, Postal Code: 700-721 **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "in order to prevent the anaesthesiologist from knowing what type of medication will be administered" (translated)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "an anaesthesiologist who does not know the patient group investigated the occurrence of nausea and vomiting" (translated)

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Kim 2007 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Kim 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 54 • *Received treatment (n)*: NA • *Analysed (n)*: 54 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 8.8 • *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 8.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 94.44 • *History of PONV/motion sickness (%)*: 1.8/29.6 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 111 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 3 µg/kg fentanyl at induction, 496 µg postoperative fentanyl via PCA • *Type of surgery*: gynaecological surgery (hysterectomy, ovarian cystectomy, salpingo-oophorectomy) Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 54 • *Received treatment (n)*: NA • *Analysed (n)*: 54 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 9.1 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 8.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 87.04

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Kim 2009 *(Continued)*

- *History of PONV/motion sickness (%)*: 1.85/33.33
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 3 µg/kg fentanyl at induction, 466 µg postoperative fentanyl via PCA
- *Type of surgery*: gynaecological surgery (hysterectomy, ovarian cystectomy, salpingo-oophorectomy)

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 54
- *Received treatment (n)*: NA
- *Analysed (n)*: 54
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 9.1
- *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 8.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 87.04
- *History of PONV/motion sickness (%)*: 5.6/42.6
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 114
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 3 µg/kg fentanyl at induction, 375 µg postoperative fentanyl via PCA
- *Type of surgery*: gynaecological surgery (hysterectomy, ovarian cystectomy, salpingo-oophorectomy)

Included criteria: female, 21 to 71 years of age, undergoing elective gynaecological surgery (hysterectomy, ovarian cystectomy, salpingo-oophorectomy), duration of surgery 35 to 190 minutes

Excluded criteria: pregnancy; body weight > 30% above ideal body weight; vomiting or retching within 24 hours before the operation; administration of antiemetics or steroids or psychoactive medications within 24 hours before the operation; respiratory, cardiovascular, renal, hepatic, endocrine, gastrointestinal, or neurological disease

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear, but stated "healthy patients". Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Interventions

Intervention characteristics

Ramosetron

- *Dose*: 0.3 mg
- *Time point of administration*: 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg, second ondansetron 4 mg

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg, second ondansetron 4 mg

Placebo

- *Dose*: saline

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Kim 2009 *(Continued)*

- *Time point of administration*: 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg, second ondansetron 4 mg

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** S.I. Kim **Institution:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Hospital **Email:** soonnim@hosp.sch.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Hospital, 657 Hannam-dong, Yongsan-gu, Seoul 140-743, Republic of Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of nausea and vomiting during the first 24 hours after operation **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated to receive one of the three study medications according to a computer-generated randomized number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "the envelopes were opened before induction of anaesthesia by a trained nurse not involved in the study. The nurse then prepared..."

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Kim 2009 *(Continued)*

		Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the envelopes were opened before induction of anaesthesia by a trained nurse not involved in the study. The nurse then prepared the appropriate study medication diluted..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all patients, investigators collecting the post-operative data, and nurses involved in the postoperative care of patients were blinded to the randomization"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "no study patient was withdrawn from the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there were no significant differences among the three groups with respect to patient characteristics, type of surgery, duration of surgery or anaesthesia, motion sickness, smoking status, or previous PONV history (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear, but stated "healthy patients". Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Kim 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 51.2 ± 7.8 • *Weight (mean ± SD, median (IQR), median (range))*: 62.5 ± 10.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 162.4 • *Use of perioperative opioids (if yes, which?)*: 0.5 µg/kg to 1 µg/kg remifentanil for induction, 0.05 µg/kg/min to 0.2 µg/kg/min remifentanil for maintenance

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Kim 2012 *(Continued)*

- *Type of surgery*: thyroidectomy

Palonosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 49.8 ± 7.3
- *Weight (mean ± SD, median (IQR), median (range))*: 59.7 ± 11.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 175.7
- *Use of perioperative opioids (if yes, which?)*: 0.5 µg/kg to 1 µg/kg remifentanil for induction, 0.05 µg/kg/min to 0.2 µg/kg/min remifentanil for maintenance
- *Type of surgery*: thyroidectomy

Included criteria: non-smoking female, healthy, over 18 years of age, undergoing thyroidectomy with general anaesthesia; ASA I and II

Excluded criteria: patients with pregnancy, severe obesity, smoker, history of PONV or motion sickness, nausea or vomiting within 24 hours before surgery, had received antiemetics

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 8 mg • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10 mg metoclopramide IV Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10 mg metoclopramide IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)*

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Kim 2012 *(Continued)*

- Outcome type: dichotomous outcome

Headache (0 to 48 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 48 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Yu Yil Kim **Institution:** Department of Anesthesiology and Pain Medicine, Presbyterian Medical Center **Email:** zion_yuyil@yahoo.co.kr **Address:** Presbyterian Medical Center, 300, Junghwasandong,1-ga, Wansan-gu, Jeonju 560-750, Korea **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly assigned to" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "a designated anesthesiologist who does not know the patient's group observed patients after 2 hours (recovery room), 24 hours and 48 hours..." (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Kim 2012 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Kim 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 40 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 6.82/20.45 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 146 • *Use of perioperative opioids (if yes, which?)*: remifentanil for anaesthesia (5 mg/mL using a target-controlled infusion device), fentanyl for postoperative pain (no participant required additional fentanyl) • *Type of surgery*: gynaecological laparoscopic surgery Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 51 • *Received treatment (n)*: NA • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 37 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 2.27/11.36 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 133

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Kim 2015 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: remifentanil for anaesthesia (5 mg/mL using a target-controlled infusion device), fentanyl for postoperative pain (no participant required additional fentanyl)
- *Type of surgery*: gynaecological laparoscopic surgery

Ramosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 48
- *Received treatment (n)*: NA
- *Analysed (n)*: 44
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 6.81/6.81
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 151
- *Use of perioperative opioids (if yes, which?)*: remifentanil for anaesthesia (5 mg/mL using a target-controlled infusion device), fentanyl for postoperative pain (no participant required additional fentanyl)
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: patients requesting IV PCA for pain control after gynaecological laparoscopic surgery

Excluded criteria: urgent or emergent case, re-operation case, allergy to egg or soybean oil, QT prolongation on preoperative electrocardiography, history of drug abuse, any current medication, other concurrent surgery, surgery within 1 hour and discharge within 72 hours

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV, dexamethasone 5 mg

Palonosetron

- *Dose*: 0.075 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV, dexamethasone 5 mg

Ramosetron

- *Dose*: 0.3 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV

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Kim 2015 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV, dexamethasone 5 mg
Outcomes	*Headache (0 to 72 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this research was supported by the Basic Science Research Programme through the National Research Foundation of Korea (NRF), funded by the Ministry of Education, Science and Technology (grant number: 2012R1A1A1001819) **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Seong-Hyop Kim **Institution:** Department ofAnesthesiology and Pain Medicine, Konkuk University Medical Center, Konkuk University School of Medicin, Seoul, Korea **Email:** yshkim75@daum.net **Address:** Department of Anesthesiology and Pain Medicine, Konkuk University Medical Center, Konkuk University School of Medicine, 120-1, Neungdong-ro (Hwayang-dong), Gwangjin-gu, Seoul 143-729, Korea **Duration of study:** September 2011 to February 2013 **Language:** English **Study's primary outcome:** PONV incidence and Rhodes index from T2 to T3 **Trial registry number:** KCT0000183
Notes	Three out of 4 groups relevant (PCA)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated using a sealed envelope method" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "were randomly allocated using a sealed envelope method" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelope" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all anesthesiologists, surgeons and nurses involved in the study were blinded to the allocation of groups"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all data were collected by trained observers who were blinded to the study and did not participate in patient care"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the two hundred and seven patients who were eligible for the study, 31 were excluded for the following reasons—7 patients refused to participate in the study, 10 patients were converted to open laparotomy (4 patients in

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Kim 2015 *(Continued)*

		P group, 2 patients in R0.3 group and 4 patients in R PCA group), 12 patients were discharged early (6 patients in C group, 3 patients in P group, 1 patient in R0.3 group, and 2 patients in R PCA group), and 2 patients had a malfunctioning PCA (1 patient in R0.3 group and 1 patient in R PCA group). Thus, 176 patients were included in the final analysis (Fig. 2)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: KCT0000183. Date of study start given in the protocol differs from that given in the study report. Unclear whether prospective or retrospective registration
Other bias	Unclear risk	Quote: "the demographic profiles of the patients were similar among the groups (Table 1)" Quote: "there were no significant differences in the number of additional doses of PCA on demand among the groups" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Kim JE 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 40 ± 11.5 • *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 6.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 69 • *Use of perioperative opioids (if yes, which?)*: none • *Type of surgery*: breast tumour resection Granisetron (group G) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40

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Kim JE 2005 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 12.2
- *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 5.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 82
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: breast tumour resection

Ramosetron (group R)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 13.3
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 5.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: breast tumour resection

Included criteria: healthy female patients with ASA body class I or II who underwent general anaesthesia for breast tumour resection

Excluded criteria: cardiovascular, respiratory, brain disease; kidney or liver abnormalities; gastritis, stomach ulcers, etc.; intestinal disease or frequent nausea; severe obesity; pregnancy; history of PONV; had received intravenous antibiotics within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Placebo (group P)

- *Dose*: saline
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: (22.5%) metoclopramide 10 mg

Granisetron (group G)

- *Dose*: 40 g/kg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: (2.5%) metoclopramide 10 mg

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Kim JE 2005 *(Continued)*

	Ramosetron (group R) • *Dose*: 6 µg/kg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (0%) metoclopramide 10 mg
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 48 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Oxy-Young **Institution:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Hospital **Email:** syok2377@hanmail.net **Address:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Hospital, 657 Hannam-dong, Yongsan-gu, Seoul, Korea **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Kim JE 2005 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: anaesthesiologists unaware of group allocation administered the drugs
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: anaesthesiologists unaware of group allocation performed outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "among the 145 patients who underwent breast tumor resection, 15 patients had gastrointestinal diseases such as gastritis and gastric ulcer, 7 patients had frequent nausea, 2 patients had severe obesity, patients with a history of PONV (1 patient) were excluded from the study (total 25 patients) and 120 patients were enrolled". Reasons for exclusions reported
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Kim SH 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 53.3 ± 10.9 • *Weight (mean ± SD, median (IQR), median (range))*: 64.5 ± 5.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 100 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 147.3 • *Use of perioperative opioids (if yes, which?)*: 896 µg remifentanil intraoperative, fentanyl postoperative • *Type of surgery*: laparoscopic surgery Ramosetron • *Assessed for eligibility (n)*: -

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Kim SH 2013 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 38
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 54.8 ± 11.1
- *Weight (mean ± SD, median (IQR), median (range))*: 65.0 ± 11.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 100
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 153.6
- *Use of perioperative opioids (if yes, which?)*: 872 µg remifentanil intraoperative, fentanyl postoperative
- *Type of surgery*: laparoscopic surgery

Palonosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 36
- *Received treatment (n)*: NA
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 54.3 ± 10.5
- *Weight (mean ± SD, median (IQR), median (range))*: 65.6 ± 9.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 100
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 169.9
- *Use of perioperative opioids (if yes, which?)*: 905 µg remifentanil intraoperative, fentanyl postoperative
- *Type of surgery*: laparoscopic surgery

Included criteria: ASA I or II, female, 20 to 65 years of age, non-smoker, history of motion sickness or previous PONV, elective laparoscopic surgery, use of postoperative intravenous patient-controlled analgesia (IV-PCA) with fentanyl

Excluded criteria: impairment of bowel motility, diabetes, pregnancy or lactation, administration of an antiemetic medication or steroids within 24 hours before surgery, presence of a cardiovascular or respiratory disease, obesity (body mass index > 35 kg/m^2), renal or hepatic dysfunction

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: (54.3%) 20 mg propofol, 10 mg metoclopramide, 4 mg ondansetron, 4 mg dexamethasone

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Kim SH 2013 *(Continued)*

	Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (34.2%) 20 mg propofol,10 mg metoclopramide, 4 mg ondansetron, 4 mg dexamethasone Palonosetron • *Dose*: 75 µg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (11.1%) 20 mg propofol, 10 mg metoclopramide, 4 mg ondansetron, 4 mg dexamethasone
Outcomes	*Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Hae Keum Kil **Institution:** Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Korea **Email:** hkkil@yuhs.ac **Address:** Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Severance Hospital, Yonsei University College of Medicine, 134, Sinchon-dong, Seodaemun-gu, Seoul 120-752, Korea **Duration of study:** July 2010 to June 2011 **Language:** English **Study's primary outcome:** PONV (nausea, vomiting, need for rescue medication) **Trial registry number:** NCT01169805 (not referenced in the published study report)
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using computer-generated random numbers"
Allocation concealment (selection bias)	Low risk	Quote: "the hospital pharmacy that prepared the study drugs assigned patients into one of 3 active treatment groups on the morning of the day of surgery"

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Kim SH 2013 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all patients, surgeons, anaesthesiologists, and nurses involved in the study were blinded to group allocation and every precaution was taken to maintain the double-blind conditions"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperative nausea and emetic episodes were assessed for 48 hours after surgery by 2 independent investigators blinded to patient group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "no patient withdrew from the study"
Selective reporting (reporting bias)	High risk	Judgement comment: NCT01169805 (prospective registration). One additional new primary outcome was added to the final study report (need to use a rescue medication). The assessment period was shortened in the study report
Other bias	Low risk	Quote: "neither patient characteristics nor intraoperative data differed among the 3 groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Kim WJ 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Midazolam (group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 32 • *Age (mean ± SD, median (IQR), median (range))*: 47.0 (39.3 to 47.8) • *Weight (mean ± SD, median (IQR), median (range))*: 60.1 ± 9.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 150 • *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg fentanyl IV 15 minutes before end of surgery, IV–PCA device connected, 20 mg/kg fentanyl in 100 mL solution at 0.2 mL/h with a bolus of 1.2 mL and lockout time of 15 minutes • *Type of surgery*: thyroidectomy

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Kim WJ 2013 *(Continued)*

	Ramosetron + midazolam (group RM) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 32 • *Received treatment (n)*: NA • *Analysed (n)*: 32 • *Age (mean ± SD, median (IQR), median (range))*: 48.5 (37.3 to 54.0) • *Weight (mean ± SD, median (IQR), median (range))*: 59.3 ± 9.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 145.0 • *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg fentanyl IV 15 minutes before end of surgery, IV–PCA device connected, 20 mg/kg fentanyl in 100 mL solution at 0.2 mL/h with a bolus of 1.2 mL and lockout time of 15 minutes • *Type of surgery*: thyroidectomy **Included criteria:** non-smoking females, 20 to 65 years of age, ASA I or II, anticipated need for opioids for postoperative pain management, 3 or 4 risk factors for PONV **Excluded criteria:** diabetes mellitus or gastrointestinal disease, smoker, menstruating or had taken an antiemetic medication 72 hours before surgery **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear
Interventions	**Intervention characteristics** Midazolam (group M) • *Dose*: 75 µg/kg • *Time point of administration*: immediately before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, dexamethasone 5 mg IV Ramosetron + midazolam (group RM) • *Dose*: ramosetron 0.3 mg, midazolam 75 µg/kg • *Time point of administration*: immediately before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, dexamethasone 5 mg IV
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2012R1A1A1003700) **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Hyun Kang

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Kim WJ 2013 *(Continued)*

Institution: Department of Anaesthesiology and Pain Medicine, College of Medicine, Chung-Ang University, Seoul, Republic of Korea

Email: roman00@cau.ac.kr

Address: Department of Anaesthesiology and Pain Medicine, Chung-Ang University College of Medicine, 224-1 Heukseok-dong, Dongjak-gu, Seoul 156-755, Republic of Korea

Language: English

Duration of study: January to September 2012

Trial registry number: ACTRN12612000757819

Study's primary outcome: primary endpoint of this study was severity of PONV

Notes	Two out of 3 groups relevant (midazolam)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomization was based on a random table, generated using the R Project for Statistical Computing (http://www. r-project.org/) Block randomization with a block size of four and equal allocation was employed to prevent imbalances in treatment assignments. The randomization sequence was generated by a statistician who was not involved with the study"
Allocation concealment (selection bias)	Unclear risk	Quote: "the randomization sequence was generated by a statistician who was not involved with the study. Patient group allocation was revealed to the anaesthetist immediately prior to induction of anaesthesia, by means of numbered and sealed envelopes" Quote: "participate in conducting the study and data collection" Quote: "decisions to enrol or exclude patients were made by an investigator at the preoperative anaesthetic evaluation who did not otherwise..." Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "patient group allocation was revealed to the anaesthetist immediately prior to induction of anaesthesia" Judgement comment: anaesthesiologists were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were questioned by an anaesthetic nurse, who was unaware of the group identities, as to the severity of nausea and incidence of retching and vomiting"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 100 patients were enrolled in the study; four patients were excluded because of incomplete data collection and two patients were excluded because of withdrawal of consent"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: ACTRN12612000757819 (retrospective registration). Date of study start given in the protocol differs from that given in the study report
Other bias	Unclear risk	Quote: "patient characteristics and operative data were similar in the three groups (Table 1)"

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Kim WJ 2013 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear

Kiran 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: 100 • *Analysed (n)*: 100 • *Age (mean ± SD, median (IQR), median (range))*: 29.5 (20 to 60) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 45 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 50.55 • *Use of perioperative opioids (if yes, which?)*: pentazocine 0.5 mg/kg IV • *Type of surgery*: appendicectomy, fibroadenoma excision, hemithyroidectomy, keloid excision, lipoma excision, lymph node excision, mastoidectomy, ORIF fracture both bone forearms, polypectomy, sebaceous cyst excision, septoplasty, SMR, thyroglossal cyst removal, tonsillectomy Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: 100 • *Analysed (n)*: 100 • *Age (mean ± SD, median (IQR), median (range))*: 30.9 (20 to 60) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 43 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 48.3 • *Use of perioperative opioids (if yes, which?)*: pentazocine 0.5 mg/kg IV

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Kiran 2013 *(Continued)*

- *Type of surgery*: appendicectomy, fibroadenoma excision, hemithyroidectomy, keloid excision, lipoma excision, lymph node excision, mastoidectomy, ORIF fracture both bone forearms, polypectomy, sebaceous cyst excision, septoplasty, SMR, thyroglossal cyst removal, tonsillectomy

Included criteria: ASA I and ASA II, 20 to 60 years of age, no history of PONV in previous surgery, motion sickness, Ryle's tube in situ in the past 24 hours, undergoing elective surgery under general anaesthesia

Excluded criteria: renal impairment and hepatic disease, neurological and endocrinal abnormalities, pregnant and lactating

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, history of PONV/motion sickness, duration of anaesthesia, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 30 seconds before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: injection of metoclopramide 0.15 mg/kg IV given for more than 2 episodes of vomiting Ondansetron + dexamethasone • *Dose*: ondansetron 4mg, dexamethasone 8 mg • *Time point of administration*: 30 seconds before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: injection of metoclopramide 0.15 mg/kg IV given for more than 2 episodes of vomiting
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 4 hours, 4 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 7 days)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** NA **Author's name:** Kiran A.V. **Institution:** Department of Anesthesiology, Sapthagiri Institute of Medical Science Research Center, Bangalore **Email:** NA

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Kiran 2013 *(Continued)*

	Address: NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a randomisation list was prepared using a mechanical randomisation device"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, history of PONV/motion sickness, duration of anaesthesia, perioperative opioids): no; (non-smoker): unclear

Kizilcik 2017

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA

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Kizilcik 2017 *(Continued)*

- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 32.83 ± 8.22
- *Weight (mean ± SD, median (IQR), median (range))*: 76.00 ± 12.90
- *BMI (mean ± SD, median (IQR), median (range))*: 25.65 ± 3.00
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 89.30
- *Use of perioperative opioids (if yes, which?)*: 231.7 µg perioperative opioids (fentanyl at induction, intraoperative remifentanil), 130 mg tramadol at end of surgery and postoperatively via PCA
- *Type of surgery*: rhinoplasty

Dexamethasone + dimenhydrinate

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 33.27 ± 8.15
- *Weight (mean ± SD, median (IQR), median (range))*: 71.30 ± 13.40
- *BMI (mean ± SD, median (IQR), median (range))*: 24.86 ± 3.48
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 110.67
- *Use of perioperative opioids (if yes, which?)*: 341.8 µg perioperative opioids (fentanyl at induction, intraoperative remifentanil), 132.33 mg tramadol at end of surgery and postoperatively via PCA
- *Type of surgery*: rhinoplasty

Included criteria: ASA I and II, 18 to 65 years of age, women scheduled for elective rhinoplasty

Excluded criteria: hypersensitivity or contraindication to study drugs; receiving an antiemetic drug or steroid within 24 hours before anaesthesia; history of diabetes, motion sickness, or PONV; pregnant or breastfeeding

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (duration of anaesthesia, perioperative opioids): yes

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Interventions

Intervention characteristics

Dexamethasone + ondansetron

- *Dose*: dexamethasone 8 mg, ondansetron 4 mg
- *Time point of administration*: dexamethasone after tracheal intubation, ondansetron 30 minutes before emergence of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: granisetron 3 mg IV, ondansetron 4 mg

Dexamethasone + dimenhydrinate

- *Dose*: dexamethasone 8 mg, dimenhydrinate 1 mg/kg

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Kizilcik 2017 *(Continued)*

	• *Time point of administration*: dexamethasone after tracheal intubation, dimenhydrinate 30 minutes before emergence of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 3 mg IV, ondansetron 4 mg
Outcomes	*Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatients, single-centre **Author's name:** Nurcan Kizilcik **Institution:** Department of Anesthesiology and Reanimation, Yeditepe University School of Medicine, Istanbul, Turkey **Email:** nurcankizilcik@gmail.com **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** prevalence of nausea, vomiting, and retching at any time in the postoperative period **Trial registry number:** NCT02382146
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "sixty patients were randomly assigned to two equal study groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "ondansetron 4 mg and dimenhydrinate 1 mg/kg were diluted with 0.09% NaCl to a volume of 5 ml by the pharmacy department and given to the blinded investigators. The patients, anesthesiologists (except for the primary author), statistician, and observers were all blinded to the study groups" Judgement comment: the role of the primary author (not blinded) in study conduct is unclear
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients, anesthesiologists (except for the primary author), statistician, and observers were all blinded to the study groups"
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Kizilcik 2017 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT02382146 (retrospective registration)
Other bias	High risk	Quote: "(p = 0.002; Table 2). The duration of surgery was longer in the DD group (mean 110.67 min) than in the DO group (mean 89.30 min; p = 0.038; Table 1). Total remifentanil consumption was higher in the DD group (p = 0.006). Baseline and 60-min VAS scores were significantly higher in the DO group compared with the DD group (p = 0.003 and p = 0.039, respectively; Tables 2, Table 3). 206 Aesth Plast Surg (2017)" Quote: "there was no difference in patient demographics or Apfel risk factors for PONV between the two groups (p > 0.05; Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (duration of anaesthesia, perioperative opioids): yes

Kizilkaya 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 45 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 63 • *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 1.5 µg/kg fentanyl at induction, 10 µg sufentanil intra-articular • *Type of surgery*: knee arthroscopic meniscectomy Methylprednisolone (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20

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Kizilkaya 2004 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 45
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 58
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 1.5 µg/kg fentanyl at induction, 10 µg sufentanil intra-articular
- *Type of surgery*: knee arthroscopic meniscectomy

Included criteria: ASA I to II, scheduled for knee arthroscopic meniscectomy

Excluded criteria: daily intake of steroids, non-steroidal antiinflammatory drugs (NSAIDs), or opioids; relevant drug allergy; need for postoperative intra-articular drainage

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo (group B) • *Dose*: saline • *Time point of administration*: before the arthroscope was removed • *Route of administration*: intra-articular • *Rescue antiemetics (if yes, which?)*: NA Methylprednisolone (group C) • *Dose*: methylprednisolone 40 mg • *Time point of administration*: before the arthroscope was removed • *Route of administration*: intra-articular • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Postoperative wound infection (time point unknown)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Mehmet Kizilkaya **Institution:** Departments of Anesthesiology and Reanimation and Orthopaedic Surgery, The School of Medicine, Ataturk University, Erzurum, Turkey **Email:** mkizilkaya65@hotmail.com **Address:** Universite Lojmanlari No:46/4, Erzurum 25240, Turkey **Duration of study:** NA

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Kizilkaya 2004 *(Continued)*

	Language: English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups eligible (sufentanil)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned to 3 groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the test drug was given to the surgeon who performed the injection through the arthroscope at the end of the procedure (without knowing the contents) to ensure that the drug would be delivered into the joint" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: 60 participants were included. No information on number of analysed participants
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic data, duration of anesthesia, and tourniquet time are summarized in Table 1. With regard to demographic data, duration of anesthesia and tourniquet time, significant differences were not observed among Groups A, B, and C" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Kocamanoglu 2005

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo (group A)

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Kocamanoglu 2005 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 29.50 ± 5.29
- *Weight (mean ± SD, median (IQR), median (range))*: 75.14 ± 14.25
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 86.7
- *History of PONV/motion sickness (%)*: 10.0/10.0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 51.44
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg meperidine IV (PACU), 1 mg/kg meperidine IV (every 6 hours)
- *Type of surgery*: caesarean section

Granisetron + dexamethasone (group B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 29.42 ± 5.39
- *Weight (mean ± SD, median (IQR), median (range))*: 77.32 ± 11.35
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 93.3
- *History of PONV/motion sickness (%)*: 6.7/10.0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 49.73
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg meperidine IV (PACU), 1 mg/kg meperidine IV (every 6 hours)
- *Type of surgery*: caesarean section

Granisetron + droperidol (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 28.62 ± 5.66
- *Weight (mean ± SD, median (IQR), median (range))*: 79.45 ± 7.34
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 90.0
- *History of PONV/motion sickness (%)*: 6.7/10.0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 53.88

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Kocamanoglu 2005 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg meperidine IV (PACU), 1 mg/kg meperidine IV (every 6 hours)
- *Type of surgery*: caesarean section

Droperidol (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 30.29 ± 5.09
- *Weight (mean ± SD, median (IQR), median (range))*: 77.30 ± 9.90
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 83.3
- *History of PONV/motion sickness (%)*: 10.0/13.3
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 50.88
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg meperidine IV (PACU), 1 mg/kg meperidine IV (every 6 hours)
- *Type of surgery*: caesarean section

Granisetron (group E)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 28.96 ± 5.95
- *Weight (mean ± SD, median (IQR), median (range))*: 74.15 ± 11.33
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 86.7
- *History of PONV/motion sickness (%)*: 10.0/13.3
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 49.29
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg meperidine IV (PACU), 1 mg/kg meperidine IV (every 6 hours)
- *Type of surgery*: caesarean section

Included criteria: ASA I or II, scheduled for caesarean section

Excluded criteria: underlying pro-emetic disease and/or taking antiemetic drugs

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Placebo (group A) • *Dose*: 5 mL saline • *Time point of administration*: immediately after clamping of the umbilical cord

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Kocamanoglu 2005 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 26.7% (metoclopramide 10 mg IV)

Granisetron + dexamethasone (group B)

- *Dose*: granisetron 40 µg/kg, dexamethasone 8 mg
- *Time point of administration*: immediately after clamping of the umbilical cord
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 0.0% (metoclopramide 10 mg IV)

Granisetron + droperidol (group C)

- *Dose*: granisetron 40 µg/kg, droperidol 1.25 mg
- *Time point of administration*: immediately after clamping of the umbilical cord
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 3.3% (metoclopramide 10 mg IV)

Droperidol (group D)

- *Dose*: 1.25 mg
- *Time point of administration*: immediately after clamping of the umbilical cord
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 16.7% (metoclopramide 10 mg IV)

Granisetron (group E)

- *Dose*: 40 µg/kg
- *Time point of administration*: immediately after clamping of the umbilical cord
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 3.3% (metoclopramide 10 mg IV)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** departmental sources **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Ismail Serhat Kocamanoglu

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Kocamanoglu 2005 *(Continued)*

Institution: Department of Anesthesiology, Onkoduz Mayis University, Samsun, Turkey

Email: serhatk@omu.edu.tr

Address: Department of Anesthesiology, Onkoduz Mayis University, Samsun, Turkey

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "prospectively and randomly assigned to one of five groups". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "total volume of antiemetic solutions were 5 ml with the saline added, and thus maintaining the anesthesiologist blinding to the study drug"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "one of the investigators, who were blinded to the treatment group, recorded all the variables observed"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Ko Iam 2015

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Metoclopramide + dexamethasone • *Assessed for eligibility (n)*: -

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Ko Iam 2015 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 52.5 ± 34.0
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23.9 ± 3.5
- *ASA I/II/III/IV (n)*: 22/28/0/0
- *Gender (female in %)*: 58
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia with thiopental and fentanyl
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 68.3 ± 22.9
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl intraoperative
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 50.9 ± 12.7
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23.7 ± 2.8
- *ASA I/II/III/IV (n)*: 19/31/0/0
- *Gender (female in %)*: 66
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia with thiopental and fentanyl
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 72.9 ± 24.6
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl intraoperative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, 18 to 75 years of age, required elective laparoscopic cholecystectomy

Excluded criteria: pregnancy; breastfeeding; > 100 kg in weight; history of motion sickness; nausea/vomiting with the use of antiemetic drugs within 24 hours before surgery; insulin-dependent diabetes mellitus; allergy to any protocol medication; contraindication for metoclopramide such as epilepsy, pheochromocytoma, and antipsychotic (haloperidol, chlorpromazine) treated patients; contraindication for dexamethasone such as tuberculosis and herpes simplex virus ophthalmic; procedure conversion to open cholecystectomy

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide + dexamethasone • *Dose*: metoclopramide 10 mg, dexamethasone 8 mg • *Time point of administration*: before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: intravenous metoclopramide 10 mg

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Ko Iam 2015 *(Continued)*

	Metoclopramide • *Dose*: 10 mg • *Time point of administration*: before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: intravenous metoclopramide 10 mg
Outcomes	*Arrhythmia (until discharge)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (until discharge)* • Outcome type: dichotomous outcome *Postoperative wound infection (until discharge)* • Outcome type: dichotomous outcome *Sedation/drowsiness (until discharge)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Research Fund for Royal College of Surgeons of Thailand **Country:** Thailand **Setting:** inpatient, single-centre **Author's name:** Wasana Ko-iam **Institution:** Department of Surgery, Faculty of Medicine, Chiang Mai **Email:** waskoiam@hotmail.com **Address:** Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand **Language:** English **Duration of study:** January 2012 to January 2014 **Trial registry number:** TCTR20140128001 **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "sampling technique was done by permuted block randomization. Ratio between treatment group (combination of metoclopramide and dexamethasone) and control group (metoclopramide) was 1:1. 'A' represented treatment group, and 'B' represented control group. Then 'Block of four' randomization was performed by a hospital pharmacist who prepared the drugs. This pharmacist was not involved in patient care or data collection. Accordingly, the 'Block of four' could be distributed into six blocks including 1) AABB, 2) ABAB, 3) ABBA, 4) BBAA, 5) BABA, and 6) BAAB, respectively. The labeled num-

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Ko Iam 2015 *(Continued)*

		bers 1 to 6 were chosen at random until the full amount of the sample size. The orders in each number represented the orders of treatment that the patient received. The chosen numbers were converted into codes A and B, as defined in each block"
Allocation concealment (selection bias)	Low risk	Quote: "concealment was performed by putting the card of assignment in an opaque envelope, and open[ing] it before the end of surgery" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the pharmacist assigned patients to interventions and supplied syringes in a blinded fashion, so that the investigators, anesthetists, patients, care providers, and outcome assessor were unaware of which of the two drugs was being administered"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "outcome assessor were unaware of which of the two drugs was being administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "with no patients being excluded after randomization"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: TCTR20140128001 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Koivuranta 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 31 • *Received treatment (n)*: 31 • *Analysed (n)*: 31 • *Age (mean ± SD, median (IQR), median (range))*: 48 (21 to 72) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27.1 ± 4.9 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 83.87 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 25.81/41.94 • *Type of general anaesthesia*: combined anaesthesia (propofol + isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 120

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Koivuranta 1996 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (NA), 110 doses of oxycodone (0.1 mg/kg)
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: 32
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 50 (21 to 72)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25.5 ± 3.5
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 71.88
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 25.0/21.88
- *Type of general anaesthesia*: combined anaesthesia (propofol + isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl (NA), 100 doses of oxycodone (0.1 mg/kg)
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: scheduled to have laparoscopic cholecystectomy, over 18 years of age, ASA I or II

Excluded criteria: pregnant or breastfeeding, evidence of hepatic dysfunction, currently receiving any antiemetic medication

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (non-smoker, perioperative opioids): unclear; (history of motion sickness): yes

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 45% (droperidol) Placebo • *Dose*: 5 ml 0.9% sodium chloride solution • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 44% (droperidol)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)*

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Koivuranta 1996 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** NA **Author's name:** M.K. Koivuranta **Institution:** Department of Anaesthesiology, Oulu University Central Hospital, Finland **Email:** NA **Address:** Department of Anaesthesiology, Oulu University Central Hospital, Kajaanintie 50, SF-90220 Oulu 22, Finland **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** main outcome measure of the study was the need to give rescue medication during the first 24 hours after surgery
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the treatment allocation codes, produced from a table of random digits"
Allocation concealment (selection bias)	Low risk	Quote: "the treatment allocation codes, produced from a table of random digits, were contained in numbered sealed opaque envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "for each new patient, the assisting nurse opened the next envelope in numerical order and prepared the study drug as outlined but did not take part in the anaesthetic or in the postoperative assessment. The randomised process and the identity of the study drugs were blinded from the anaesthetist throughout the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all observations were recorded without knowledge of the treatment given"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 63 patients participated in the study and underwent scheduled laparoscopic cholecystectomy. Thirty-one patients received ondansetron and 32 placebo" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Koivuranta 1996 *(Continued)*

Other bias	High risk	Quote: "there were no essential differences between the groups in age, body mass index, previous history of PONV and history of migraine (Table 1). There were, however, more male patients in the placebo group than in the on-dansetron group and a history of motion sickness was more common in the ondansetron group. The duration of anaesthesia and surgery were similar in both groups" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (non-smoker, perioperative opioids): unclear; (history of motion sickness): yes

Koivuranta 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 195 • *Received treatment (n)*: NA • *Analysed (n)*: 195 • *Age (mean ± SD, median (IQR), median (range))*: 43 (16 to 75) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25 (19 to 41) • *ASA I/II/III/IV (n)*: 126/62/7/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 73 • *History of PONV/motion sickness (%)*: 42/36 • *Type of general anaesthesia*: combined anaesthesia (propofol, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 110 • *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 2 µg/kg fentanyl intraoperative, 94% of patients receiving oxycodone • *Type of surgery*: general surgical or gynaecological laparoscopy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 193 • *Received treatment (n)*: NA • *Analysed (n)*: 193 • *Age (mean ± SD, median (IQR), median (range))*: 40 (18 to 80) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25 (17 to 46) • *ASA I/II/III/IV (n)*: 130/54/9/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 74

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Koivuranta 1997 *(Continued)*

- *History of PONV/motion sickness (%)*: 32/39
- *Type of general anaesthesia*: combined anaesthesia (propofol, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 2 µg/kg fentanyl intraoperative, 91% of patients receiving oxycodone
- *Type of surgery*: general surgical or gynaecological laparoscopy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 51
- *Received treatment (n)*: NA
- *Analysed (n)*: 51
- *Age (mean ± SD, median (IQR), median (range))*: 41 (22 to 75)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24 (17 to 34)
- *ASA I/II/III/IV (n)*: 31/17/3/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: 35/33
- *Type of general anaesthesia*: combined anaesthesia (propofol, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 2 µg/kg fentanyl intraoperative, 94% of patients receiving oxycodone
- *Type of surgery*: general surgical or gynaecological laparoscopy

Included criteria: female inpatients scheduled for general surgical or gynaecological laparoscopy, over 15 years of age, ASA I to III

Excluded criteria: pregnant or breastfeeding, evidence of hepatic dysfunction, Parkinson's disease, currently received opioids or drugs with antiemetic properties

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV (10% difference)/motion sickness): no; (perioperative opioids): unclear

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Interventions

Intervention characteristics

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 34%; metoclopramide 10 mg IV

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 28%; metoclopramide 10 mg IV

Placebo

- *Dose*: 0.9% sodium chloride solution
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV

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Koivuranta 1997 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: 49%; metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 2 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** the work was financially supported by the Emil Aaltonen Foundation of Finland **Country:** Finland **Setting:** inpatient, multi-centre (2) **Author's name:** M. Koivuranta **Institution:** Departments of Anaesthesiology, Oulu University Hospital and Lappi Central Hospital, Finland **Email:** NA **Address:** Department of Anaesthesiology, Oulu University Hospital, Kajaanintie 50, FIN-90220 Oulu, Finland **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of nausea **Trial registry number:** NA
Notes	None
Risk of bias	

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Koivuranta 1997 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the patients were randomised by a research nurse using a table of random permuted blocks of 20 numbers (13)"
Allocation concealment (selection bias)	Unclear risk	Quote: "...of 20 numbers (13) with the treatment codes put into sealed envelopes. For each consecutive recruited patient, the assisting nurses opened the next envelope in order, prepared the study drug but did not participate in the postoperative assessment. The drugs were masked from the participating physicians by dilution to the same volume of saline. Anaesthesia was standardised" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "put into sealed envelopes. For each consecutive recruited patient, the assisting nurses opened the next envelope in order, prepared the study drug but did not participate in the postoperative assessment. The drugs were masked..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all observations were made without the interviewer being aware of the study treatment..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 439 patients entered and all of them completed the study on planned schedule: 195 patients received ondansetron, 193 droperidol and 51 placebo"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "193 droperidol and 51 placebo. The treatment groups were fairly comparable as to some demographic and clinical characteristics (Table 1). However, some disparity appeared in the prognostic factors for PONV. There were more patients in the ondansetron group with a history of migraine and with a history of previous postoperative sickness than in the other groups. The duration of anaesthesia and surgery were similar in all groups. The treatment groups were also comparable with regard to the type of surgery performed (Table 1). Overall, 203 of the patients..." Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV (10% difference)/motion sickness): no; (perioperative opioids): unclear

Koivuranta 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Droperidol + ondansetron • *Assessed for eligibility (n)*: -

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Koivuranta 1999 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 45
- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 42 (21 to 62)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23.5 (18.2 to 34.5)
- *ASA I/II/III/IV (n)*: 33/11/1/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 67
- *History of PONV/motion sickness (%)*: 100/51
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95
- *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl intraoperative, 24.6 mg oxycodone post-operative
- *Type of surgery*: gynaecological laparoscopic surgery

Droperidol + tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 43
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 38 (25 to 51)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24.0 (17.1 to 37.5)
- *ASA I/II/III/IV (n)*: 33/10/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 79
- *History of PONV/motion sickness (%)*: 100/35
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 70
- *Use of perioperative opioids (if yes, which?)*: 250 µg fentanyl intraoperative, 25.6 mg oxycodone post-operative
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: female, history of previous PONV, scheduled to have elective gynaecological laparoscopic surgery, over 18 years of age, ASA I to III

Excluded criteria: pregnant, breastfeeding, evidence of hepatic or other metabolic dysfunction, Parkinson's disease, currently received opioids or medication with antiemetic activity

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, perioperative opioids, non-smoker, history of PONV/motion sickness): no; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Droperidol + ondansetron • *Dose*: droperidol 0.75 mg, ondansetron 8 mg • *Time point of administration*: droperidol after induction of anaesthesia, ondansetron at the end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 31% (droperidol 0.75 mg)

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Koivuranta 1999 *(Continued)*

	Droperidol + tropisetron • *Dose*: droperidol 0.75 mg, tropisetron 5 mg • *Time point of administration*: droperidol after induction of anaesthesia, tropisetron at the end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 40% (droperidol 0.75 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 2 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatients, multi-centre (2) **Author's name:** M. Koivuranta **Institution:** Department of Anaesthesiology, Oulu University Hospital, Ouluandt Department of Anaesthesiology, Lappland Central Hospital, Rovaniemi, Finland **Email:** NA **Address:** Department of Anaesthesiology, Oulu University Hospital, Kajaanintie 50,FIN-90220 Oulu, Finland **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

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Koivuranta 1999 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Low risk	Judgement comment: quote: "the treatment allocation codes were contained in sealed opaque envelopes and for each consecutive patient recruited the assisting nurses opened the next envelope in order and administered the study drug but did not participate in the post-operative assessment"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "in a random double-blind fashion to receive intravenously (i.v.) (...) either a slow injection of ondansetron 8 mg or tropisetron 5 mg, diluted to the same volume of saline"; "the assisting nurses opened the next envelope in order and administered the study drug but did not participate in the post-operative assessment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "all observations were made without the interviewer being aware of the study treatment"; "all observations were made without the interviewer being aware of the study treatment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "two patients were excluded from the final analysis because of a protocol violation"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: quote: "furthermore, this was in spite of the fact that the patients in the ondansetron group had a higher incidence of motion sickness, received a longer anaesthetic and larger dose of fentanyl" Baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, perioperative opioids, non-smoker, history of PONV/motion sickness): no; (duration of anaesthesia): yes

Koo 2001

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: 15 • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 59.2 ± 14.3 • *Weight (mean ± SD, median (IQR), median (range))*: 57.3 ± 8.1

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Koo 2001 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane/isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 204.0
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, morphine as premedication and for postoperative analgesia
- *Type of surgery*: gastric resection

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 12
- *Received treatment (n)*: 12
- *Analysed (n)*: 12
- *Age (mean ± SD, median (IQR), median (range))*: 56.3 ± 9.3
- *Weight (mean ± SD, median (IQR), median (range))*: 59.9 ± 12.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane/isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 190.4
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, morphine as premedication and for postoperative analgesia
- *Type of surgery*: gastric resection

Included criteria: patients with gastric cancer undergoing gastric resection, ASA I or II

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: saline 2 mL • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone • *Dose*: 10 mg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome

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Koo 2001 *(Continued)*

	PONV (0 to 24 hours) • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Duck Mi Yoon **Institution:** Department of Anaesthesiology, Yonsei University College of Medicine, Seoul, Korea, 50 Yonsei-ro, Sinchon-dong, Seodaemun-gu, South Korea **Email:** dmyoon@yumc.yonsei.ac.kr **Address:** Department of Anaesthesiology, Yonsei University College of Medicine, Seoul, Korea, 50 Yonsei-ro, Sinchon-dong, Seodaemun-gu, Seoul, Korea **Duration of study:** NA **Language:** Korean (translated by Woocheol Sim) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "drawing lots" (translated)
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: an anaesthetist not further involved in the study prepared and injected the syringes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Korttila 1979

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Domperidone (5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 40 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 94 • *Use of perioperative opioids (if yes, which?)*: 0.15 mg/kg oxycodone as premedication, 23 mg oxycodone postoperatively, 0.29 mg fentanyl intraoperative • *Type of surgery*: orthopaedic surgery Domperidone (10 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 78 • *Use of perioperative opioids (if yes, which?)*: 0.15 mg/kg oxycodone as premedication, 24 mg oxycodone postoperatively, 0.27 mg fentanyl intraoperative • *Type of surgery*: orthopaedic surgery Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: NA

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Korttila 1979 *(Continued)*

- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 107
- *Use of perioperative opioids (if yes, which?)*: 0.15 mg/kg oxycodone as premedication, 22 mg oxycodone postoperatively, 0.33 mg fentanyl intraoperative
- *Type of surgery*: orthopaedic surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 37
- *Received treatment (n)*: NA
- *Analysed (n)*: 37
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 85
- *Use of perioperative opioids (if yes, which?)*: 0.15 mg/kg oxycodone as premedication, 24 mg oxycodone postoperatively, 0.25 mg fentanyl intraoperative
- *Type of surgery*: orthopaedic surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95
- *Use of perioperative opioids (if yes, which?)*: 0.15 mg/kg oxycodone as premedication, 20 mg oxycodone postoperatively, 0.31 mg fentanyl intraoperative
- *Type of surgery*: orthopaedic surgery

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Korttila 1979 *(Continued)*

Included criteria: women undergoing elective orthopaedic surgery, ASA I or II, during the 2 weeks before the operation had not taken any drugs with an antiemetic action

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia,perioperative opioids): yes

Interventions	**Intervention characteristics** Domperidone (5 mg group) • *Dose*: 5 mg • *Time point of administration*: 5 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: domperidone 5 mg IM, droperidol 1.25 mg IM Domperidone (10 mg group) • *Dose*: 10 mg • *Time point of administration*: 5 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: domperidone 10 mg IM, droperidol 1.25 mg IM Droperidol • *Dose*: 1.25 mg • *Time point of administration*: 5 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg IM Metoclopramide • *Dose*: 10 mg • *Time point of administration*: 5 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM, droperidol 1.25 mg Placebo • *Dose*: saline • *Time point of administration*: 5 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Orion Pharmaceutical Company provided the drugs **Country:** Finland

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Korttila 1979 *(Continued)*

Setting: inpatient, single-centre

Author's name: K. Korttila

Institution: Department of Anesthesia, Helsinki University Central Hospital

Email: NA

Address: Department of Anesthesia, University of Iowa Hospitals and Clinics, Iowa City, IA 52242

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "a double-blind randomized fashion" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the slightly longer duration of anesthesia, as well as the slightly greater amount of fentanyl, in patients given droperidol should have contributed to a higher incidence of emetic sequelae than that associated with shorter duration of anesthesia and a smaller amount of fentanyl.2*3" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia, perioperative opioids): yes

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Korttila 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 128 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 95/32/1/0 • *Gender (female in %)*: 91 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 30/18 • *Type of general anaesthesia*: inhalational anaesthesia (iso-/enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl/sufentanil at induction • *Type of surgery*: different surgical procedures (mainly laparoscopic and gynaecological surgeries) Dolasetron (25 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 127 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 98/28/2/0 • *Gender (female in %)*: 94 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 22/13 • *Type of general anaesthesia*: inhalational anaesthesia (iso-/enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl/sufentanil at induction • *Type of surgery*: different surgical procedures (mainly laparoscopic and gynaecological surgeries) Dolasetron (50 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 129 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 11

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- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 106/23/0/0
- *Gender (female in %)*: 95
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 33/15
- *Type of general anaesthesia*: inhalational anaesthesia (iso-/enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl/sufentanil at induction
- *Type of surgery*: different surgical procedures (mainly laparoscopic and gynaecological surgeries)

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 130
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 107/23/2/0
- *Gender (female in %)*: 96
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 30/19
- *Type of general anaesthesia*: inhalational anaesthesia (iso-/enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl/sufentanil at induction
- *Type of surgery*: different surgical procedures (mainly laparoscopic and gynaecological surgeries)

Included criteria: male and non-pregnant female, 18 to 65 years of age, ASA I to III, undergoing surgical procedure with general anaesthesia

Excluded criteria: scheduled for postoperative gastric suctioning or ingested any drug with antiemetic efficacy within 24 hours before surgery, clinically significant cardiac or liver disease, abnormal pre-study serum potassium levels, obesity (> 40% above ideal body weight), nausea and vomiting within 24 hours before surgery, previous treatment with dolasetron, use of any investigational drug within 30 days of dolasetron administration, known alcohol abuse

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (non-smoker, duration of anaesthesia, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (36%) investigator's choice Dolasetron (25 mg group) • *Dose*: 25 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (29%) investigator's choice

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Korttila 1997 *(Continued)*

	Dolasetron (50 mg group) • *Dose*: 50 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (19%) investigator's choice Ondansetron • *Dose*: 4 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (24%) investigator's choice
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by a research grant from Hoechst Marion Roussel **Country:** Finland **Setting:** inpatient, multi-centre (24) **Author's name:** Kari Korttila **Institution:** Department of Obstetrics and Gynaecology, University of Helsinki, Finland **Email:** kari.korttila@)helsinki.fi **Address:** Department of Obstetrics and Gynaecology, University of Helsinki, Haartmaninkatu-2, Fin-00290, Helsinki, Finland **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were stratified by gender and randomized to receive one of four treatments"

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Korttila 1997 *(Continued)*

		Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "gender and investigative site. Of 518 patients enrolled, 517 were included in safety analyses (one patient withdrew from the study after randomization but before receiving study drug), and 514 were included in the intent-to-treat data set for efficacy analyses (3 patients were withdrawn from the study before cessation of anesthesia: two experienced serious adverse events not related to study drug during surgery and one patient required nasogastric suction during and after surgery). There were no statistically..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no statistically significant imbalances across treatment groups with respect to gender, race, age, previous surgery, ASA physical status, history of POW, or history of motion sickness. There was a statistically but not clinically significant imbalance in weight among treat- ment groups (P=0.004), with patients in the ondansetron group weighing less on average than patients in the other treatment groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (non-smoker, duration of anaesthesia, perioperative opioids): unclear

Kothari 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 47.9 • *Weight (mean ± SD, median (IQR), median (range))*: 87.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Kothari 2000 *(Continued)*

- *ASA I/II/III/IV (n)*: 22/24/4/0
- *Gender (female in %)*: 72
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/24
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 65.1
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Dimenhydrinate

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 58
- *Age (mean ± SD, median (IQR), median (range))*: 49.7
- *Weight (mean ± SD, median (IQR), median (range))*: 85.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 25/27/6/0
- *Gender (female in %)*: 74.14
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/22.41
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 61.1
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I to III, undergoing elective laparoscopic cholecystectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 34% (patients given their choice of antiemetic at the discretion of the anaesthesiologist) Dimenhydrinate • *Dose*: 50 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 29% (patients given their choice of antiemetic at the discretion of the anaesthesiologist)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome

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Kothari 2000 *(Continued)*

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** W.C. Boyd **Institution:** Departments of Surgery and Anesthesiology, Gundersen Lutheran, La Crosse, WI 54601, USA **Email:** AN **Address:** Departments of Surgery and Anesthesiology, Gundersen Lutheran, 1836 South Avenue, La Crosse, WI 54601, USA **Duration of study:** 1 November 1998 to 1 June 1999 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "randomization was performed using a computer-generated randomized list''
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "nurses blinded to which antiemetic the patients had received recorded all episodes of nausea, vomiting, and retching in the re-

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Kothari 2000 *(Continued)*

		covery room by direct questioning, spontaneous complaint of the patient, or side effects''
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "of the 20 patient excluded, 15 had received an additional antiemetic preoperatively 4 were converted to open cholecystectomy, and the case of 1 was aborted because of the intraoperative finding of carcinomatosis. Of the 108 remaining patients available for analysis, 50 [of] whom were randomized to receive ondansetron (group 1) and 58 to receive dimenhydrinate (group 2)''
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: quote: "patient demographics were similar in both treatment groups" Baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Kovac 1992

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 142 • *Age (mean ± SD, median (IQR), median (range))*: 30.2 ± 0.5 • *Weight (mean ± SD, median (IQR), median (range))*: 64.2 ± 1.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 32/NA • *Type of general anaesthesia*: inhalational anaesthesia (oxygen, N_2O, additional isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 41.4 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopy for tubal sterilization, diagnostic laparoscopy, laser laparoscopy, laparotomy, minilaparotomy, dilatation curettage, no surgery Ondansetron (1 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Kovac 1992 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 139
- *Age (mean ± SD, median (IQR), median (range))*: 30.3 ± 0.5
- *Weight (mean ± SD, median (IQR), median (range))*: 64.4 ± 1.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 32/NA
- *Type of general anaesthesia*: inhalational anaesthesia (oxygen, N_2O, additional isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 39.3
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopy for tubal sterilization, diagnostic laparoscopy, laser laparoscopy, laparotomy, minilaparotomy, dilatation curettage, no surgery

Ondansetron (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 152
- *Age (mean ± SD, median (IQR), median (range))*: 30.7 ± 0.5
- *Weight (mean ± SD, median (IQR), median (range))*: 65.8 ± 1.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 33/NA
- *Type of general anaesthesia*: inhalational anaesthesia (oxygen, N_2O, additional isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 41.3
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopy for tubal sterilization, diagnostic laparoscopy, laser laparoscopy, laparotomy, minilaparotomy, dilatation curettage, no surgery

Ondansetron (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 147
- *Age (mean ± SD, median (IQR), median (range))*: 30.5 ± 0.5
- *Weight (mean ± SD, median (IQR), median (range))*: 66.0 ± 1.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 33/NA
- *Type of general anaesthesia*: inhalational anaesthesia (oxygen, N_2O, additional isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 40.7
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopy for tubal sterilization, diagnostic laparoscopy, laser laparoscopy, laparotomy, minilaparotomy, dilatation curettage, no surgery

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Kovac 1992 *(Continued)*

Included criteria: ASA I or II; non-pregnant female; between 18 and 70 years of age; scheduled for diagnostic laparoscopy, laparoscopy for tubal sterilization, or laparoscopy including laser surgery; intubated with an endotracheal tube and received a balanced anaesthetic

Excluded criteria: > 100% over ideal body weight, scheduled to undergo liver or peritoneal biopsy during the laparoscopy, to undergo continuous gastric suction via an intragastric tube during the surgical procedure, received any antiemetic medication within the 24 hours before surgery, had received an investigational drug within 30 days of the study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: citrate puffer
- *Time point of administration*: infused over 5 minutes, before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 27% (droperidol, prochlorperazine, metoclopramide, promethazine)

Ondansetron (1 mg group)

- *Dose*: 1 mg
- *Time point of administration*: infused over 5 minutes, before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 21% (droperidol, prochlorperazine, metoclopramide, promethazine)

Ondansetron (4 mg group)

- *Dose*: 4 mg
- *Time point of administration*: infused over 5 minutes, before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 12% (droperidol, prochlorperazine, metoclopramide, promethazine)

Ondansetron (8 mg group)

- *Dose*: 8 mg
- *Time point of administration*: infused over 5 minutes, before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 11% (droperidol, prochlorperazine, metoclopramide, promethazine)

Outcomes

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

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Kovac 1992 *(Continued)*

	Adverse events (general notes in the publication, 24 hours' observation) • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatients, multi-centre (8) **Author's name:** A.L. Kovac **Institution:** University of Kansas Medical Center, Kansas City, Kansas, USA **Email:** NA **Address:** Department of Anesthesiology, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160-7415, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "of the 580 patients, 36 had protocol deviations which caused them to be excluded from the efficacy analysis. Efficacy analysis was performed on the remaining population. The safety of ondansetron was evaluated in all patients"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

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Kovac 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 136 • *Age (mean ± SD, median (IQR), median (range))*: 50 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 49/83/4/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 85 • *History of PONV/motion sickness (%)*: 46 • *Type of general anaesthesia*: inhalational anaesthesia (any inhaled anaesthetic, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 43% postoperative opioids (fentanyl) • *Type of surgery*: gynaecological or breast surgery Palonosetron (0.025 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 136 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 65/67/4/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 86 • *History of PONV/motion sickness (%)*: 47 • *Type of general anaesthesia*: inhalational anaesthesia (any inhaled anaesthetic, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 46% postoperative opioids (fentanyl) • *Type of surgery*: gynaecological or breast surgery Palonosetron (0.05 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 137 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 10

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Kovac 2008 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 62/71/4/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 85
- *History of PONV/motion sickness (%)*: 47
- *Type of general anaesthesia*: inhalational anaesthesia (any inhaled anaesthetic, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 46% postoperative opioids (fentanyl)
- *Type of surgery*: gynaecological or breast surgery

Palonosetron (0.075 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 135
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 67/65/3
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 84
- *History of PONV/motion sickness (%)*: 47
- *Type of general anaesthesia*: inhalational anaesthesia (any inhaled anaesthetic, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 46% postoperative opioids (fentanyl)
- *Type of surgery*: gynaecological or breast surgery

Included criteria: women, ASA I to III, at least 18 years of age, scheduled to undergo elective inpatient gynaecological surgery (e.g. abdominal hysterectomy, vaginal hysterectomy) or breast surgery (except aesthetic/cosmetic plastic surgery), surgery expected to last a minimum of 1 hour, scheduled to be hospitalized for at least 72 hours after surgery, at least 1 of the 2 following risk factors for PONV: (1) history of PONV and/or currently prone to motion sickness, and (2) non-smoking status (never smoked or quit at least 12 months ago)

Excluded criteria: had received cancer chemotherapy within 4 weeks or emetogenic radiotherapy within 8 weeks before study entry

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 2 mL normal saline • *Time point of administration*: immediately (no more than 5 minutes) before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 64% (all, except palonosetron, dolasetron) Palonosetron (0.025 mg group) • *Dose*: 0.025 mg • *Time point of administration*: immediately (no more than 5 minutes) before induction of anaesthesia • *Route of administration*: IV

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Kovac 2008 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: all, except palonosetron, dolasetron Palonosetron (0.05 mg group) • *Dose*: 0.05 mg • *Time point of administration*: immediately (no more than 5 minutes) before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: all, except palonosetron, dolasetron Palonosetron (0.075 mg group) • *Dose*: 0.075 mg • *Time point of administration*: immediately (no more than 5 minutes) before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 27% (all, except palonosetron, dolasetron)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** sponsored by Helsinn Healthcare SA and supported by MGI PHARMA **Country:** Germany, Poland, Czech Republic **Setting:** inpatient, multi-centre (28 centres in Europe: 13 in Germany, 10 in Poland, and 5 in the Czech Republic) **Author's name:** Giuseppina Clerici **Institution:** Research and Development Department, Helsinn Healthcare SA, Lugano, Switzerland **Email:** gcl@helsinn.com **Address:** P.O. Box 357, 6915 Pambio-Noranco (Lugano), Switzerland **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response (CR: no emesis and no use of rescue medications) evaluated at 0 to 24 and 24 to 72 hours after surgery
Notes	None
Risk of bias	

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Kovac 2008 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "treatment randomization was stratified by type of surgery, history of PONV, and smoking status. A dynamic adaptive stratification type of randomization method was used to balance the four treatment groups across the entire study and not within each individual site"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "at each study site, palonosetron and placebo were prepared for administration to patients by an unblinded research pharmacist or designee who was otherwise not involved in the conduct of the study"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: emetic episodes and nausea were assessed with patient's reported diary cards. No statement on assessment of adverse events
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "significance level of 0.05. The incidence rates for adverse events were summarized; formal statistical comparisons were not performed. After the first 130 patients were enrolled in this study, a potential unblinding event with the clinical supplies label was discovered by a representative of the sponsor. If the labels were closely examined, there was a remote possibility that unblinding information of palonosetron versus placebo could have been revealed to the pharmacist. However, neither patient nor investigator was likely unblinded and the dose of palonosetron could not have been revealed. The decision was made to exclude these 130 patients and enroll an additional 130 patients to replace them. For this reason, the first 130 patients were included in the safety analysis (n 673) but excluded from the efficacy analysis (n 544)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): unclear

Koyuncu 2017

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 51 (46 to 54)

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Koyuncu 2017 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 29.4 (25.8 to 31.3)
- *ASA I/II/III/IV (n)*: 8/52/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102
- *Use of perioperative opioids (if yes, which?)*: 441 (280 to 578) mg tramadol consumption, fentanyl (2 µg/kg) at end of surgery for all participants
- *Type of surgery*: hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: 60
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 49 (44 to 57)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 29.4 (26.8 to 33.2)
- *ASA I/II/III/IV (n)*: 12/48/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 132
- *Use of perioperative opioids (if yes, which?)*: 412 (309 to 574) mg tramadol consumption, fentanyl (2 µg/kg) at end of surgery for all participants
- *Type of surgery*: hysterectomy

Included criteria: ASA I or II, women, 18 to 80 years of age, scheduled for hysterectomy with general anaesthesia. The study was restricted to hysterectomies with horizontal abdominal skin incision, and to patients who were able to operate a patient-controlled analgesia (PCA) device

Excluded criteria: emergency procedures; pre-existing chronic pain at any site requiring opioid analgesia; history of significant Axis I psychiatric disease (major depressive disorder, bipolar disorder, schizophrenia, etc.); significant hepatic (ALT or AST 2 times normal) or renal (serum creatinine 2 mg/dL) impairment; reporting allergy to acetaminophen or ondansetron

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 8 mg • *Time point of administration*: skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 25% (metoclopramide 10 mg) Placebo • *Dose*: 2 mL saline

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Koyuncu 2017 *(Continued)*

- *Time point of administration*: skin closure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 17% (metoclopramide 10 mg)

Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by internal funds only. The Department of Outcomes Research receives research support from Mallinckrodt unrelated to this project. None of the authors has a personal financial interest in this research **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Onur Koyuncu **Institution:** Department of Anesthesiology, Department of Outcomes Research, Anesthesiology Institute, Mustafa Kemal University Tayfur Ata Sokmen Medicine Faculty, Hatay, Turkey **Email:** okoyuncu@mku.edu.tr **Address:** Department of Anesthesiology, Mustafa Kemal UniversityTayfur Ata Sokmen Medicine Faculty, Serinyol, Hatay, Turkey **Language:** English **Duration of study:** May to December 2014 **Trial registry number:** NCT02296333 **Study's primary outcome:** postoperative pain scores
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization 1:1 without stratification was web-based using computer-generated codes"
Allocation concealment (selection bias)	Low risk	Quote: "the system was accessed shortly before induction of anesthesia to mask allocation until the last practical moment. Drugs were covered by opaque plastic to keep the surgical team and anesthesiologists blinded"
Blinding of participants and personnel (performance bias)	Low risk	Quote: "the system was accessed shortly before induction of anesthesia to mask allocation until the last practical moment. Drugs were covered by

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Koyuncu 2017 *(Continued)*

All outcomes		opaque plastic to keep the surgical team and anesthesiologists blinded to treatment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all postoperative measurements were conducted by a research assistant who was blinded to group allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT02296333 (retrospective registration)
Other bias	High risk	Quote: "the two randomized groups were poorly balanced on duration of anesthesia and duration of surgery, with absolute standardized differences of 0.66 and 0.70, respectively (Table 1). We thus adjusted for each when comparing the two groups on outcomes" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia): yes

Kranke 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 51 • *Received treatment (n)*: 51 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 51.2 (20 to 76) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27.1 (18.1 to 40.9) • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 88.2 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, isoflurane, or sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: all patients except 1 received opioids • *Type of surgery*: hysterectomy, other laparoscopic surgery, breast surgery Buspirone (0.3 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Kranke 2012 *(Continued)*

- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 48
- *Age (mean ± SD, median (IQR), median (range))*: 49.4 (19 to 86)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26.9 (15.1 to 42.9)
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 98.0
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, isoflurane, or sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: all patients except 1 received opioids
- *Type of surgery*: hysterectomy, other laparoscopic surgery, breast surgery

Buspirone (1 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 49
- *Received treatment (n)*: 49
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 49.5 (21 to 85)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26.8 (17.7 to 40.2)
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 87.8
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, isoflurane, or sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: all patients except 1 received opioids
- *Type of surgery*: hysterectomy, other laparoscopic surgery, breast surgery

Buspirone (2 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 52
- *Received treatment (n)*: 52
- *Analysed (n)*: 51
- *Age (mean ± SD, median (IQR), median (range))*: 52.3 (25 to 86)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26.7 (19.1 to 47.0)
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 86.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, isoflurane, or sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: all patients except 1 received opioids
- *Type of surgery*: hysterectomy, other laparoscopic surgery, breast surgery

Buspirone (3 mg group)

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Kranke 2012 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 55
- *Received treatment (n)*: 55
- *Analysed (n)*: 54
- *Age (mean ± SD, median (IQR), median (range))*: 50.3 (25 to 78)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26.9 (17.1 to 42.6)
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 89.1
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, isoflurane, or sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: all patients except 1 received opioids
- *Type of surgery*: hysterectomy, other laparoscopic surgery, breast surgery

Included criteria: adults; due to have an inpatient operation under general anaesthesia (other than intrathoracic, transplant, or central nerve system surgery) that was expected to last at least 1 hour and during which inhalational anaesthetics were to be used as maintenance agents; had at least 2 of 4 prespecified risk factors for developing PONV: female sex, non-smoking status, history of PONV or motion sickness, expectation of receiving opioids for postoperative analgesia; adequate haematological, renal, and hepatic function (alanine aminotransferase and aspartate aminotransferase levels 2.5× upper limit of normal (ULN); bilirubin and creatinine levels 1.5× ULN; haemoglobin ≥ 9.5 g/dL; white cell count range 4.0 to 11.0 × 10^9/L; platelet count range 150 to 400 × 10^9/L)

Excluded criteria: expected to require postoperative ventilation, Parkinson's disease, clinically significant cardiac arrhythmia, epilepsy

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 39.2%; NA

Buspirone (0.3 mg group)

- *Dose*: 0.3 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 56.0%; NA

Buspirone (1 mg group)

- *Dose*: 1 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 30.6%; NA

Buspirone (2 mg group)

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Kranke 2012 *(Continued)*

- *Dose*: 2 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 53.8%; NA

Buspirone (3 mg group)

- *Dose*: 3 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 41.8%; NA

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours) or PONV* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** the study was funded by Acacia Pharma Ltd., the manufacturer of the study drug. The study design was developed by a steering committee (CCA, PD, TJG, PK, MRT) in collaboration with Acacia Pharma Ltd. Acacia Pharma Ltd. edited the study protocol in collaboration with steering committee members, organized meetings for steering committee members and investigators, supplied study drugs, and was responsible for data analysis **Country:** France, Germany, Switzerland, USA **Setting:** inpatient, multi-centre (17) **Author's name:** Martin R. Tramèr **Institution:** Division of Anaesthesiology, Geneva University Hospitals, Geneva, Switzerland **Email:** martin.tramer@hcuge.ch **Address:** Division of Anaesthesiology, Geneva University Hospitals, Rue Gabrielle-Perret-Gentil 4,1211 Geneva 14, Switzerland **Duration of study:** NA **Language:** English **Study's primary outcome:** cumulative incidence of PONV (i.e. vomiting or significant nausea) in the 24-hour period after end of surgery **Trial registry number:** NCT00895830
Notes	None

Risk of bias

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Kranke 2012 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "by means of an interactive telephone- and internet-based randomisation service, the site obtained a randomised treatment allocation for each subject to one of five groups"
Allocation concealment (selection bias)	Low risk	Quote: "the site obtained a randomised treatment allocation for each subject to one of five groups: 0.3, 1, 2 or 3 mg of buspirone or placebo" Quote: "the randomisation was stratified by country and by number of risk factors (2 vs. 3 or 4). An unblinded pharmacist at each site, with no other study involvement, made up a treatment syringe of equal volume (28 ml) containing placebo or the appropriate dose of buspirone for each subject. Syringes were matching and were labelled with the randomisation number only to ensure that allocation was concealed" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...and that the investigators, other study personnel, and subjects were all blinded as to treatment group" Quote: "syringes were matching and were labelled with the randomisation number only to ensure that allocation was concealed and that the investigators, other study personnel and subjects were all blinded as to treatment group"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were asked prospectively by blinded dedicated research assistants about nausea every 30 min after surgery up to and including the 1-h mark and then again at 6 and 24 h"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "in total, 298 patients were screened and 281 were randomised into the study (Fig. 1). Twenty-four patients did not receive the study drug, mostly because their operation was cancelled or postponed (11 cases), the study drug was unavailable (5 cases) or they withdrew consent prior to surgery (5 cases). This left 257 patients"
Selective reporting (reporting bias)	Low risk	Judgement comment: NCT00895830 (prospective registration). The prospectively registered primary outcome (PONV) was reported in the prespecified way in the final study report
Other bias	Unclear risk	Quote: "primary safety and efficacy analyses. Study arms were well balanced for age, sex, body mass index and race (Table 1). The mean age of patients at enrolment was 50.6 years, and 89.9% were female. There were no significant differences between study arms in terms of past medical history, baseline physical examination, vital signs and type of operation. Hysterectomy occurred in 22.6% of patients, laparoscopic surgery other than hysterectomy or cholecystectomy in 19.8%, and breast surgery in 14.4%. There were no significant differences between study arms in terms of anaesthetic technique. All patients except one received opioids, and 93% received a volatile anaesthetic (desflurane, isoflurane or sevoflurane). Among the few who did..." Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Kranke 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 55 • *Received treatment (n)*: 54 • *Analysed (n)*: 54 • *Age (mean ± SD, median (IQR), median (range))*: 50.0 (19 to 75) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.8 (18 to 40) • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 87 • *Non-smoker (%)*: 85 • *History of PONV/motion sickness (%)*: 39 • *Type of general anaesthesia*: at investigators' discretion (sevo-/desflurane; TIVA not permitted) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, remifentanil, or sufentanil (61%) • *Type of surgery*: abdominal operation, breast surgery, axillary surgery APD421 (1 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 61 • *Received treatment (n)*: 58 • *Analysed (n)*: 58 • *Age (mean ± SD, median (IQR), median (range))*: 48.5 (22 to 83) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.6 (17 to 46) • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 91 • *Non-smoker (%)*: 64 • *History of PONV/motion sickness (%)*: 36 • *Type of general anaesthesia*: at investigators' discretion (sevo-/desflurane; TIVA not permitted) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, remifentanil, or sufentanil (67%) • *Type of surgery*: abdominal operation, breast surgery, axillary surgery APD421 (5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 51 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 50.5 (20 to 80) • *Weight (mean ± SD, median (IQR), median (range))*: NA

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Kranke 2013 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 26.1 (18 to 40)
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 96
- *Non-smoker (%)*: 84
- *History of PONV/motion sickness (%)*: 40
- *Type of general anaesthesia*: at investigators' discretion (sevo-/desflurane; TIVA not permitted)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, remifentanil, or sufentanil (62%)
- *Type of surgery*: abdominal operation, breast surgery, axillary surgery

APD421 (20 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 56
- *Received treatment (n)*: 53
- *Analysed (n)*: 53
- *Age (mean ± SD, median (IQR), median (range))*: 51.0 (22 to 82)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26.2 (20 to 43)
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 92
- *Non-smoker (%)*: 75
- *History of PONV/motion sickness (%)*: 38
- *Type of general anaesthesia*: at investigators' discretion (sevo-/desflurane; TIVA not permitted)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, remifentanil, or sufentanil (70%)
- *Type of surgery*: abdominal operation, breast surgery, axillary surgery

Included criteria: adults who had given written informed consent; inpatient operation (other than intrathoracic, transplant, or central nervous system (CNS) surgery) expected to last at least 1 hour under general anaesthesia; had at least 2 of the following risk factors for developing PONV: (1) female sex; (2) non-smoking status; (3) prior history of PONV or motion sickness; and (4) expected to receive postoperative opioid analgesia; adequate haematological, renal, and hepatic function (haemoglobin ≥ 9 g/dL, white cells ≥ 3×10^9/L, platelets ≥ 100×10^9/L, creatinine 2 × upper limit of normal (ULN), bilirubin 3 × ULN, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) both 5× ULN)

Excluded criteria: expected to require postoperative ventilation or to need a nasogastric or orogastric tube in situ after surgery, Parkinson's disease, pre-existing vestibular disorder or history of dizziness, history of alcohol abuse, clinically significant cardiac arrhythmia, epilepsy

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): unclear

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Interventions

Intervention characteristics

placebo

- *Dose*: 2 mL saline
- *Time point of administration*: at the time of induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 67% 5-HT3 antagonist IV, or a different class

APD421 (1 mg group)

- *Dose*: 1 mg

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Kranke 2013 *(Continued)*

- *Time point of administration*: at the time of induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 47% 5-HT3 antagonist IV, or a different class

APD421 (5 mg group)

- *Dose*: 5 mg
- *Time point of administration*: at the time of induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 38% 5-HT3 antagonist IV, or a different class

APD421 (20 mg group)

- *Dose*: 20 mg
- *Time point of administration*: at the time of induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 55% 5-HT3 antagonist IV, or a different class

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** the study was funded by Acacia Pharma Ltd., Cambridge, UK, the manufacturer of the study drug. **Country:** Germany, France, USA **Setting:** inpatient, multi-centre (10) **Author's name:** Peter Kranke **Institution:** Department of Anaesthesia and Critical Care, University Hospital of Würzburg **Email:** kranke_p@klinik.uni-wuerzburg.de

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Kranke 2013 *(Continued)*

Address: Department of Anaesthesia and Critical Care, University Hospital of Würzburg, Oberdürrbacher Str. 6, Würzburg 97080, Germany

Duration of study: January to April 2012

Language: English

Study's primary outcome: PONV (vomiting/retching or antiemetic rescue) in the 24 hour period after surgery.

Trial registry number: NCT01510704, EUCTR2011-004267-71

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "an internet-based randomization system provided sites on demand with a subject number for each patient randomized"
Allocation concealment (selection bias)	Low risk	Quote: "an internet-based randomization system provided sites on demand with a subject number for each patient randomized, which could then be matched to the subject number on the appropriate vial of study medication held at the site" Judgement comment: central allocation (web-based)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all vials were identically labelled except for an individual subject number derived from a master randomization list available to the contract manufacturer of the study medication, but not to the sponsor, any site research personnel, or study participants"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the final constitution of study analysis populations was determined on a fully blinded basis before database closure"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "two hundred and twenty-three subjects were randomized into the study (Fig. 1), eight not receiving study drug, mostly because of withdrawal of consent, cancellation of surgery, or a preoperative episode of nausea and vomiting. The ITT and safety analysis populations, therefore, comprised 215 individuals"
Selective reporting (reporting bias)	Low risk	Judgement comment: NCT01510704 (prospective registration), EUCTR2011-004267-71 (prospective registration). The prospectively registered primary outcome (PONV) was reported in the pre-specified way in the final study report
Other bias	Unclear risk	Quote: "therefore, comprised 215 individuals. Study arms were generally well balanced for age, body mass index, and PONV risk factor profile (Table 1). Most patients were female (92%) and non-smokers (77%), including ex-smokers who had ceased 2 yr previously. Two-thirds of the population had three or four risk factors. There were no significant differences" Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): unclear

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Krobbuaban 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 191 • *Received treatment (n)*: 191 • *Analysed (n)*: 189 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 31/12 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 66 ± 2 • *Use of perioperative opioids (if yes, which?)*: 68 ± 20 µg fentanyl intraoperative • *Type of surgery*: major gynaecological surgery Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 191 • *Received treatment (n)*: 191 • *Analysed (n)*: 191 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 34/19 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 66 • *Use of perioperative opioids (if yes, which?)*: 61 ± 18 µg fentanyl intraoperative • *Type of surgery*: major gynaecological surgery **Included criteria:** female, 20 to 65 years of age **Excluded criteria:** laboratory or clinical evidence of cardiovascular, haematological, pulmonary, renal, hepatic, neurological, or endocrine abnormalities; gastrointestinal disease; pregnancy; morbid obesity; history of substance abuse; antiemetic antipsychoactive medication within 24 hours before surgery; need for a nasogastric tube postoperatively **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Krobbuaban 2008 *(Continued)*

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dimenhydrinate 50 mg IV Metoclopramide • *Dose*: 10 mg • *Time point of administration*: immediately before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dimenhydrinate 50 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 1 hour, 1 to 6 hours, 6 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 1 hour, 1 to 6 hours, 6 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 1 hour, 1 to 6 hours, 6 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 1 hour, 1 to 6 hours, 6 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** the present study is not supported by any funds of drug commercials **Country:** Thailand **Setting:** inpatient, single-centre **Author's name:** Banjong Krobbuaban **Institution:** Department of Anesthesiology, Chaiyaphum Hospital **Email:** albkb@diamond.mahidol.ac.th **Address:** Department of Anesthesiology, Chaiyaphum Hospital, Bannakan Rd, Maung, Chaiyaphum 36000, Thailand **Language:** English

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Krobbuaban 2008 *(Continued)*

	Duration of study: NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	(Erratum appears in Journal of the Medical Association of Thailand 2008 Jul;91(7):1154. Note: dosage error in text)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "a randomization list and sealed envelopes were prepared before anaesthesia according to a list of randomized numbers generated by the method of block randomization, with block size varying from 2 to 6"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "according to the list, identical syringes containing each antiemetic were prepared by a nurse anaesthetist not involved in the study. In this way, the anaesthesiologist, anaesthetist, patients, and PACU nurses were all blinded to the identity of the prophylactic treatment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "according to the list, identical syringes containing each antiemetic were prepared by a nurse anaesthetist not involved in the study. In this way, the anaesthesiologist, anaesthetist, patients, and PACU nurses were all blinded to the identity of the prophylactic treatment"; "the details of any other adverse effects were recorded by a nurse anesthetist, not apprised of which drug had been administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "two patients in the ondansetron group were excluded from the trial due to complications in surgery (final operations were bowel surgery)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Kumar 1996

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Kumar 1996 *(Continued)*

- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 43.87 ± 10.7
- *Weight (mean ± SD, median (IQR), median (range))*: 49.67 ± 7.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 97.5
- *Use of perioperative opioids (if yes, which?)*: 0.1 mg/kg morphine at induction
- *Type of surgery*: major gynaecological surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 41.13 ± 12.5
- *Weight (mean ± SD, median (IQR), median (range))*: 52.07 ± 10.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102.5
- *Use of perioperative opioids (if yes, which?)*: 0.1 mg/kg morphine at induction
- *Type of surgery*: major gynaecological surgery

Included criteria: female, ASA I or II, scheduled for elective gynaecological surgery under general anaesthesia

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Metoclopramide • *Dose*: 10 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV

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Kumar 1996 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** CIPLA Limited supplied ondansetron ampoules **Country:** India **Setting:** inpatient, single-centre **Author's name:** A. Kumar **Institution:** Department of Anaesthesiology Critical Care, UCMS GTB Hospital, Delhi **Email:** NA **Address:** Department of Anaesthesiology Critical Care, UCMS GTB Hospital, Delhi-110095 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote "randomly distributed into two groups". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "patients were studied by an independent observer who was blinded as to which group the patient belonged"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no information on number of analysed participants
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Kumar 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: 80 • *Analysed (n)*: 80 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: balanced general anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group II) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: 80 • *Analysed (n)*: 80 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: balanced general anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Dexamethasone (group III) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: 80 • *Analysed (n)*: 80 • *Age (mean ± SD, median (IQR), median (range))*: NA

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Kumar 2013 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced general anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron + dexamethasone (group IV)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: 80
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced general anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: both sexes, scheduled for elective laparoscopic cholecystectomy

Excluded criteria: older than 60 years and younger than 18 years, smoker, alcoholics, history of hypersensitivity to any drug, impaired liver and kidney functions, history of previous PONV, receiving antidepressants or calcium channel blockers, converted to open cholecystectomy

Pretreatment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (non-smoker, history of PONV): no; (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): unclear

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Interventions

Intervention characteristics

Placebo (group I)

- *Dose*: 2 ml of distilled water
- *Time point of administration*: before general anaesthesia administered
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Ondansetron (group II)

- *Dose*: 4 mg
- *Time point of administration*: before general anaesthesia administered
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Dexamethasone (group III)

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Kumar 2013 *(Continued)*

	• *Dose*: 8 mg • *Time point of administration*: before general anaesthesia administered • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Ondansetron + dexamethasone (group IV) • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: before general anaesthesia administered • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** NA **Author's name:** Ashwani Kumar **Institution:** Department of Surgery, Rajindra Hospital, Patiala, Punjab, India **Email:** ashwanicmc@hotmail.com **Address:** Medical College Campus, Near Senior Boys Hostel, Government Medical College, Patiala-147001. Punjab, India **Language:** English **Duration of study:** July 2007 to June 2010 **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated to four groups of 80 patients each" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement

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Kumar 2013 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (non-smoker, history of PONV): no; (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): unclear

Kurz 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 296 • *Received treatment (n)*: NA • *Analysed (n)*: 283 • *Age (mean ± SD, median (IQR), median (range))*: 53 ± 17 • *Weight (mean ± SD, median (IQR), median (range))*: 80 ± 20 • *BMI (mean ± SD, median (IQR), median (range))*: 27 ± 6 • *ASA I/II/III/IV (n)*: 36/172/75/0 • *Gender (female in %)*: 45 • *Non-smoker (%)*: 82 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (des-/sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 210 • *Use of perioperative opioids (if yes, which?)*: 0.60 mg fentanyl intraoperative, postoperative morphine/hydromorphone • *Type of surgery*: colorectal resection Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 290 • *Received treatment (n)*: NA • *Analysed (n)*: 272 • *Age (mean ± SD, median (IQR), median (range))*: 52 ± 16 • *Weight (mean ± SD, median (IQR), median (range))*: 80 ± 22

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Kurz 2015 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 28 ± 7
- *ASA I/II/III/IV (n)*: 41/160/71/0
- *Gender (female in %)*: 52
- *Non-smoker (%)*: 73
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (des-/sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 204
- *Use of perioperative opioids (if yes, which?)*: 0.48 mg fentanyl intraoperative, postoperative morphine/hydromorphone
- *Type of surgery*: colorectal resection

Included criteria: adults younger than 80 years of age, scheduled for elective colorectal resection expected to last 2 to 6 hours

Excluded criteria: chemotherapy within 6 months, anticipated secondary wound closure, fever (≥ 38°C) or infection at admission, severe chronic obstructive pulmonary disease (forced expiratory volume in the first second (FEV1)/forced vital capacity (FVC) 70%; FEV1 150% predicted, with or without chronic symptoms), unstable angina pectoris, hypertensive cardiomyopathy, congestive heart failure (according to the Modified Framingham criteria), myocardial infarction within 6 months, bowel obstruction (confirmed or suspected by the primary surgeon), ASA ≥ 4

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness): unclear; (perioperative opioids, non-smoker): yes

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 4 mg • *Time point of administration*: within 15 minutes of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: not standardized, ondansetron recommended, dexamethasone forbidden Placebo • *Dose*: saline 0.9% • *Time point of administration*: within 15 minutes of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: not standardized, ondansetron recommended, dexamethasone forbidden
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this study was supported in part by the Gheens Foundation (Louisville, KY, USA) and the Mater College for Postgraduate Research (Ireland). Viasys Healthcare (Wheeling, IL, USA) provided the Hi-Ox oxygen masks **Country:** USA, Austria, Ireland, Switzerland **Setting:** inpatient, multi-centre (5) **Authors name:** D.I. Sessler **Institution:** Department of Outcomes Research, Cleveland Clinic, Cleveland, OH, USA **Email:** ds@or.org

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Kurz 2015 *(Continued)*

	Address: NA **Language:** English **Duration of study:** 2002 to 2007 **Trial registry number:** NCT00273377 **Study's primary outcome:** incidence of surgical site infection within 30 days
Notes	Factorial trial design (normocapnia and hypercapnia)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "all assignments were based on computer-generated randomizations"
Allocation concealment (selection bias)	Low risk	Quote: "all assignments were based on computer-generated randomizations that were kept in opaque, sealed, sequentially numbered envelopes until shortly before surgery"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "anaesthesiologists were not blinded to group assignments, but flow meters and gas monitors were shielded to prevent surgeons from determining randomisation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "after giving the handoff report to the post-anaesthesia care unit, the anaesthesia record was sealed in an envelope as part of the blinding process until discharge" Quote: "wounds were evaluated daily throughout hospitalisation by an investigator blinded to treatment. Subsequently subjects were called on the 15th and 30th day and a scripted interview was used to enquire about SSI. When answers suggested that infection was likely, efforts were made to obtain relevant records. An investigator blinded to treatment adjudicated infections and complications using all available data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "≤ 0.05 were retained. We enrolled 586 subjects in five centres (Bern, 29; Cleveland, 295; Dublin, 29; Louisville, 102; Vienna, 131); data from 555 subjects were analysable (Fig. 1)..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00273377 (retrospective registration)
Other bias	High risk	Quote: "clinical characteristics, diagnoses, surgical procedures, duration of surgery, haemodynamic values, and anaesthetic management were generally similar in subjects randomized to each intervention. However, an open surgical approach was used slightly more often in subjects assigned to 80% rather than 30% inspired oxygen, and subjects assigned to dexamethasone were given slightly more fentanyl and volatile anaesthesia (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness): unclear; (perioperative opioids, non-smoker): yes

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Kyokong 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 207 • *Received treatment (n)*: 207 • *Analysed (n)*: 201 • *Age (mean ± SD, median (IQR), median (range))*: 50.36 ± 14.17 • *Weight (mean ± SD, median (IQR), median (range))*: 58.65 ± 10.92 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 59.70 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced general anaesthesia (fentanyl, N_2O, isoflurane, or halothane (if necessary)) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: gastrointestinal and biliary tract surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 201 • *Received treatment (n)*: 201 • *Analysed (n)*: 199 • *Age (mean ± SD, median (IQR), median (range))*: 50.07 ± 15.47 • *Weight (mean ± SD, median (IQR), median (range))*: 57.19 ± 12.08 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 61.31 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced general anaesthesia (fentanyl, N_2O, isoflurane, or halothane (if necessary)) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: gastrointestinal and biliary tract surgery **Included criteria:** 18 to 75 years of age, ASA I or II, scheduled for gastrointestinal and biliary tract surgery under general anaesthesia **Excluded criteria:** received any other antiemetic agent within 24 hours before the study began, had vomited or retched within 24 hours, pregnant or breastfeeding, > 100 kg in weight, scheduled for inguinal hernia repair, recent history of drug or alcohol abuse, any other contraindications to ondansetron

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Kyokong 1999 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: on discretion of the investigator Placebo • *Dose*: NA • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: on discretion of the investigator
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by Glaxo Wellcome (Thailand) **Country:** Thailand **Setting:** NA, multi-centre (5) **Author's name:** Oranuch Kyokong **Institution:** Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330 **Email:** NA **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA

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Kyokong 1999 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "patients were randomized within each center...". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "each medication was coded and contained in identical ampoules so that the patient and investigator were unaware of the nature of the drug being administered"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "six of the 207 patients who received ondansetron and 2 of the 201 patients who received the placebo were not included in the analysis of efficacy because of major protocol violations that may have altered the interpretation of results. These protocol violations included receipt of other antiemetics in addition to ondansetron or surgery was cancelled after study drug administration"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Laha 2013

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 43.3 ± 14.25 • *Weight (mean ± SD, median (IQR), median (range))*: 57.1 ± 9.61 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Laha 2013 *(Continued)*

- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 10.20
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl intraoperative
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 44.9 ± 13.36
- *Weight (mean ± SD, median (IQR), median (range))*: 60.4 ± 9.99
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 24.49
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79.2 ± 24.3
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl intraoperative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: over 18 years age, either sex, undergoing elective laparoscopic cholecystectomy at a tertiary care hospital

Excluded criteria: pregnancy; body weight > 30% of ideal body weight; distinct spells of nausea, vomiting, or retching within 24 hours before surgery; use of corticosteroids, psychoactive drugs, or any other medication with known emetic or antiemetic effect within 24 hours before surgery; significant disease of major organs like liver, kidneys, heart, lungs, and bone marrow; known hypersensitivity to study medication; history of alcohol or substance abuse; participation in any other clinical trial within the last month

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Palonosetron • *Dose*: 75 µg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg PO Ondansetron • *Dose*: 4 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg PO

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Laha 2013 *(Continued)*

Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (time point unknown)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** nil **Country:** India **Setting:** inpatient, single-centre **Author's name:** Avijit Hazra **Institution:** NA **Email:** ni.oc.oohay@snafwolb **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "simple randomization was done in 1:1 ratio on the basis of a computer generated random number list"
Allocation concealment (selection bias)	Low risk	Quote: "generated random number list and allocation was concealed till the point of drug administration using serially numbered opaque sealed envelopes. The medication was administered..."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "single blind manner, taking care to ensure that the patient was not aware of the exact identity of the antiemetic drug" Judgement comment: personnel was aware of the study drug
Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: personnel was aware of the study drug
Incomplete outcome data (attrition bias)	Low risk	Quote: "the study was completed by all recruited subjects"

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Laha 2013 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Lahsaei 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: NA • *Analysed (n)*: 100 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: induction fentanyl (1 mg/kg to 2 mg/kg), morphine (0.1 mg/kg to 0.2 mg/kg) • *Type of surgery*: orthopaedic operations Cetirizine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: 100 • *Analysed (n)*: 100 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)

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Lahsaei 2012 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: induction fentanyl (1 mg/kg to 2 mg/kg), morphine (0.1 mg/kg to 0.2 mg/kg)
- *Type of surgery*: orthopaedic operations

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 100
- *Received treatment (n)*: 100
- *Analysed (n)*: 100
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: induction fentanyl (1 mg/kg to 2 mg/kg), morphine (0.1 mg/kg to 0.2 mg/kg)
- *Type of surgery*: orthopaedic operations

Included criteria: 18 to 65 years of age, ASA I or II

Excluded criteria: history of diabetes mellitus, motion sickness, ischaemic cardiomyopathy, nausea and vomiting in previous operations, asthma, pregnancy

Pretreatment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (history of PONV/motion sickness): no; (gender, non-smoker, duration of anaesthesia, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: NA • *Time point of administration*: 30 to 60 minutes before anaesthesia • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: NA Cetirizine • *Dose*: 10 mg • *Time point of administration*: 30 to 60 minutes before anaesthesia • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 8 mg • *Time point of administration*: 30 to 60 minutes before anaesthesia • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 2 hours)*

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Lahsaei 2012 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (2 to 12 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** nil **Country:** Iran **Setting:** single-centre **Author's name:** Afshin Amini **Institution:** Department of Anesthesiology, Anesthesiology Research Center, Shiraz **Email:** ri.ca.smus@inimaa **Address:** Shiraz Medical Science University Managing Building, Fars Province, Shiraz, Zand, Iran **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "simple random sampling method" Judgement comment: insufficient information on randomization provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "only the anesthetist was aware of the content"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "neither the interviewer nor the patient was aware of the capsule content"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (history of PONV/motion sickness): no; (gender, non-smoker, duration of anaesthesia, perioperative opioids): unclear

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Laiq 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 32.5 ± 2.47 • *Weight (mean ± SD, median (IQR), median (range))*: 59.2 ± 7.86 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 54.5 • *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction • *Type of surgery*: laparoscopic gynaecological surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 33.1 ± 1.46 • *Weight (mean ± SD, median (IQR), median (range))*: 60.4 ± 8.77 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 56.2 • *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction • *Type of surgery*: laparoscopic gynaecological surgery **Included criteria:** ASA I and II, undergoing gynaecological laparoscopic surgery **Excluded criteria:** severe systemic or endocrine disorder with predisposing factors for delayed gastric emptying such as diabetes, chronic cholecystitis, or neuromuscular disorders; had postoperative nausea and vomiting; had received an antiemetic drug or narcotic medications within the last 24 hours

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Laiq 2005 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 10 mg • *Time point of administration*: at the time of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16% (Marzine) Placebo • *Dose*: saline • *Time point of administration*: at the time of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 28% (Marzine)
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 10 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Pakistan **Setting:** single-centre **Author's name:** Dr. Nasreen Laiq **Institution:** Hayatabad Medical Complex, Peshawar **Email:** nasreennaeem@hotmail.com **Address:** H.No: 156.Street No.3. SectorN-2, Phase 4, Hayatabad, Peshawar. N.W.F.P, Pakistan **Duration of study:** December 2001 to June 2002 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "using a computer generated random number table"

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Laiq 2005 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "study medications were prepared by one of the investigators and were admitted, using a double blind design". Insufficient information on blinding. Unclear whether anaesthetists were blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Larsson 1988

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Dixyrazine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 129 • *Use of perioperative opioids (if yes, which?)*: 3.9 µg/kg/h fentanyl intraoperative, pethidine postoperative • *Type of surgery*: abdominal, minor orthopaedic, thyroid, mammary Scopolamine

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Larsson 1988 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 29
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (fentanyl, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 148
- *Use of perioperative opioids (if yes, which?)*: 3.9 µg/kg/h fentanyl intraoperative, pethidine postoperative, morphine 0.15 mg/kg
- *Type of surgery*: abdominal, minor orthopaedic, thyroid, mammary

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 26
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 53
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (fentanyl, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 128
- *Use of perioperative opioids (if yes, which?)*: 4.7 µg/kg/h fentanyl intraoperative, pethidine postoperative
- *Type of surgery*: abdominal, minor orthopaedic, thyroid, mammary

Included criteria: 20 to 60 years of age; ASA I or II; scheduled for abdominal, minor orthopaedic, thyroid, or mammary surgery expected to last at least 1 hour; no patient was on continuous sedative or analgesic medication

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Dixyrazine • *Dose*: 0.5 mg/kg • *Time point of administration*: 1 hour before anaesthesia induction • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: droperidol

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Larsson 1988 *(Continued)*

	Scopolamine • *Dose*: scopolamine 0.0065 mg/kg, morphine 0.15 mg/kg • *Time point of administration*: 1 hour before anaesthesia induction • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: droperidol Placebo • *Dose*: saline • *Time point of administration*: 1 hour before anaesthesia induction • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: droperidol
Outcomes	*Sedation/drowsiness (at 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 6 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Sweden **Setting:** NA, single-centre **Author's name:** Sylvia Larsson **Institution:** Department of Anesthesiology, University Hospital, Lund, Sweden **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly divided into three groups with 30 patients each" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "in equal volume and in a double-blind fashion" Judgement comment: insufficient information on blinding

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Larsson 1988 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "two patients excluded because of thyrotoxic symptoms before induction of anaesthesia. 8 patients were later excluded because of following reasons: delays in operating room schedule, major surgical bleeding, anaesthesia >1 h, reoperation"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Lee 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 31.5 ± 6.32 • *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 6.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 30/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickn(ess (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 79 • *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg for induction • *Type of surgery*: gynaecological laparoscopy Ondansetron (4 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 30.8 ± 5.6

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Lee 2000 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 53.1 ± 7.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 30/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 78
- *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg for induction
- *Type of surgery*: gynaecological laparoscopy

Ondansetron (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 30.55 ± 4.2
- *Weight (mean ± SD, median (IQR), median (range))*: 51.5 ± 4.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 30/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 74
- *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg for induction
- *Type of surgery*: gynaecological laparoscopy

Prochlorperazine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 31.5 ± 5.2
- *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 6.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 30/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 85
- *Use of perioperative opioids (if yes, which?)*: fentanyl 3 µg/kg for induction
- *Type of surgery*: gynaecological laparoscopy

Included criteria: women, ASA I, scheduled to undergo ambulatory gynaecological laparoscopy

Excluded criteria: antiemetic or psychoactive medication within 24 hours before surgery; pregnancy; obesity (50% above ideal body weight), history of smoking

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Lee 2000 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: NaCl 0.9% • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (4 mg group) • *Dose*: 4 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (8 mg group) • *Dose*: 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Prochlorperazine • *Dose*: 5 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** outpatient, single-centre **Author's name:** Lin-Cheng Yang **Institution:** Department of Anesthesiology, Chang Gung Memorial Hospital, Taiwan **Email:** LCYANG@ons13.hinet.net **Address:** Department of Anesthesiology, Chang Gung Memorial Hospital, 123Ta-Pei Road, Niao Shung Hsiang, Kaobsiung Hsien 833, Taiwan **Duration of study:** NA **Language:** English **Study's primary outcome:** NA

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Lee 2000 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "computer generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "POV assessments were made throughout this period by an observer who was unaware of the type of prophylactic antiemetic drug administrated"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: 15 participants were excluded due to protocol violations
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a sturdy protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Lee 2003

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group MS+) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 42 • *Received treatment (n)*: NA • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 39.6 ± 7.7 • *Weight (mean ± SD, median (IQR), median (range))*: 56.4 ± 5.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Lee 2003 *(Continued)*

- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/100
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 141.5
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction 1 µg/kg
- *Type of surgery*: gynaecological laparoscopic procedures

Placebo (group MS+)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 42
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 38.7 ± 8.1
- *Weight (mean ± SD, median (IQR), median (range))*: 57.5 ± 6.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/100
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138.3
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction 1 µg/kg
- *Type of surgery*: gynaecological laparoscopic procedures

Dexamethasone (group MS-)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 42
- *Received treatment (n)*: NA
- *Analysed (n)*: 42
- *Age (mean ± SD, median (IQR), median (range))*: 40.5 ± 6.8
- *Weight (mean ± SD, median (IQR), median (range))*: 58.2 ± 7.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 136.6
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction 1 µg/kg
- *Type of surgery*: gynaecological laparoscopic procedures

Placebo (group MS-)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 42
- *Received treatment (n)*: NA
- *Analysed (n)*: 41
- *Age (mean ± SD, median (IQR), median (range))*: 38.4 ± 9.3
- *Weight (mean ± SD, median (IQR), median (range))*: 55.6 ± 7.6

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Lee 2003 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 135.6
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction 1 µg/kg
- *Type of surgery*: gynaecological laparoscopic procedures

Included criteria: female; ASA I or II; 28 to 58 years of age; with (n = 84) or without (n = 84) history of motion sickness; undergoing gynaecological laparoscopic procedures including salpingo-oophorectomy, oophorectomy, salpingostomy, myomectomy, tubal ligation, and diagnostic laparoscopy

Excluded criteria: pregnant; obese (body mass index > 30 kg/m^2); current smoker; needing long-term steroid therapy; diagnosed with gastrointestinal, liver, or renal dysfunction; vestibular disease; preoperative vomiting; currently receiving antiemetic therapy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness, perioperative opioids): no; (history of PONV): unclear

Interventions	**Intervention characteristics** Dexamethasone (group MS+) • *Dose*: 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo (group MS+) • *Dose*: saline 2 ml • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone (group MS-) • *Dose*: 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo (group MS-) • *Dose*: saline 2 ml • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours, 0 to 6 hours)* • Outcome type: dichotomous outcome

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Lee 2003 *(Continued)*

Vomiting (6 to 12 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Yi Lee **Institution:** Department of Anesthesiology, Tzu-Chi Medical Center, Hualien, Taiwan, R.O.C **Email:** drleeyi@sinamail.com **Address:** Department of Anesthesiology, Tzu-Chi Medical Center, No. 707, Sec. 3, Chung-Yang Road, Hualien, Taiwan, R.O.C. **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	Four groups (participants with or without history of motion sickness) pooled into 2 groups for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients with or without motion sickness history (designated MS+ and MS- groups, respectively) were randomly assigned to one of two treatment regimens" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study medications (2 mL) were prepared by personnel blinded to the study protocols, and were administered intravenously immediately prior to the induction of anesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all data were collected by a team of trained nurse anesthetists blinded to the type of treatment received"

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Lee 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 168 patients enrolled, four were excluded from the analysis: two required further surgery (laparotomy) during the procedure and two were lost to follow-up"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "no additional opioid drugs were administered during the operation" Quote: "except for history of motion sickness, no significant differences were demonstrated between patient groups when comparing demographic data, duration of surgery, CO2 insufflation and anesthesia (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness, perioperative opioids): no; (history of PONV): unclear

Lee 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 57.4 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 58.3 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 35.14 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 240.8 • *Use of perioperative opioids (if yes, which?)*: fentanyl via epidural infusor • *Type of surgery*: subtotal gastrectomy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 54.8 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 59.7 ± 8

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Lee 2006 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 34.29
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 254.4
- *Use of perioperative opioids (if yes, which?)*: fentanyl via epidural infusor
- *Type of surgery*: subtotal gastrectomy

Included criteria: ASA I or II, diagnosed with cancer of the stomach, undergoing elective subtotal gastrectomy

Excluded criteria: recent use of opioids; any cutaneous pathology with pruritus; administration of antiemetic medication within 24 hours before surgery; history of motion sickness, convulsion, parkinsonism, or psychiatric problems; inability to answer questions

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: on surgical commencement of skin closure
- *Route of administration*: epidural
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg or ondansetron 4 mg IV

Droperidol

- *Dose*: 2.5 mg
- *Time point of administration*: on surgical commencement of skin closure
- *Route of administration*: epidural
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg or ondansetron 4 mg IV

Outcomes

Arrhythmia (0 to 48 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 48 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: South Korea

Setting: inpatient, single-centre

Author's name: Il Ok Lee

Institution: Korea University College of Medicine, Guro Hospital, Department of Anesthesiology, Seoul, South Korea

Email: iloklee@korea.ac.kr

Address: Department of Anesthesiology, Guro Hospital, Guro ku Gurodong gil 97 Korea University College of Medicine, Seoul, South Korea 152-703

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Lee 2006 *(Continued)*

Duration of study: March 2000 to October 2001

Language: English

Study's primary outcome: incidence of PONV and pruritus

Trial registry number: NA

Notes	Two out of 3 groups relevant (continuous infusion of droperidol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated to one of the following three groups (n 40 each) according to a random-number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "an independent pharmacist prepared three sets of 10 mL syringe and infusions (Infusor LV5; Baxter Healthcare Corp., USA) according to the Group A, B and C and these sets were kept concealed in numbered envelopes and all study personnel and participants were blinded to treatment assignment for the duration of the study" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all study personnel and participants were blinded to treatment assignment for the duration of the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the severity of pruritus, PONV, pain and sedation were evaluated by an anaesthesiologist who was blinded to the study treatments at 1, 6, 24 and 48 h postoperatively"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "twelve patients were excluded. An epidural catheter could not be placed in seven patients for technical reasons and patient discomfort preoperatively, therefore epidural analgesia was placed postoperatively. In three patients who have shown far advanced gastric cancer during operation, gastrojejunostomy was performed instead of a gastrectomy. There were missing data from two patients. Data from the remaining 108 patients were analysed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "all groups were demographically similar, and there were no differences in epidural levels or surgery duration (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Lee 2008a

Study characteristics

Methods	**Study design:** randomized controlled trial

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Lee 2008a *(Continued)*

Study grouping: 3 groups, monoprophylaxis, different routes of administration

Participants

Baseline characteristics

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 77
- *Age (mean ± SD, median (IQR), median (range))*: 47.4 ± 6.9
- *Weight (mean ± SD, median (IQR), median (range))*: 56.1 ± 6.5
- *BMI (mean ± SD, median (IQR), median (range))*: 22.8 ± 2.9
- *ASA I/II/III/IV (n)*: 11/66/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 250.9 ± 85
- *Use of perioperative opioids (if yes, which?)*: 652.3 ± 139.0 µg fentanyl-PCA 15 µg/h (mean ± SD in 24 hours)
- *Type of surgery*: partial/complete mastectomy with/without LN dissection

Ramosetron (0.1 mg IV group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 79
- *Age (mean ± SD, median (IQR), median (range))*: 46.1 ± 6.2
- *Weight (mean ± SD, median (IQR), median (range))*: 57.7 ± 8.9
- *BMI (mean ± SD, median (IQR), median (range))*: 23.0 ± 3.1
- *ASA I/II/III/IV (n)*: 16/63/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 277.1
- *Use of perioperative opioids (if yes, which?)*: 655.7 ± 99.8 µg fentanyl-PCA 15 µg/h (mean ± SD in 24 hours)
- *Type of surgery*: partial/complete mastectomy with/without LN dissection

Ramosetron (0.1 mg oral group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: 47.1 ± 8.6
- *Weight (mean ± SD, median (IQR), median (range))*: 57.8 ± 8.5
- *BMI (mean ± SD, median (IQR), median (range))*: 23.4 ± 3.7
- *ASA I/II/III/IV (n)*: 20/60/0/0

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Lee 2008a *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 255.1
- *Use of perioperative opioids (if yes, which?)*: 620.0 ± 97.6 µg fentanyl-PCA 15 µg/h (mean ± SD in 24 hours)
- *Type of surgery*: partial/complete mastectomy with/without LN dissection

Included criteria: women 24 to 60 years of age, ASA I or II, scheduled for elective breast cancer surgery

Excluded criteria: history of smoking, PONV, motion sickness, gastrointestinal disease, an antiemetic medication within 48 hours before surgery, pregnant

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

Interventions	**Intervention characteristics** Placebo • *Dose*: 0.9% normal saline 2 mL • *Time point of administration*: end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 50 µg/kg IV Ramosetron (0.1 mg IV group) • *Dose*: 0.1 mg mixed with 0.9% normal saline to a total 2 mL • *Time point of administration*: at completion of surgery but before recovery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 50 µg/kg IV Ramosetron (0.1 mg oral group) • *Dose*: 0.1 mg and 0.9% normal saline 2 mL • *Time point of administration*: 30 minutes before induction and saline at end of surgery • *Route of administration*: ramosetron PO and saline IV • *Rescue antiemetics (if yes, which?)*: ondansetron 50 µg/kg IV
Outcomes	*Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)*

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Lee 2008a *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** grant from Medical Research Institute, Pusan National University, Busan, Korea **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Jae-Young Kwon **Institution:** Department of Anesthesia and Pain Medicine, School of Medicine, Pusan National University **Email:** lhjksk@pusan.ac.kr **Address:** Pusan National University, 1-10, Ami-dong, Seo-gu, Busan, 602-739, Republic of Korea **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were assigned to three groups using computer-generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Quote: "patients were assigned to three groups using computer-generated random numbers inserted into sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: different routes of administration without sham treatment
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all episodes of nausea and vomiting were recorded by nurses who were blinded to the treatment assignment"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "two hundred and forty patients were enrolled. Four patients were excluded from the study because of the onset of intolerable dizziness (n 5 3) and headache (n 5 1)" Judgement comment: reasons for exclusion related to outcomes of interest (adverse events -> headache)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Lee 2008a *(Continued)*

Other bias	Low risk	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids, history of PONV/motion sickness): no

Lee 2008b

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 47 • *Age (mean ± SD, median (IQR), median (range))*: 46.4 ± 10.8 • *Weight (mean ± SD, median (IQR), median (range))*: 61.1 ± 10.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 206 • *Use of perioperative opioids (if yes, which?)*: 72.4 mL PCA volume (1.500 µg fentanyl) • *Type of surgery*: breast, gynaecological, orthopaedic, otolaryngological Ramosetron (group N) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 42.1 ± 10.7 • *Weight (mean ± SD, median (IQR), median (range))*: 58.7 ± 8.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 228 • *Use of perioperative opioids (if yes, which?)*: 72.9 mL PCA volume (1.500 µg fentanyl) • *Type of surgery*: breast, gynaecological, orthopaedic, otolaryngological **Included criteria:** ASA I or II, 18 to 65 years of age, undergoing elective surgery

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Lee 2008b *(Continued)*

	Excluded criteria: smoker, over 65 years of age, history of nausea and vomiting, experience of motion sickness **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): no; (gender): unclear
Interventions	**Intervention characteristics** Control (group C) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: (23.4%) ondansetron 50 µg/kg Ramosetron (group N) • *Dose*: 0.1 mg • *Time point of administration*: 30 minutes before induction • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: (8.2%) ondansetron 50 µg/kg
Outcomes	*Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by a grant from the Pusan National University Hospital **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Kim Hae-gyu **Institution:** Department of Anesthesiology and Pain Medicine, Pusan National University Hospital **Email:** hakykim@pusan.ac.kr **Address:** Amidong 1-ga, Seo-gu, Busan, Korea, Postal Code: 602-739 **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (continuous infusion of ondansetron)

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Lee 2008b *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly assigned". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no placebo intervention in the control group. No blinding of personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the evaluation is performed by the same observer, who does not know the patient's group" (translated)
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: quote: "three patients in group C and one patient in group N were excluded from the analysis because of severe nausea and vomiting and dissatisfaction with PCA during the study period" (translated). There is still 1 participant missing. The reason for exclusion is related to the outcome of interest (nausea and vomiting)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: quote: "there were no significant differences in the age, weight, height, type of surgery, VAS count, and PCA dose for 48 hours after surgery (Table 1)" (translated) Baseline characteristics (age, weight, ASA): no. Potential effect modifiers (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): no; (gender): unclear

Lee 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 42 • *Received treatment (n)*: NA • *Analysed (n)*: 42 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 10.4 • *Weight (mean ± SD, median (IQR), median (range))*: 61.3 ± 12.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Lee 2012 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 92.86
- *History of PONV/motion sickness (%)*: 7.14/ 19.05
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 158.8
- *Use of perioperative opioids (if yes, which?)*: 247.2 mg remifentanil intraoperative, postoperative fentanyl via PCA
- *Type of surgery*: gynaecological

Aprepitant + ramosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 42
- *Received treatment (n)*: NA
- *Analysed (n)*: 42
- *Age (mean ± SD, median (IQR), median (range))*: 43.8 ± 8.2
- *Weight (mean ± SD, median (IQR), median (range))*: 61.2 ± 8.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 95.24
- *History of PONV/motion sickness (%)*: 4.76/14.29
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 145.0 ± 62
- *Use of perioperative opioids (if yes, which?)*: 332.79 mg remifentanil intraoperative, postoperative fentanyl via PCA
- *Type of surgery*: gynaecological

Included criteria: women between 20 and 70 years of age, ASA I or II, scheduled to undergo gynaecological surgery with general anaesthesia and received IV PCA

Excluded criteria: refusal to participate in the research, history of drug abuse, hypersensitivity reaction, nausea, received antiemetics before surgery within 24 hours, pregnancy, breastfeeding, cancer, inadequate participation in clinical trials for other reasons

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Interventions

Intervention characteristics

Ramosetron

- *Dose*: 0.3 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 10 mg metoclopramide, 4 mg ondansetron additionally

Aprepitant + ramosetron

- *Dose*: aprepitant 80 mg, ramosetron 0.3 mg
- *Time point of administration*: aprepitant 2 to 3 hours before induction of anaesthesia, ramosetron after induction of anaesthesia
- *Route of administration*: aprepitant PO, ramosetron IV
- *Rescue antiemetics (if yes, which?)*: 10 mg metoclopramide, 4 mg ondansetron additionally

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Lee 2012 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Soon Im Kim **Institution:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Seoul Hospital, Seoul, Korea **Email:** soonnim@schmc.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Seoul Hospital, 22, Daesagwan-gil, Yongsan-gu, Seoul 140-887, Korea. Tel: 82-2-705-9294, Fax: 82-2-790-0394 **Duration of study:** 10 April to 30 November 2011 **Language:** English **Study's primary outcome:** PONV incidence **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to computer-based random number generation, patients were divided into an aprepitant group (n = 42) and a control group (n = 42)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	High risk	Judgement comment: open-label trial; no placebo intervention in the control group

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Lee 2012 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "in the recovery room, the anesthesiologist visited with each patient, being blinded to the conditions"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the patient's age, weight, surgery time, anesthesia time, past history of nausea, past history of PONV, smoking and amount of usage of remifentanil was recorded. There was no statistically significant difference between the two groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Lee 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group S) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 52.9 ± 7.0 • *Weight (mean ± SD, median (IQR), median (range))*: 55.7 ± 7.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 90 • *History of PONV/motion sickness (%)*: 0/30 • *Type of general anaesthesia*: TIVA (propofol, remifentanil), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 87.2 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil • *Type of surgery*: breast and thyroid cancer Palonosetron (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30

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Lee 2014 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 53.2 ± 9.2
- *Weight (mean ± SD, median (IQR), median (range))*: 57.3 ± 6.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 97
- *History of PONV/motion sickness (%)*: 0/26.7
- *Type of general anaesthesia*: TIVA (propofol, remifentanil), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 87.5
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil
- *Type of surgery*: breast and thyroid cancer

Included criteria: women aged 20 to 65 years, scheduled to undergo general anaesthesia for breast and thyroid cancer surgery, ASA I or II

Excluded criteria: history of severe cardiovascular or respiratory distress, morbid obesity, drug or alcohol abuse, history of adverse medication reactions and chronic pain, had received any antiemetics, sedatives, or analgesics within 24 hours before surgery, if we could not get intravenous access to the desired vein on the dorsum of the hand apart from the surgical field

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo (group S) • *Dose*: saline • *Time point of administration*: after venous occlusion at the forearm • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg or ondansetron 4 mg IV Palonosetron (group P) • *Dose*: 75 µg • *Time point of administration*: after venous occlusion at the forearm • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg or ondansetron 4 mg IV
Outcomes	*Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Ji Heui Lee **Institution:** Department of Anesthesiology and Pain Medicine, Korean Cancer Center Hospital, Seoul, Korea

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Lee 2014 *(Continued)*

Email: jiheui0255@naver.com

Address: Department of Anesthesiology and Pain Medicine, Korean Cancer Center Hospital, 75, Nowon-ro, Nowon-gu, Seoul 139-240, Korea

Duration of study: NA

Language: English

Study's primary outcome: reduction in pain scores

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated to one of two groups by the investigator using a sealed envelope system" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "using a sealed envelope system" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "all syringes of the pretreatment drugs were prepared by an anesthetic nurse under the supervision of the investigator" Judgement comment: no information on blinding of participants and anaesthesiologists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "12 and 24 hours after surgery, a blinded researcher assessed allergic reactions, edema, pain at the injection site, PONV, shivering, VAS, and the use of rescue antiemetics and analgesics" Quote: "a blinded nurse assessed the patients in the PACU"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all 60 patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the two groups with regard to age, body" Quote: "2014 palonosetron and injection pain weight, height, duration of surgery, and risk factors including history of PONV, motion sickness, non-smoking, and type of surgery (Table 1). The overall incidence of pain..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

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Lee D 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different routes of administration
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 110 • *Use of perioperative opioids (if yes, which?)*: 2.5 ng/mL to 3.5 ng/mL remifentanil intraoperative (target blood concentration, total amount of intraoperative remifentanil per group not reported), 2 patients received pethidine as rescue analgesia • *Type of surgery*: gynaecological laparoscopy Ramosetron (IV group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 111 • *Use of perioperative opioids (if yes, which?)*: 2.5 ng/mL to 3.5 ng/mL remifentanil intraoperative (target blood concentration, total amount of intraoperative remifentanil per group not reported), 3 patients received pethidine as rescue analgesia • *Type of surgery*: gynaecological laparoscopy Ramosetron (PO group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Lee D 2009 *(Continued)*

- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105
- *Use of perioperative opioids (if yes, which?)*: 2.5 ng/mL to 3.5 ng/mL remifentanil intraoperative (target blood concentration, total amount of intraoperative remifentanil per group not reported), 2 patients received pethidine as rescue analgesia
- *Type of surgery*: gynaecological laparoscopy

Included criteria: women, ASA I or II, 18 to 60 years of age, undergoing general anaesthesia for gynaecological laparoscopy

Excluded criteria: gastrointestinal disease, history of motion sickness, previous episode of PONV, menstruating, had taken an antiemetic medication within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: saline, placebo • *Time point of administration*: IV immediately after induction of anaesthesia, PO 1 hour before surgery • *Route of administration*: IV/PO • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV, dexamethasone 5 mg IV Ramosetron (IV group) • *Dose*: 0.3 mg • *Time point of administration*: ramosetron immediately after induction of anaesthesia, placebo 1 hour before surgery • *Route of administration*: IV (ramosetron)/PO • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV, dexamethasone 5 mg IV Ramosetron (PO group) • *Dose*: 0.1 mg • *Time point of administration*: ramosetron 1 hour before surgery, placebo immediately after induction of anaesthesia • *Route of administration*: PO (ramosetron)/IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 4 mg IV, dexamethasone 5 mg IV
Outcomes	*Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)*

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Lee D 2009 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this study was supported by Gil Medical Center, Incheon, Korea **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** H.J. Kwak **Institution:** Department of Anesthesiology and Pain Medicine, Gil Medical Center **Email:** NA **Address:** Gachon University of Medicine and Science, 1198 Guwol-dong, Namdong-gu, Incheon 405-760, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of complete response (no nausea, no retching, no vomiting) **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "effects on postoperative nausea 47 0.3 mg IV ramosetron (IV group), or 0.1 mg oral ramosetron (PO group), using a sealed envelope system. An independent researcher prepared..." Quote: "patients were allocated randomly to one of three groups (n = 40 in each), to receive saline (control group)" Judgement comment: insufficient information on random sequence generation (shuffling envelopes?)
Allocation concealment (selection bias)	Unclear risk	Quote: "...using a sealed envelope system. An independent researcher prepared the study solutions, which consisted of a drinking cup containing 10 ml saline and a syringe with 2 ml normal saline in the control group, a cup containing 10 ml saline and a syringe with 0.3 mg ramosetron in the IV group, and a cup containing completely dissolved ramosetron tablets in 10 ml saline and a syringe with 2 ml saline in the PO group. The oral test drug..." Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the oral test drug was administered 1 hour before surgery and the IV test drug was injected immediately after the induction of anaesthesia by an investigator who was blinded to the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all episodes of PONV (nausea, retching, and vomiting) during the periods 0 to 1 hour and 1 to 24 hours after anaesthesia were recorded by nursing staff who were unaware of which treatment each patient had been given"
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Lee D 2009 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no differences in patient characteristics among the three groups (Table 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Lee DC 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 65 • *Received treatment (n)*: NA • *Analysed (n)*: 65 • *Age (mean ± SD, median (IQR), median (range))*: 47.7 ± 9.8 • *Weight (mean ± SD, median (IQR), median (range))*: 61.7 ± 9.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 9/22 • *Type of general anaesthesia*: TIVA (propofol, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 240 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 624.2 µg fentanyl via PCA • *Type of surgery*: total thyroidectomy Ramosetron (group R) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 65 • *Received treatment (n)*: NA • *Analysed (n)*: 65 • *Age (mean ± SD, median (IQR), median (range))*: 46.4 ± 9.2 • *Weight (mean ± SD, median (IQR), median (range))*: 60.4 ± 8.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100

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Lee DC 2011 *(Continued)*

- *History of PONV/motion sickness (%)*: 12/22
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 240
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 601.7 µg fentanyl via PCA
- *Type of surgery*: total thyroidectomy

Included criteria: female, 18 to 65 years of age, scheduled for total thyroidectomy, non-smoking status, anticipated to require postoperative opioids

Excluded criteria: severe bowel motility impairment, insulin-dependent diabetes mellitus, pregnancy, breastfeeding, administration of an antiemetic before surgery, systemic treatment with steroids before surgery, history of cardiovascular or respiratory disease, impaired renal and/or hepatic function

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions

Intervention characteristics

Control (group C)

- *Dose*: saline
- *Time point of administration*: 20 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ramosetron (group R)

- *Dose*: 0.3 mg
- *Time point of administration*: 20 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Outcomes

Vomiting (0 to 6 hours)

- Outcome type: dichotomous outcome

Vomiting (6 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 48 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 48 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Korea

Setting: inpatient, single-centre

Author's name: Ji Yeon Lee

Institution: Department of Anesthesiology and Pain Medicine, Gachon University of Medicine and Science, Incheon, Korea

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Lee DC 2011 *(Continued)*

	Email: easy95@gilhospital.com **Address:** Department of Anesthesiology and Pain Medicine, Gachon University of Medicine and Science, 1198, Guwol-dong, Namdong-gu, Incheon 405-220, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of complete response (no nausea, no retching, no vomiting) **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated to either a control group (n = 65) or a ramosetron group (n = 65) using a computerized generated randomization table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "injected drugs were prepared in identical syringes by personnel not otherwise involved in this study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "these variables were assessed by investigators unaware of the group identities"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients' characteristics, including a history of PONV and/or motion sickness, and operative data were similar in both groups (Table 1), as were the expected risks for PONV using the Apfel scoring system [13]" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Lee HS 2004

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, monoprophylaxis and combination prophylaxis, dose-finding study

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Lee HS 2004 *(Continued)*

Participants

Baseline characteristics

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 44.6 ± 8.5
- *Weight (mean ± SD, median (IQR), median (range))*: 59.9 ± 10.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0/36
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 111.2
- *Use of perioperative opioids (if yes, which?)*: sufentanil (IV-PCA)
- *Type of surgery*: gynaecological

Dexamethasone (D4 group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 41.1 ± 10.8
- *Weight (mean ± SD, median (IQR), median (range))*: 60.7 ± 7.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 84
- *History of PONV/motion sickness (%)*: 8/32
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 117.6
- *Use of perioperative opioids (if yes, which?)*: sufentanil (IV-PCA)
- *Type of surgery*: gynaecological

Dexamethasone (D8 group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 40.3 ± 10.6
- *Weight (mean ± SD, median (IQR), median (range))*: 58.4 ± 8.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 96
- *History of PONV/motion sickness (%)*: 0/36

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Lee HS 2004 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 112.4
- *Use of perioperative opioids (if yes, which?)*: sufentanil (IV-PCA)
- *Type of surgery*: gynaecological

Ondansetron (O4 group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 38.6 ± 9.4
- *Weight (mean ± SD, median (IQR), median (range))*: 61.1 ± 9.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 88
- *History of PONV/motion sickness (%)*: 4/36
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 113.8
- *Use of perioperative opioids (if yes, which?)*: sufentanil (IV-PCA)
- *Type of surgery*: gynaecological

Ondansetron (O8 group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 42.3 ± 7.5
- *Weight (mean ± SD, median (IQR), median (range))*: 60.9 ± 11.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 84
- *History of PONV/motion sickness (%)*: 4/16
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 141.0
- *Use of perioperative opioids (if yes, which?)*: sufentanil (IV-PCA)
- *Type of surgery*: gynaecological

Dexamethasone + ondansetron (D4O4 group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 42.0 ± 9.9
- *Weight (mean ± SD, median (IQR), median (range))*: 58.1 ± 7.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0

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Lee HS 2004 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: 92
- *History of PONV/motion sickness (%)*: 8/20
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138.4
- *Use of perioperative opioids (if yes, which?)*: sufentanil (IV-PCA)
- *Type of surgery*: gynaecological

Included criteria: 45 to 81 kg, 19 to 62 years of age, ASA I and II, scheduled for gynaecological surgery and pain management after surgery

Excluded criteria: history of substance abuse, hypersensitivity to any drug used in this study, vomiting within 24 hours before surgery, taking medication, pregnant women, patients with renal or liver disease

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids, non-smoker, history of PONV/motion sickness): no; (duration of anaesthesia): yes

Interventions

Intervention characteristics

Control

- *Dose*: saline
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone (D4 group)

- *Dose*: 4 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone (D8 group)

- *Dose*: 8 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron (O4 group)

- *Dose*: 4 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron (O8 group)

- *Dose*: 8 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone + ondansetron (D4O4 group)

- *Dose*: dexamethasone 4 mg, ondansetron 4 mg
- *Time point of administration*: after induction of anaesthesia
- *Route of administration*: IV

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Lee HS 2004 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 12 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Hye Jin Park **Institution:** Department of Anesthesiology and Pain Medicine, College of Medicine, Inha University, Incheon, Korea **Email:** anesthjin@hanmail.net **Address:** 7-206 Shinheung-dong, Jung-gu, Incheon, Korea Department of Anesthesiology, Inha University Hospital, Postal Code: 400-711 **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "one designated anaesthesiologist who does not know the patient's group observed 2 hours, 2-12 hours, 12-24, 24-48 hours after surgery..." (translated)

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Lee HS 2004 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids, non-smoker, history of PONV/motion sickness): no; (duration of anaesthesia): yes

Lee IH 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 57 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 47.22 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 246 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, postoperatively via PCA • *Type of surgery*: surgical resection for colorectal cancer Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 34 • *Age (mean ± SD, median (IQR), median (range))*: 55 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 47.06 • *Non-smoker (%)*: NA

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Lee IH 2007 *(Continued)*

- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 250
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, postoperatively via PCA
- *Type of surgery*: surgical resection for colorectal cancer

Included criteria: ASA I and II, underwent surgical resection for colorectal cancer under general anaesthesia combined with epidural anaesthesia

Excluded criteria: recent use of opioids; any cutaneous pathology with pruritus; administration of antiemetic medication within 24 hours before surgery; history of motion sickness, convulsion, parkinsonism, or psychiatric problems; inability to answer questions; could not tolerate the preoperative epidural procedure because of pain or discomfort; epidural failure; dural puncture

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: placebo • *Time point of administration*: at skin closure • *Route of administration*: epidural • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg or ondansetron 4 mg IV Droperidol • *Dose*: 2.5 mg • *Time point of administration*: at skin closure • *Route of administration*: epidural • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg or ondansetron 4 mg IV
Outcomes	*Arrhythmia (0 to 48 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Il Ok Lee **Institution:** Department of Anesthesiology, Cheil General Hospital, and Women's Healthcare Center, Kwandong University College of Medicine, Seoul, Korea; and Department of Anesthesiology, Korea University College of Medicine, Seoul, Korea. **Email:** iloklee@korea.ac.kr **Address:** Department of Anesthesiology, Guro Hospital, Guro gu Gurodonggil 97, Korea University College of Medicine, Seoul, South Korea

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Lee IH 2007 *(Continued)*

	Duration of study: June 2000 to October 2001 **Language:** English **Study's primary outcome:** incidence of pruritus **Trial registry number:** NA
Notes	Two out of 4 groups relevant (continuous infusion of droperidol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a random-number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "an independent pharmacist prepared four sets of 10 mL syringes and infusions (Infusor LV5; Baxter Healthcare, USA) for Groups A, B, C, and D. These sets were kept concealed in numbered envelopes" Judgement comment: not stated; "sequentially numbered, opaque. and sealed envelopes" (SNOSE). Syringes and infusions are not stated as identical
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the participants and researchers were blinded as to group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the severity of pruritus, PONV, pain, and sedation were evaluated at 1, 6, 24,and 48 hours postoperatively by an anaesthesiologist who was blinded to the study treatments"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "eighteen patients were excluded from the study. An epidural catheter could not be placed in eight patients because of technical reasons and preoperative patient discomfort; therefore, an epidural catheter was placed postoperatively. Five patients were excluded because of epidural failure (catheter dislocation in two patients and dural puncture in three patients). There were missing data from five patients. The data from the remaining 142 patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "all the groups were demographically similar, and there were no differences in the epidural levels or the duration of surgery (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Lee JW 2011

Study characteristics

Methods	**Study design:** randomized controlled trial

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Lee JW 2011 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 45.0 ± 5.5 • *Weight (mean ± SD, median (IQR), median (range))*: 58.3 ± 7.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 27 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 111.2 • *Use of perioperative opioids (if yes, which?)*: end of surgery fentanyl 50 µg IV, PCA fentanyl 800 µg • *Type of surgery*: abdominal hysterectomy Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 46.0 ± 6.8 • *Weight (mean ± SD, median (IQR), median (range))*: 60.3 ± 7.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 20 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 121.0 • *Use of perioperative opioids (if yes, which?)*: end of surgery fentanyl 50 µg IV, PCA fentanyl 800 µg • *Type of surgery*: abdominal hysterectomy **Included criteria:** healthy women, ASA I or II, undergoing abdominal hysterectomy, 18 to 60 years of age, PONV risk factors (i.e. non-smokers, use of opioid-based PCA) **Excluded criteria:** history of allergy to any study medication, gastrointestinal disease, Insulin dependent diabetes mellitus, administration of antiemetics or steroids 24 hours before surgery, active pregnancy, major cardiac or neurological disease, impaired hepatic/renal function **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoke, history of PONV/motion sickness): no; (perioperative opioids): unclear
Interventions	**Intervention characteristics** Ramosetron • *Dose*: 0.3 mg

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Lee JW 2011 *(Continued)*

	• *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 18.3% (metoclopramide) Ondansetron • *Dose*: 4 mg • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 15.0% (metoclopramide)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 2 hours, 2 to 24 hours, 24 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** HyeJin Park **Institution:** Department of Anesthesiology and Pain Medicine, Eulji General Hospital, College of Medicine Eulji University, Seoul, Korea **Email:** anesthjin@hanmail.net **Address:** Department of Anesthesiology and Pain Medicine, Eulji General Hospital, College of Medicine Eulji University, Hagye-dong, Nowon-gu, Seoul 139-711, Korea **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response (no PONV and no requirement for another rescue medication)
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "by a computerized randomization table"

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Lee JW 2011 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "injected drugs were prepared in identically shaped syringes by personnel not involved in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all episodes of PONV were recorded through direct questioning by one anaesthesiologist blinded to the study group or by complaints from patients during the 3 interval study periods within the first 48 hours after anaesthesia: 0-2 h, 2-24 h and 24-48 h"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences in the demographic data (Table 1). Additional inclusion criteria included patients aged 18 to 60 years having PONV risk factors (i.e. non-smokers, use of opioid-based PCA)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoke, history of PONV/motion sickness): no; (perioperative opioids): unclear

Lee MJ 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Control (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 52.4 ± 8.3 • *Weight (mean ± SD, median (IQR), median (range))*: 60.1 ± 4.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 86.11 • *Non-smoker (%)*: 92 • *History of PONV/motion sickness (%)*: 11/0 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 140.2 • *Use of perioperative opioids (if yes, which?)*: remifentanil

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Lee MJ 2015 *(Continued)*

- *Type of surgery*: thyroid surgery

Ramosetron (group R)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 36
- *Received treatment (n)*: NA
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 53.0 ± 8.2
- *Weight (mean ± SD, median (IQR), median (range))*: 58.84 ± 6.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 88.89
- *Non-smoker (%)*: 94
- *History of PONV/motion sickness (%)*: 8/0
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 143.5
- *Use of perioperative opioids (if yes, which?)*: remifentanil
- *Type of surgery*: thyroid

Ramosetron + dexamethasone (group RD)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 36
- *Received treatment (n)*: NA
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 54.3 ± 7.7
- *Weight (mean ± SD, median (IQR), median (range))*: 60.5 ± 5.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 83.33
- *Non-smoker (%)*: 94
- *History of PONV/motion sickness (%)*: 11/0
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 141.5
- *Use of perioperative opioids (if yes, which?)*: remifentanil
- *Type of surgery*: thyroid

Included criteria: elective thyroid surgery, between 20 and 65 years of age, ASA I or II

Excluded criteria: history of allergy to any drugs used in the study, gastrointestinal disease, motion sickness, diabetes mellitus, obesity (body mass index ≥ 35 kg/m^2), renal or hepatic functional impairment, pregnancy, menstruation, use of antiemetic drugs or a systemic steroid 24 hours before surgery, chronic pain disorder

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV): no; (history of motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control (group C) • *Dose*: NaCl • *Time point of administration*: immediately after induction of anaesthesia

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Lee MJ 2015 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ramosetron (group R)

- *Dose*: 0.3
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ramosetron + dexamethasone (group RD)

- *Dose*: ramosetron 0.3 mg, dexamethasone 5 mg
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Outcomes	*Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, NA **Author's name:** Cheol Lee **Institution:** Department of Anesthesiology and Pain Medicine, Wonkwang University College of Medicine, Iksan, Korea **Email:** ironyii@wku.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Wonkwang University College of Medicine, 344-2, Sinyong-dong, Iksan 570-711, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of nausea, vomiting, and rescue antiemetic drug use within 48 hours postoperatively **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly (envelope randomization) allocated to three groups"

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Lee MJ 2015 *(Continued)*

		Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "(envelope randomization)" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "all patients, investigators collecting the postoperative data, and nurses involved in the post-operative care of patients were blinded to the randomization" Judgement comment: no information on blinding of anaesthesiologists provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "investigators collecting the postoperative data, and nurses involved in the post-operative care of patients were blinded to the randomization"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patient characteristics including the history of PONV, tympanic temperature, as well as operative data were similar among the groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV): no; (history of motion sickness, perioperative opioids): unclear

Lee SY 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 28 • *Received treatment (n)*: NA • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 44.9 ± 10.9 • *Weight (mean ± SD, median (IQR), median (range))*: 61.4 ± 8.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 82.14 • *Non-smoker (%)*: NA

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Lee SY 2001 *(Continued)*

- *History of PONV/motion sickness (%)*: 17.86/17.86
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 156.7
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: thyroidectomy

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 23
- *Received treatment (n)*: NA
- *Analysed (n)*: 23
- *Age (mean ± SD, median (IQR), median (range))*: 38.2 ± 9.1
- *Weight (mean ± SD, median (IQR), median (range))*: 59.6 ± 10.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 91.30
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 8.70/13.04
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 170.7
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: thyroidectomy

Tropisetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 17
- *Received treatment (n)*: NA
- *Analysed (n)*: 17
- *Age (mean ± SD, median (IQR), median (range))*: 34.1 ± 9.8
- *Weight (mean ± SD, median (IQR), median (range))*: 58.7 ± 7.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 94.12
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/11.76
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 176.2
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: thyroidectomy

Included criteria: ASA I or II, 18 to 65 years of age, undergoing thyroidectomy

Excluded criteria: abdominal organ disease, more than 50% of normal body weight, vomiting within 24 hours before surgery, taking antiemetics, and non-normal thyroid function are excluded

Pretreatment: baseline characteristics (weight): no; (ASA): unclear; (age): yes > 20% difference. Potential effect modifiers (gender, duration of anaesthesia): no; (non-smoker, perioperative opioids): unclear; (history of PONV/motion sickness): yes > 20% difference

Interventions	**Intervention characteristics**
	Control

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Lee SY 2001 *(Continued)*

- *Dose*: saline
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Tropisetron

- *Dose*: 30 µg/kg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Tropisetron + dexamethasone

- *Dose*: tropisetron 30 µg/kg, dexamethasone 5 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Outcomes

Vomiting or retching (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Korea

Setting: inpatient, single-centre

Author's name: Sook-Young Lee

Institution: Department of Anesthesiology, Ajou University School of Medicine, Suwon, Korea

Email: anesylee@madang.ajou.ac.kr

Address: Department of Anesthesiology, Ajou University School of Medicine, Suwon, Korea 5, Won-cheon-dong, Paldal-gu, Gyeonggi-do, Korea, Postal Code: 442-721

Duration of study: June 1998 to February 2000

Language: Korean (Google translated)

Study's primary outcome: NA

Trial registry number: NA

Notes

None

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Lee SY 2001 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided". Insufficient information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (weight, ASA): no; (age): yes > 20% difference. Potential effect modifiers (gender, duration of anaesthesia): no; (non-smoker, perioperative opioids): unclear; (history of PONV/motion sickness): yes > 20% difference

Lee SY 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: 41 • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 42.22 ± 11.34 • *Weight (mean ± SD, median (IQR), median (range))*: 59.59 ± 8.14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 93 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 9.8/26.8

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Lee SY 2002 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 177.32
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 36
- *Received treatment (n)*: 36
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 37.70 ± 9.96
- *Weight (mean ± SD, median (IQR), median (range))*: 60.31 ± 7.82
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 94
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 2.8/16.7
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 168.47
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Ramosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 36
- *Received treatment (n)*: 36
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 38.61 ± 9.50
- *Weight (mean ± SD, median (IQR), median (range))*: 58.25 ± 7.32
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 89
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/30.6
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 173.75
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: thyroidectomy

Included criteria: ASA I or II, 18 to 65 years of age, undergoing general anaesthesia for elective thyroidectomy

Excluded criteria: > 50% over ideal body weight, gastrointestinal disease, had taken antiemetics within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo

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Lee SY 2002 *(Continued)*

- *Dose*: 0.9% NaCl
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 31.7% (metoclopramide 10 mg)

Granisetron

- *Dose*: 20 µg/kg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 11.1% (metoclopramide 10 mg)

Ramosetron

- *Dose*: 4 µg/kg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 19.4% (metoclopramide 10 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Sook-Young Lee **Institution:** Ajou UniversitySchool of Medicine, 5 Wonchon Dong, Paldal Gu,Suwon, Korea **Email:** anesylee@hotmail.com **Address:** Department of Anesthesiology, Ajou UniversitySchool of Medicine, 5 Wonchon Dong, Paldal Gu,Suwon, Korea **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

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Lee SY 2002 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated to receive placebo (0.9% NaCl), granisetron 20 µg/kg or ramosetron 4 µg/kg i.v." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "specially trained nurses performed the questioning, and they were blinded to study groups"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Lee WS 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: 35 • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 51.5 ± 16.3 • *Weight (mean ± SD, median (IQR), median (range))*: 60.1 ± 4.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 23/12/0/0 • *Gender (female in %)*: 100

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Lee WS 2015 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: combined anaesthesia (propofol + remifentanil + sevoflurane + N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 128.1
- *Use of perioperative opioids (if yes, which?)*: induction and maintenance of anaesthesia with remifentanil
- *Type of surgery*: laparoscopic hysterectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: 35
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 52.5 ± 15.7
- *Weight (mean ± SD, median (IQR), median (range))*: 59.3 ± 5.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/11/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: combined anaesthesia (propofol + remifentanil + sevoflurane + N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 123.5
- *Use of perioperative opioids (if yes, which?)*: induction and maintenance of anaesthesia with remifentanil
- *Type of surgery*: laparoscopic hysterectomy

Ramosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: 35
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 48.2 ± 12.1
- *Weight (mean ± SD, median (IQR), median (range))*: 56.3 ± 4.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 26/9/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: combined anaesthesia (propofol + remifentanil + sevoflurane + N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.1
- *Use of perioperative opioids (if yes, which?)*: induction and maintenance of anaesthesia with remifentanil
- *Type of surgery*: laparoscopic hysterectomy

Included criteria: healthy female undergoing laparoscopic hysterectomy under general anaesthesia

Excluded criteria: allergy to any of the experimental drugs, opioid dependence, history of PONV and motion sickness, use of antiemetic medication within 24 hours before surgery, pregnancy, inability to use patient-controlled analgesia (PCA) IV device or to comprehend 10 cm visual analogue scale (VAS; 0, none; 10, maximum) for pain and nausea assessment, unwillingness to be enrolled in the study

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Lee WS 2015 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: at the end of surgery, before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Granisetron • *Dose*: 3 mg • *Time point of administration*: at the end of surgery, before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: at the end of surgery, before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** CKDpharm **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Won-Suk Lee **Institution:** Department of Anesthesiology Surgery, Gil Medical Center, Gachon University, School of Medicine, Incheon, South Korea **Email:** gachonlws@gmail.com **Address:** Department of Anesthesiology Surgery, Gil Medical Center, Gachon University, School of Medicine, Incheon, South Korea **Duration of study:** November 2011 to June 2013 **Language:** English **Study's primary outcome:** incidence of complete responders during the study period **Trial registry number:** NCT01752374

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Lee WS 2015 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "this investigator-initiated, prospective, non-blinded, randomized controlled trial"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "the incidence of nausea and vomiting was recorded during the assessment periods by ward nursing staff not blinded to the treatment drugs"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01752374 (retrospective registration)
Other bias	Unclear risk	Quote: "the groups were comparable with respect to age, weight, duration of surgery, and ASA score" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Lee Y 2001

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo (group S) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0

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Lee Y 2001 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 182
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction
- *Type of surgery*: thyroidectomy

Dexamethasone (group D5)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: 45
- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 179
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction
- *Type of surgery*: thyroidectomy

Dexamethasone (group D8)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: 45
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 187
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction
- *Type of surgery*: thyroidectomy

Included criteria: women, ASA I or II, scheduled for thyroidectomy

Excluded criteria: history of gastrointestinal disease, motion sickness, received antiemetic medication within 24 hours before surgery, obese BMI > 25 kg/m^2, smoking ≥ 5 cigarettes per day, previously sustained difficult intubation during induction of anaesthesia

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

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Lee Y 2001 *(Continued)*

Interventions	**Intervention characteristics** Placebo (group S) • *Dose*: saline • *Time point of administration*: right before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 64% (droperidol 1.25 mg IV) Dexamethasone (group D5) • *Dose*: 5 mg • *Time point of administration*: right before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 33% (droperidol 1.25 mg IV) Dexamethasone (group D8) • *Dose*: 8 mg • *Time point of administration*: right before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 12% (droperidol 1.25 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (during stay in hospital)* • Outcome type: dichotomous outcome *Postoperative wound infection (during stay in hospital)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Yi Lee **Institution:** Department of Anesthesiology, Buddhist Tzu Chi General Hospital, Taiwan

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Lee Y 2001 *(Continued)*

Email: drleeyi@sinamail.com

Address: Department of Anesthesiology. Buddhist Tzu Chi General Hospital. No 707. Section 3, Chung Yang Road. Hualien. Taiwan. R.O.C.

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "computer generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the study drugs (4 ml) prepared by personnel blinded to the study were administered intervenously right before induction of anaesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "were recorded by a nurse anaesthetist or one of the investigators without the knowledge of which treatment the patients had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "two patients in group D8 suffered from difficult intubation and were deleted from the study. One patient in Group S sustained re-operation because of postoperative bleeding"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

Lee Y 2002

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: -

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Lee Y 2002 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 42.3 (28 to 67)
- *Weight (mean ± SD, median (IQR), median (range))*: 65 (52 to 90)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 131
- *Use of perioperative opioids (if yes, which?)*: 43 (25 to 77) mg morphine, fentanyl (2 µg/kg) for induction
- *Type of surgery*: total hip/knee replacement, corrective spinal surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 44
- *Age (mean ± SD, median (IQR), median (range))*: 44.6 (32 to 69)
- *Weight (mean ± SD, median (IQR), median (range))*: 67 (54 to 84)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 0
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 127
- *Use of perioperative opioids (if yes, which?)*: 40 (26 to 72) mg morphine, fentanyl (2 µg/kg) for induction
- *Type of surgery*: total hip/knee replacement, corrective spinal surgery

Included criteria: female, ASA I or II, 28 to 69 years of age, major orthopaedic procedures

Excluded criteria: history of gastrointestinal, liver, or renal disease; received any antiemetic medication in the 24 hours before surgery or complained of preoperative nausea or vomiting; obesity (body mass index > 30 kg/m^2); smoked ≥ 5 cigarettes per day; difficult intubation during induction of anaesthesia

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 37% (metoclopramide 10 mg) Placebo • *Dose*: 2 mL saline

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Lee Y 2002 *(Continued)*

- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 50% (metoclopramide 10 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Y. Lee **Institution:** Tzu-Chi Medical Center **Email:** drleeyi@sinamail.com **Address:** Tzu-Chi Medical Center, Tzu-Chi University School of Medicine, no. 707, Sec 3, Chung-Yang Road, Hualien, Taiwan, ROC **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated by means of computer-generated numbers to one of two treatment regimens"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Lee Y 2002 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study medications (2 ml), prepared by personnel blinded to the study, were administered intravenously immediately before induction of anaesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "for the first 24 hours after anaesthesia, the presence or absence of nausea and vomiting was recorded by a trained nurse anaesthetist blinded to which treatment the patients had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "of the 90 patients enrolled in the study, three were excluded from analysis, one required a further operation 24 hours after spinal surgery because of continuous postoperative bleeding and two were not followed up adequately. Therefore, 87 recruited patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Lee Y 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Dexamethasone (12 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 51 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: 51.4 ± 7.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 92.1 • *History of PONV/motion sickness (%)*: 23.7/47.4 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 143 • *Use of perioperative opioids (if yes, which?)*: 37.3 mg morphine postoperative, fentanyl 2 µg/kg for induction • *Type of surgery*: major orthopaedic (total hip or knee replacement, corrective spinal procedures), general (laparotomy), gynaecological (abdominal total hysterectomy, myomectomy) Dexamethasone (8 mg group)

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Lee Y 2004 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 54 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 52.5 ± 6.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 94.4
- *History of PONV/motion sickness (%)*: 19.4/44.4
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138
- *Use of perioperative opioids (if yes, which?)*: 38.6 mg morphine postoperative, fentanyl 2 µg/kg for induction
- *Type of surgery*: major orthopaedic (total hip or knee replacement, corrective spinal procedures), general (laparotomy), gynaecological surgery (abdominal total hysterectomy, myomectomy)

Dexamethasone (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 55 ± 16
- *Weight (mean ± SD, median (IQR), median (range))*: 52.8 ± 7.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 92.1
- *History of PONV/motion sickness (%)*: 15.8/50.0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 148
- *Use of perioperative opioids (if yes, which?)*: 35.8 mg morphine postoperative, fentanyl 2 µg/kg for induction
- *Type of surgery*: major orthopaedic (total hip or knee replacement, corrective spinal procedures), general (laparotomy), gynaecological surgery (abdominal total hysterectomy, myomectomy)

Dexamethasone (2 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 53.2 ± 7.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 88.4
- *History of PONV/motion sickness (%)*: 25.0/55.6

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Lee Y 2004 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 150
- *Use of perioperative opioids (if yes, which?)*: 32.4 mg morphine postoperative, fentanyl 2 µg/kg for induction
- *Type of surgery*: major orthopaedic (total hip or knee replacement, corrective spinal procedures), general (laparotomy), gynaecological surgery (abdominal total hysterectomy, myomectomy)

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 52 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 53.6 ± 7.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 88.6
- *History of PONV/motion sickness (%)*: 22.9/42.9
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 135
- *Use of perioperative opioids (if yes, which?)*: 31.2 mg morphine postoperative, fentanyl 2 µg/kg for induction
- *Type of surgery*: major orthopaedic (total hip or knee replacement, corrective spinal procedures), general (laparotomy), gynaecological surgery (abdominal total hysterectomy, myomectomy)

Included criteria: ASA I or II; female; scheduled for major orthopaedic (total hip or knee replacement or corrective spinal procedures), general (laparotomy), or gynaecological surgery (abdominal total hysterectomy, myomectomy) under general anaesthesia

Excluded criteria: had received any antiemetic medications in the 24 hours before surgery, complained of preoperative nausea or vomiting, history of immunosuppression, significant gastric reflux, peptic ulcer disease, diabetes mellitus, recent tuberculosis, Cushing's syndrome, liver/renal disease, intubation during induction of anaesthesia was difficult

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dexamethasone (12 mg group) • *Dose*: 12 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 13.2% (metoclopramide 10 mg IV) Dexamethasone (8 mg group) • *Dose*: 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16.7% (metoclopramide 10 mg IV) Dexamethasone (4 mg group)

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Lee Y 2004 *(Continued)*

- *Dose*: 4 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 31.6% (metoclopramide 10 mg IV)

Dexamethasone (2 mg group)

- *Dose*: 2 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 47.2% (metoclopramide 10 mg IV)

Placebo

- *Dose*: 0.9% saline
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 45.7% (metoclopramide 10 mg IV)

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (0 to 2 hours)

- Outcome type: dichotomous outcome

Vomiting (2 to 12 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Taiwan

Setting: inpatient, single-centre

Author's name: Yi Lee

Institution: Department of Anesthesiology, Tzu-Chi Medical Cen- ter, Tzu-Chi University School of Medicine, no. 707, Sec 3, Chung-Yang Road, Hualien, Taiwan, ROC

Email: drleeyi@sinamail.com

Address: Department of Anesthesiology, Tzu-Chi Medical Center, Tzu-Chi University School of Medicine, no. 707, Sec 3, Chung-Yang Road, Hualien, Taiwan, ROC

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

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Lee Y 2004 *(Continued)*

	Trial registry number: NA
Notes	Five out of 6 groups relevant (continuous infusion of droperidol via PCA)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all patients were blinded to the nature of the drug administered. The study medication preparations were performed by a specially trained nurse-anaesthetist who was not involved in any subsequent assessments"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...recorded by specially trained nurse anaesthetists who were blinded as to the treatment groups"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 240 patients were recruited. Among these patients, 20 were later withdrawn for comparisons for the following reasons: 2 patients in the droperidol group experienced excessive drowsiness and PCA had to be discontinued; 2 patients underwent further surgery within 24 h; 6 patients had difficult intubation; and 10 patients had inadequate follow-up. The remaining 220 patients completed this study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "patient characteristics, surgical types, duration of anaesthesia, and numbers of risk factors for PONV (12), including prior PONV, motion sickness, and nonsmokers, were similar in the 6 groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Lee Y 2007

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Haloperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA

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Lee Y 2007 *(Continued)*

- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 19/47
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 154
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction 2 µg/kg
- *Type of surgery*: gynaecological, urologic, thyroid, breast, or plastic surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: NA
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 23/40
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction 2 µg/kg
- *Type of surgery*: gynaecological, urologic, thyroid, breast, or plastic surgery

Included criteria: ASA I and II; non-smoking female scheduled for gynaecological, urologic, thyroid, breast, or plastic surgery

Excluded criteria: obvious airway problems; obesity (body mass index > 25 kg/m^2); pregnant; had a chronic cough, psychiatric illness, or clinically significant major organ disease; had consumed an antiemetic medication within 24 hours before commencement of the study

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Haloperidol

- *Dose*: 2 mg
- *Time point of administration*: approximately 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 23% (metoclopramide 25 mg IV)

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: approximately 30 minutes before end of surgery
- *Route of administration*: IV

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Lee Y 2007 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: 19% (metoclopramide 25 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Arrhythmia (10 minutes after administration of study medication)* • Outcome type: dichotomous outcome *QT prolongation (10 minutes after administration of study medication)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Jhi-Joung Wang **Institution:** Department of Anesthesiology and Department of Medical Research, Chi- Mei Medical Center, Tainan County, Taiwan **Email:** jjw400002@hotmail.com **Address:** Chi- Mei Medical Center, Tainan County, Taiwan, No. 901, Chung- Hwa Road, Yung- Kang City, Tainan county, Taiwan **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None
Risk of bias	

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Lee Y 2007 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "syringes by personnel blinded to the study protocol, and were administered in a double-blind fashion"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "were recorded by a trained investigator without knowledge of which treatment the patients had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "ninety patients were screened, and of the 90 patients enrolled in the study, four were later withdrawn for incomplete data collection. The remaining 86 completed the protocol"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "patient characteristics, duration of anaesthesia, surgical types, the risk factors for PONV, 11 estimated risk of PONV 12 and postoperative pain scores (VAS) at the three different time intervals were similar in the two groups (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Lee YC 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Hartmann's solution (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 50.5 ± 10.5 • *Weight (mean ± SD, median (IQR), median (range))*: 61.1 ± 9.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: 66.67

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Lee YC 2009 *(Continued)*

- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 60.2
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl intraoperative, 0.5 mg/kg meperidine as rescue analgesia
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron (group 3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 49.2 ± 8.5
- *Weight (mean ± SD, median (IQR), median (range))*: 62.0 ± 9.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: 63.33
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 59.8
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl intraoperative, 0.5 mg/kg meperidine as rescue analgesia
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, presented for laparoscopic cholecystectomy, 19 to 60 years of age

Excluded criteria: previous cardiopulmonary disease, endocrine disease, obesity, renal disease, received intravenous antibiotics within 1 week of operation, history of nausea and vomiting or motion sickness, were operated on for longer than 80 minutes, switched laparoscopic surgery for laparotomy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Hartmann's solution (group 1) • *Dose*: 5 ml/kg/h • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg Ondansetron (group 3) • *Dose*: ondansetron 4 mg, Hartmann's solution 5 mL/kg/h • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA

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Lee YC 2009 *(Continued)*

Country: South Korea

Setting: inpatient, single-centre

Author's name: Yong Cheol Lee

Institution: Department of Anesthesiology and Pain Medicine, School of Medicine, Keimyung University

Email: yclee@dsmc.or.kr

Address: 194, Dongsan-dong, Jung-gu, Daegu 700-712, Korea

Duration of study: NA

Language: Korean (Google Translator)

Study's primary outcome: NA

Trial registry number: NA

Notes	Two out of 3 groups relevant (large fluid volume)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "one of the recovery anaesthesiologists who did not know the group of the study subjects observed the condition of the patient or interviewed the patient at 1 hour in the recovery room, and 12 hours and 24 hours after the operation" (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Lekprasert 1996

Study characteristics

Methods	**Study design:** randomized controlled trial

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Lekprasert 1996 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: NA • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 50.95 ± 11.49 • *Weight (mean ± SD, median (IQR), median (range))*: 61.96 ± 12.49 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 76 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane/ isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 120 (n = 34), ≥ 120 (n = 7) • *Use of perioperative opioids (if yes, which?)*: 21 patients received fentanyl/morphine/nalbuphine • *Type of surgery*: gastrointestinal surgery (cholecystectomy, appendectomy, etc.) Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: NA • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 49.22 ± 14.79 • *Weight (mean ± SD, median (IQR), median (range))*: 58.48 ± 10.09 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 74 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane/ isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 33 patients received fentanyl/morphine/nalbuphine • *Type of surgery*: gastrointestinal surgery (cholecystectomy, appendectomy, etc.) **Included criteria:** Thai male and female patients, ASA I or II, 12 to 75 years of age, scheduled for gastrointestinal surgery (cholecystectomy, appendectomy, etc.) **Excluded criteria:** female patients weighing over 100 kg and male patients weighing over 120 kg; ASA III, IV, V; experienced emesis in the 24 hours before administration of study medication; received an antiemetic drug in the 24 hours before administration of study drug; pregnant; breastfeeding; recent history of drug or alcohol abuse; hypersensitivity to any component of the preparation **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes
Interventions	**Intervention characteristics** Ondansetron

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Lekprasert 1996 *(Continued)*

- *Dose*: 4 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo

- *Dose*: placebo
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Thailand **Setting:** inpatient, single-centre **Author's name:** Varinee Lekprasert **Institution:** Department of Anesthesia, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand **Email:** NA **Address:** Department of Anesthesia, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Lekprasert 1996 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "we randomized the patients ...". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Li 2015-1

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron (CP group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 70 • *Received treatment (n)*: NA • *Analysed (n)*: 70 • *Age (mean ± SD, median (IQR), median (range))*: 48.63 ± 8.13 • *Weight (mean ± SD, median (IQR), median (range))*: 62.24 ± 8.89 • *BMI (mean ± SD, median (IQR), median (range))*: 24.22 ± 2.97 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 8.6 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.96 • *Use of perioperative opioids (if yes, which?)*: 15.03 µg sufentanil intraoperative, 145.83 mg tramadol postoperative

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Li 2015-1 *(Continued)*

- *Type of surgery*: modified radical mastectomy

Dexamethasone + ondansetron (DP group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 70
- *Received treatment (n)*: NA
- *Analysed (n)*: 70
- *Age (mean ± SD, median (IQR), median (range))*: 46.09 ± 8.26
- *Weight (mean ± SD, median (IQR), median (range))*: 60.79 ± 8.30
- *BMI (mean ± SD, median (IQR), median (range))*: 23.66 ± 2.84
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 7.1
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 126.06
- *Use of perioperative opioids (if yes, which?)*: 14.87 µg sufentanil intraoperative, 125.00 mg tramadol postoperative
- *Type of surgery*: modified radical mastectomy

Included criteria: female, breast cancer, undergoing modified radical mastectomy with neoadjuvant chemotherapy, 18 to 60 years of age

Excluded criteria: neurological disease, severe cardiac disease, severe respiratory impairment, chronic disease of the digestive tract, long-term preoperative use of analgesics, use of antiemetics, smoker

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ondansetron (CP group) • *Dose*: 8 mg (TIVA) • *Time point of administration*: placebo before anaesthetic induction, ondansetron 30 minutes before end of surgical procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone + ondansetron (DP group) • *Dose*: dexamethasone 10 mg, ondansetron 8mg (TIVA) • *Time point of administration*: dexamethasone before anaesthetic induction, ondansetron 30 minutes before end of surgical procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre

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Li 2015-1 *(Continued)*

Author's name: Zhi-yi Fan

Institution: Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Anesthesiology, Peking University Cancer Hospital Institute, Beijing, China

Email: 13911114196@163.com

Address: Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Anesthesiology, Peking University Cancer Hospital Institute, Beijing 100142, China

Duration of study: NA

Language: Chinese (Google Translator)

Study's primary outcome: NA

Trial registry number: NA

Notes	Four groups divided into 2 sub-studies (2 different anaesthesia regimens: TIVA, inhalational anaesthesia): Li 2015-1 and Li 2015-2

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Li 2015-2

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis

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Li 2015-2 *(Continued)*

Participants	**Baseline characteristics** Ondansetron (CS group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 70 • *Received treatment (n)*: NA • *Analysed (n)*: 70 • *Age (mean ± SD, median (IQR), median (range))*: 48.74 ± 8.21 • *Weight (mean ± SD, median (IQR), median (range))*: 63.26 ± 8.61 • *BMI (mean ± SD, median (IQR), median (range))*: 24.50 ± 2.95 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 7.1 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 126.93 • *Use of perioperative opioids (if yes, which?)*: 15.58 µg sufentanil intraoperative, 110.00 mg tramadol postoperative • *Type of surgery*: modified radical mastectomy Dexamethasone + ondansetron (DS group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 70 • *Received treatment (n)*: NA • *Analysed (n)*: 70 • *Age (mean ± SD, median (IQR), median (range))*: 48.87 ± 7.48 • *Weight (mean ± SD, median (IQR), median (range))*: 62.17 ± 8.18 • *BMI (mean ± SD, median (IQR), median (range))*: 24.27 ± 3.11 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 7.1 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 112.60 • *Use of perioperative opioids (if yes, which?)*: 14.68 µg sufentanil intraoperative, 131.25 mg tramadol postoperative • *Type of surgery*: modified radical mastectomy **Included criteria:** female, breast cancer, undergoing modified radical mastectomy with neoadjuvant chemotherapy, 18 to 60 years of age **Excluded criteria:** neurological disease, severe cardiac disease, severe respiratory impairment, chronic disease of the digestive tract, long-term preoperative use of analgesics, use of antiemetics, smoker **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Ondansetron (CS group) • *Dose*: 8 mg (sevoflurane)

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Li 2015-2 *(Continued)*

- *Time point of administration*: placebo before anaesthetic induction, ondansetron 30 minutes before end of surgical procedure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone + ondansetron (DS group)

- *Dose*: dexamethasone 10 mg, ondansetron 8 mg (sevoflurane)
- *Time point of administration*: dexamethasone before anaesthetic induction, ondansetron 30 minutes before end of surgical procedure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Zhi-yi Fan **Institution:** Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Anesthesiology, Peking University Cancer Hospital Institute, Beijing, China **Email:** 13911114196@163.com **Address:** Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Anesthesiology, Peking University Cancer Hospital Institute, Beijing 100142, China **Duration of study:** NA **Language:** Chinese (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Four groups divided into 2 sub-studies (2 different anaesthesia regimens: TIVA, inhalational anaesthesia): Li 2015-1 and Li 2015-2

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement comment: no statement

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Li 2015-2 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Lim 1991

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Droperidol (2.5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range))*: 27.4 ± 5.7 • *Weight (mean ± SD, median (IQR), median (range))*: 54.6 ± 11.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: termination of pregnancy Droperidol (1.25 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 59 • *Age (mean ± SD, median (IQR), median (range))*: 29.0 ± 5.0 • *Weight (mean ± SD, median (IQR), median (range))*: 52.6 ± 9.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Lim 1991 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: termination of pregnancy

Droperidol (0.25 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 86
- *Age (mean ± SD, median (IQR), median (range))*: 28.8 ± 6.6
- *Weight (mean ± SD, median (IQR), median (range))*: 54.1 ± 9.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: termination of pregnancy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 58
- *Age (mean ± SD, median (IQR), median (range))*: 28.7 ± 7.3
- *Weight (mean ± SD, median (IQR), median (range))*: 56.8 ± 13.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: termination of pregnancy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 71
- *Age (mean ± SD, median (IQR), median (range))*: 29.2 ± 5.6
- *Weight (mean ± SD, median (IQR), median (range))*: 54.8 ± 11.6

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Lim 1991 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: termination of pregnancy

Included criteria: women, ASA I or II, undergoing termination of pregnancy as day-cases

Excluded criteria: received medication with antiemetic properties or ergometrine during the procedure, pre-existing nausea and vomiting

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Droperidol (2.5 mg group)

- *Dose*: 2.5 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg

Droperidol (1.25 mg group)

- *Dose*: 1.25 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg

Droperidol (0.25 mg group)

- *Dose*: 0.25 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg

Placebo

- *Dose*: placebo
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg

Outcomes

Sedation/drowsiness (0 to 2 hours)

- Outcome type: dichotomous outcome

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Lim 1991 *(Continued)*

	Adverse events (general notes in the publication, 24 hours' observation) • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Singapore **Setting:** outpatient, single-centre **Author's name:** K.S. Lim **Institution:** Department of Anaesthesia, Alexandra Hospital, Singapore **Email:** NA **Address:** Alexandra Road, Singapore 0314 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "immediately before the induction of anaesthesia, each patient received intravenously in random one of the studied drugs" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: high rate of exclusions (23%). Reasons described (preoperative nausea or vomiting, Syntometrine given)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Lim 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis, dose-finding study
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 25 • *Non-smoker (%)*: 67 • *History of PONV/motion sickness (%)*: 4.17/NA • *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 84 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil • *Type of surgery*: rhinolaryngological surgery Ondansetron + aprepitant (AP80 group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 35.71 • *Non-smoker (%)*: 75 • *History of PONV/motion sickness (%)*: 3.57/NA • *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 105 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil • *Type of surgery*: rhinolaryngological Ondansetron + aprepitant (AP125 group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 26

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Lim 2013 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 23.08
- *Non-smoker (%)*: 65
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil
- *Type of surgery*: rhinolaryngological

Included criteria: 18 to 65 years of age, ASA I or II, scheduled for rhinolaryngological surgery

Excluded criteria: pregnant; administered perioperative antiemetics, steroids, antihistamine, or psychiatric drugs

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV, non-smoker): no; (history of motion sickness, perioperative opioids): unclear; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before completion of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 3 mg IV Ondansetron + aprepitant (AP80 group) • *Dose*: aprepitant 80 mg, ondansetron 4 mg • *Time point of administration*: aprepitant on the morning of the operation, ondansetron immediately before completion of the operation • *Route of administration*: aprepitant PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: granisetron 3 mg IV Ondansetron + aprepitant (AP125 group) • *Dose*: aprepitant 125 mg, ondansetron 4 mg • *Time point of administration*: aprepitant on the morning of the operation, ondansetron immediately before completion of the operation • *Route of administration*: aprepitant PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: granisetron 3 mg IV
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this work was supported by research fund of Chungnam National University **Country:** South Korea **Setting:** inpatient, single-centre

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Lim 2013 *(Continued)*

Author's name: Young-Kwon Ko

Institution: Department of Anesthesiology and Pain Medicine, College of Medicine, Chungnam National University, Daejeon, Korea

Email: ane84@cnu.ac.kr

Address: Department of Anesthesiology and Pain Medicine, College of Medicine, Chungnam National University, Deasa-dong, Jung-gu, Daejeon 301-721, Korea

Duration of study: NA

Language: English

Study's primary outcome: PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random allocation was utilized for the random allocation..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 78 (Control: Ap80: Ap125 = 24: 28: 26) out of the 90 subject patients, excluding 12 patients who were administered with a steroid during or after the operations, were the final subjects of comparison. Data on the patients..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "were the final subjects of comparison. The data on the patients and the operative information is shown on Table 3. There was no significant statistical difference in the comparison of the groups. One patient in the Ap125 group had symptoms" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV, non-smoker): no; (history of motion sickness, perioperative opioids): unclear; (duration of anaesthesia): yes

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Lind 1970

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Hyoscine (scopolamine) + metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 95 • *Age (mean ± SD, median (IQR), median (range))*: 36.8 ± 9.4 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 10 mg morphine as premedication, 41% of patients received pethidine as rescue medication • *Type of surgery*: gynaecological laparotomy Hyoscine (scopolamine) + perphenazine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 93 • *Age (mean ± SD, median (IQR), median (range))*: 38.9 ± 9.9 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 10 mg morphine as premedication, 65% of patients received pethidine as rescue medication • *Type of surgery*: gynaecological laparotomy **Included criteria:** healthy women admitted for planned gynaecological laparotomy **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear; (perioperative opioids): yes

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Lind 1970 *(Continued)*

Interventions	**Intervention characteristics** Hyoscine (scopolamine) + metoclopramide • *Dose*: hyoscine 4 mg, metoclopramide 10 mg • *Time point of administration*: hyoscine premedication, metoclopramide at end of operation • *Route of administration*: NA, IM • *Rescue antiemetics (if yes, which?)*: perphenazine 5 mg IM Hyoscine (scopolamine) + perphenazine • *Dose*: hyoscine 4 mg, perphenazine 5 mg • *Time point of administration*: hyoscine premedication, perphenazine at end of operation • *Route of administration*: NA, IM • *Rescue antiemetics (if yes, which?)*: perphenazine 5 mg IM
Outcomes	*Retching and vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Norway **Setting:** inpatient, single-centre **Author's name:** Bjorn Lind **Institution:** Department of Anaesthetics, University of Oslo, Akershus Central Hospital, Nordbyhagen, Norway **Email:** NA **Address:** Department of Anaesthetics, University of Oslo, Akershus Central Hospital, 1474 Nordbyhagen, Norway **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the ampoules had been code-numbered according to a list of random numbers"
Allocation concealment (selection bias)	Unclear risk	Quote: "controlled throughout the entire procedure. Either perphenazine 5 mg or metoclopramide 10 mg from coded ampoules was given intramuscularly at the end of the operation. The ampoules had been code-numbered according to a list of random numbers. For 6 hours..."

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Lind 1970 *(Continued)*

		Judgement comment: not stated that the ampoules were identical
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "significance tests were used. There was no difference between the two groups as to age, distribution or type of operation performed (table I)" Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear; (perioperative opioids): yes

Liu 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane/isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl (5 µg/kg) at induction, postoperative morphine (14.4 mg) via PCA • *Type of surgery*: major gynaecological procedure

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Liu 1998 *(Continued)*

	Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 93 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane/isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl (5 µg/kg) at induction, postoperative morphine (16.9 mg) via PCA • *Type of surgery*: major gynaecological procedure **Included criteria:** ASA I or II, undergoing major gynaecological procedure **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 10 mg • *Time point of administration*: before surgical incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% (prochlorperazine 10 mg IM) Placebo • *Dose*: saline • *Time point of administration*: before surgical incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 26.67% (prochlorperazine 10 mg IM)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan, ROC **Setting:** inpatient, single-centre **Author's name:** K. Liu

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Liu 1998 *(Continued)*

Institution: Department of Anaesthesiology, Veteran General Hospital-Kaohsiung, Taiwan, ROC

Email: NA

Address: Department of Anaesthesiology, Veteran General Hospital-Kaohsiung, Kaohsiung, 386, Ta-Chung 1st Rd, Kaohsiung 813, Taiwan, ROC

Duration of study: NA

Language: English

Study's primary outcome: morphine requirement

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: insufficient information on sequence generation provided ("randomized")
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "in a double-blind manner during induction of anaesthesia" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgment comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear

Liu 1999

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo

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Liu 1999 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 56.0 ± 7.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane/ halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 139
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, 19.3 mg morphine via PCA
- *Type of surgery*: abdominal total hysterectomy, myomectomy, radical hysterectomy

Dexamethasone (1.25 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 57.1 ± 7.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane/ halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 140
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, 16.9 mg morphine via PCA
- *Type of surgery*: abdominal total hysterectomy, myomectomy, radical hysterectomy

Dexamethasone (2.5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 18
- *Weight (mean ± SD, median (IQR), median (range))*: 56.1 ± 7.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane/halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 168
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, 15.5 mg morphine via PCA

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Liu 1999 *(Continued)*

- *Type of surgery*: abdominal total hysterectomy, myomectomy, radical hysterectomy

Dexamethasone (5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 49 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 54.7 ± 7.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane/halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 167
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, 14.4 mg morphine via PCA
- *Type of surgery*: abdominal total hysterectomy, myomectomy, radical hysterectomy

Dexamethasone (10 group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 58.1 ± 8.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane/ halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 122
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, 13.7 mg morphine via PCA
- *Type of surgery*: abdominal total hysterectomy, myomectomy, radical hysterectomy

Included criteria: ASA I or II, undergoing general anaesthesia for elective major gynaecological procedure

Excluded criteria: history of motion sickness, gastrointestinal disturbances, postoperative nausea and vomiting (PONV) after general anaesthesia, menstruating or under hormonal therapy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (non-smoker): unclear; (duration of anaesthesia, perioperative opioids): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV

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Liu 1999 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: prochlorperazine 10 mg IM

Dexamethasone (1.25 mg group)

- *Dose*: 1.25 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 10 mg IM

Dexamethasone (2.5 mg group)

- *Dose*: 2.5 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 10 mg IM

Dexamethasone (5 mg group)

- *Dose*: 5 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 10 mg IM

Dexamethasone (10 mg group)

- *Dose*: 10 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 10 mg IM

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was supported by the Veterans General Hospital-Kaohsiung (VGHKS88-02) **Country:** China **Setting:** inpatient, single-centre **Author's name:** Yuan-Yi Chia **Institution:** Department of Anesthesia, Veterans General Hospital-Kaohsiung, Taiwan, Republic of China **Email:** NA **Address:** Department of Anesthesia, Veterans General Hospital-Kaohsiung, Taiwan, Republic of China **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of vomiting **Trial registry number:** NA

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Liu 1999 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "anesthesia, patients were randomly assigned to 5 groups..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "which was prepared as 2 mL of clear solution in an identical syringe" Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind," "identical syringes")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind," "identical syringes")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there was no significant difference among groups with respect to age, weight, height, ASA status, surgery time, and duration of hospital stay (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (non-smoker): unclear; (duration of anaesthesia, perioperative opioids): yes

Liu 2001

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 36 ± 5

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Liu 2001 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 57.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 182
- *Use of perioperative opioids (if yes, which?)*: 350 µg fentanyl intraoperative
- *Type of surgery*: tympanomastoid surgery

Placebo (group 2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 176
- *Use of perioperative opioids (if yes, which?)*: 350 µg fentanyl intraoperative
- *Type of surgery*: tympanomastoid surgery

Included criteria: adult, ASA I or II, undergoing general anaesthesia for elective tympanomastoid surgery

Excluded criteria: gastrointestinal disorders or previous history of PONV, had received antiemetic within 48 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV. perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone (group 1) • *Dose*: 10 mg • *Time point of administration*: after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (15%) 1 mg droperidol IV Placebo (group 2) • *Dose*: 2 mL saline • *Time point of administration*: after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (40%) 1 mg droperidol IV
Outcomes	*Nausea (0 to 24 hours)*

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Liu 2001 *(Continued)*

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Postoperative wound infection (during hospital stay)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Jhi-Joung Wang **Institution:** Department of Anesthesiology, Chi-Mei Medical Center **Email:** 400003@mail.chimei.org.tw **Address:** Chi-Mei Medical Center,Tainan,Taiwan **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response was defined as no vomiting and no antiemetic medication during a 24-hour postoperative period **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...study, a randomization table was used to assign patients into one of the two groups"
Allocation concealment (selection bias)	Unclear risk	Quote: "the randomized process and the identity of the study drugs were blinded from the patients" Judgement comment: no statement on who performed the randomization
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the randomized process and the identity of the study drugs were blinded from the patients, the surgeon, the anesthetists during surgery"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...and the investigators who collected the postoperative data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all 80 patients completed the study"

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Liu 2001 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the subject's characteristics (e.g., age, weight, and gender), duration of anesthesia and surgery, and the total doses of perioperative fentanyl were similar between the two groups (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV. perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Liu 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 40.9 ± 11.8 • *Weight (mean ± SD, median (IQR), median (range))*: 53.5 ± 8.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, sufentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 81 • *Use of perioperative opioids (if yes, which?)*: 43 µg fentanyl intraoperative • *Type of surgery*: gynaecological laparoscopic surgery Ondansetron + droperidol + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 41.3 ± 12.4 • *Weight (mean ± SD, median (IQR), median (range))*: 56.1 ± 10.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Liu 2011 *(Continued)*

- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 86
- *Use of perioperative opioids (if yes, which?)*: 47 µg fentanyl intraoperative
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: underwent gynaecological laparoscopic surgery (laparoscopic lower uterus, oviduct, uterus, or ovarian benign tumour resection surgery); 18 to 65 years of age; no significant organ function disorder

Excluded criteria: ASA ≥ III, obesity (body mass index > 27), taking antiemetic drugs within 24 hours, gastrointestinal disease, liver and kidney dysfunction, abnormal coagulation, history of drug allergy or drug abuse, pregnant women, breastfeeding women

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM (40%) Ondansetron + droperidol + dexamethasone • *Dose*: ondansetron 4 mg, droperidol 1.25 mg, dexamethasone 2.5 mg • *Time point of administration*: at the end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM (18%)
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Z.Q. Liu **Institution:** First Maternal and Infant Health Hospital, Tongji University, Tongji **Email:** drliuzhq@hotmail.com **Address:** NA **Duration of study:** NA **Language:** Chinese (translated by Hong Sun) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (different anaesthesia regimen)
Risk of bias	

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Liu 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly divided". (translated) No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: blinding of anaesthetists impossible due to different interventions
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "preoperative and postoperative visits were performed by a blinded anesthesiologist who did not know the group allocation" (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "a total of 88 statistically valid cases, 2 patients in group B were changed to open surgery due to surgical factors, and were excluded from the results" (translated)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Loewen 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 33 • *Received treatment (n)*: 32 • *Analysed (n)*: 31 • *Age (mean ± SD, median (IQR), median (range))*: 49.5 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 94 • *History of PONV/motion sickness (%)*: 64/24 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 234

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Loewen 2003 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 40 mg morphine equivalents intraoperative, 26 mg morphine equivalents postoperative
- *Type of surgery*: TRAM flap breast reconstruction surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 38
- *Received treatment (n)*: 35
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 49.7
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 95
- *History of PONV/motion sickness (%)*: 42/26
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 234
- *Use of perioperative opioids (if yes, which?)*: 40 mg morphine equivalents intraoperative, 33 mg morphine equivalents postoperative
- *Type of surgery*: TRAM flap breast reconstruction surgery

Included criteria: women scheduled to undergo TRAM flap breast reconstruction surgery

Excluded criteria: absolute contraindication to either of the study drugs (tardive dyskinesia, parkinsonism, hypersensitivity or previous adverse reaction to droperidol or dolasetron, significant hepatic or renal dysfunction, history of cardiac arrhythmia, history of seizures), contraindication to the standardized anaesthetic regimen, organic causes of nausea or vomiting (e.g. gastrointestinal obstruction, metastatic cancer), actual or possible pregnancy, language or cognitive barriers to understanding the screening questions, current or recent drug or alcohol abuse, receipt of an antiemetic within 24 hours before the scheduled procedure

Pretreatment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness, perioperative opioids): no; (history of PONV): yes

Interventions	**Intervention characteristics** Droperidol • *Dose*: 1 mg • *Time point of administration*: 15 minutes before discontinuation of general anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 75% (NA) Ondansetron • *Dose*: 50 mg • *Time point of administration*: 15 minutes before discontinuation of general anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 79% (NA)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)*

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Loewen 2003 *(Continued)*

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this study was funded by a grant from the Vancouver Hospital Health Sciences Center Breast Cancer Research Fund **Country:** Canada **Setting:** inpatient, single-centre **Author's name:** Peter Loewen **Institution:** Vancouver Hospital Health Sciences Centre and the University ofBritish Columbia, Vancouver, British Columbia, Canada **Email:** ploewen@interchange.ubc.ca **Address:** Pharmaceutical Sciences Clinical Service Unit, Vancouver Coastal Health Authority, 2211 Wesbrook Mall, Vancouver, BC V6T 2B5 **Duration of study:** May 2000 to December 2001 **Language:** English **Study's primary outcome:** incidence of PONV within 24 hours after surgery **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomized using a computer-generated balanced-block randomization scheme on the day of surgery to receive either droperidol 1 mg or dolasetron 50 mg"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the drug-containing syringes were prepared identically, including the volume of solution administered. The investigators, patients, and anesthesiologists were therefore blinded to treatment allocation throughout the study period"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all assessors were blinded to treatment allocation" Quote: "the investigators, patients, and anesthesiologists were therefore blinded to treatment allocation throughout the study period"

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Loewen 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...in the study was halted. Two patients were not included in the intention- to-treat analysis because they did not undergo surgery as scheduled, resulting in an intention-to-treat population of 71. Five of these patients did not receive study drug because of transportation errors (n 1), received non-study antiemetics inadvertently (n 3), or returned to the operating room within 24 hours (n 1). Therefore, the on-treatment population included 66 patients. Baseline characteristics and demographics..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "baseline characteristics and demographics of the study population are described in Table 1" Judgement comment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of motion sickness, perioperative opioids): no; (history of PONV): yes

Logie 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Alizapride • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 73 • *Age (mean ± SD, median (IQR), median (range))*: 42.3 ± 14.3 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: 24.8 ± 5.0 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, sufentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 112 • *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, piritramide as postoperative rescue analgesics • *Type of surgery*: laparoscopic gynaecological surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA

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Logie 2010 *(Continued)*

- *Analysed (n)*: 53
- *Age (mean ± SD, median (IQR), median (range))*: 41.9 ± 14.2
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: 23.5 ± 5.0
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, sufentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: intraoperative sufentanil, piritramide as postoperative rescue analgesics
- *Type of surgery*: laparoscopic gynaecological surgery

Included criteria: adult women scheduled for elective laparoscopic gynaecological surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Alizapride • *Dose*: 100 mg • *Time point of administration*: 30 minutes before end of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: first-line droperidol 1.25 + dexamethasone 5 mg, second-line ondansetron 4 mg + alizapride 100 mg Placebo • *Dose*: saline • *Time point of administration*: 30 minutes before end of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: first-line droperidol 1.25 + dexamethasone 5 mg, second-line ondansetron 4 mg + alizapride 100 mg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Belgium **Setting:** NA **Author's name:** Nathalie Logie **Institution:** NA **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English

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Logie 2010 *(Continued)*

	Study's primary outcome: NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomised". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Long 2014

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Aprepitant + dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 125 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 60 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Long 2014 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 153
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/morphine/hydromorphone
- *Type of surgery*: hysterectomy

Placebo + dexamethasone + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 131
- *Received treatment (n)*: NA
- *Analysed (n)*: 59
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100,
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 159
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/morphine/hydromorphone
- *Type of surgery*: hysterectomy

Included criteria: female; older than 18 years of age; fluent in English language; scheduled for inpatient elective hysterectomy requiring general anaesthesia of at least 30 minutes' duration; ASA I, II, or III

Excluded criteria: positive urine or serum pregnancy test done within 7 days of the study; currently breastfeeding; undergoing concomitant bowel surgery other than appendectomy; known hypersensitivity to the study medication (aprepitant) or to any of the antiemetic rescue medications (ondansetron, hydroxyzine, or promethazine), level of preoperative nausea > 4 on the visual rating scale (VRS); severe hepatic insufficiency as determined by a Child-Pugh score > 9 or any condition that impaired the patient's ability to complete study assessments; currently taking rifampin, carbamazepine, and phenytoin and other drugs that strongly induce CYP3A4 activity; had used antiemetics within 12 hours before surgery; history of clinically significant abuse of substances (alcohol, illicit, or prescribed medications) such that the patient was unable to provide informed consent or to reliably complete any of the study assessments; history of a psychiatric illness that may impair the patient's ability to provide informed consent or to complete any of the study assessments

Pretreatment: baseline characteristics (age not for all participants, weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Aprepitant + dexamethasone + ondansetron • *Dose*: aprepitant 40 mg, dexamethasone 8 mg, ondansetron 4 mg • *Time point of administration*: aprepitant 30 minutes before induction of anaesthesia, dexamethasone at induction of anaesthesia, ondansetron within 15 minutes of end of surgery • *Route of administration*: aprepitant PO, dexamethasone + ondansetron IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, promethazine 12.5 mg IV/PO/IM/PR, hydroxyzine 25 mg IV/PO/IM; in PACU at discretion of the anaesthesiologist

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Long 2014 *(Continued)*

	Placebo + dexamethasone + ondansetron • *Dose*: placebo, dexamethasone 8 mg, ondansetron 4 mg • *Time point of administration*: placebo 30 minutes prior to induction of anaesthesia, dexamethasone at induction of anaesthesia, ondansetron within 15 minutes of end of surgery • *Route of administration*: placebo PO, dexamethasone + ondansetron IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, promethazine 12.5 mg IV/PO/IM/PR, hydroxyzine 25 mg IV/PO/IM; in PACU at discretion of the anaesthesiologist
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (PACU to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Jaime B. Long **Institution:** Department of Obstetrics and Gynecology at Reading Health System, West Reading, USA **Email:** Jaime.Long@readinghealth.org **Address:** NA **Duration of study:** July 2007 to October 2011 **Language:** English **Study's primary outcome:** incidence of vomiting **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computerized random number generator was used to create the treatment allocation schedule, which was stored by the pharmacy"
Allocation concealment (selection bias)	Unclear risk	Quote: "which was stored by the pharmacy"

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Long 2014 *(Continued)*

		Judgement comment: schedule was stored by the pharmacy, but no information on whether it remained concealed or who was aware of this schedule, and how study medication was prepared
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "subjects received either oral aprepitant 40 mg or oral placebo approximately 30 minutes prior to induction of standardized anesthesia" Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "there were 125 women allocated to receive aprepitant treatment and 131 allocated to receive placebo treatment (Table 1). The number of women who were excluded during screening and the number who declined consent to participate were not recorded. Six women allocated to aprepitant and 9 women allocated to placebo were excluded during surgery. The primary outcome measure was recorded for 35 women in the Aprepitant group and 59 women in the Placebo group. Adverse events within 6 weeks after surgery were recorded for 34 women in the Aprepitant group and 37 women in the Placebo group" Judgement comment: large dropout rate. Reasons for missing outcome data unclear
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "baseline characteristics are summarized in Table 2. Mean age was 56 years, and the mean duration of surgery was 160 minutes" Judgement comment: baseline characteristics (age not for all participants, weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Loo 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 33.7 ± 8.5 • *Weight (mean ± SD, median (IQR), median (range))*: 57.5 ± 11.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Loo 1997 *(Continued)*

- *ASA I/II/III/IV (n)*: 40/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 6.6
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction
- *Type of surgery*: first trimester termination of pregnancy

Droperidol + metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 33.6 ± 8.8
- *Weight (mean ± SD, median (IQR), median (range))*: 59.3 ± 11.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 40/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 6.0
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl at induction
- *Type of surgery*: first trimester termination of pregnancy

Included criteria: Chinese, female, ASA I, undergoing first trimester termination of pregnancy in day surgery

Excluded criteria: complained of nausea/vomiting preoperatively, received prostaglandin pessary

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids)): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Droperidol • *Dose*: 0.625 mg • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% Droperidol + metoclopramide • *Dose*: droperidol 0.625 mg, metoclopramide 10 mg • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0%
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 2 hours)*

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Loo 1997 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 2 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Singapore **Setting:** outpatient, single-centre **Author's name:** C.C. Loo **Institution:** KK Women's and Children's Hospital, Singapore **Email:** NA **Address:** KK Women's and Children's Hospital, 100 Bukit Timah Road, Singapore 229899 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "using sealed envelope technique"
Allocation concealment (selection bias)	Unclear risk	Quote: "the patients were divided randomly into 2 groups using sealed envelope technique" Judgement comment: not stated; "sequentially numbered, opaque" envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no sham intervention; therefore no blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were assessed for nausea vomiting, sedation and pain at 1 and 2 hours postoperatively and upon discharge by the same nurse blinded to the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the 2 groups were comparable with regard to age, weight, gestational age and duration of operation"

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Loo 1997 *(Continued)*

Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids)): no; (history of PONV/motion sickness, non-smoker): unclear

Lopez Olaondo 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 47 (22 to 65) • *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 12/16 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 132 • *Use of perioperative opioids (if yes, which?)*: 5.9 ± 0.9 µg/kg fentanyl, 32 ± 14.8 mg/48 h morphine • *Type of surgery*: major elective gynaecological surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 47 (21 to 63) • *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 16/32 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 137 • *Use of perioperative opioids (if yes, which?)*: 6.0 ± 1.2 µg/kg fentanyl, 32 ± 18.7 mg/48 h morphine • *Type of surgery*: major elective gynaecological surgery Dexamethasone

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Lopez Olaondo 1996 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 46 (26 to 65)
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 16/28
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 137
- *Use of perioperative opioids (if yes, which?)*: 5.7 ± 0.8 µg/kg fentanyl, 39 ± 22.4 mg/48 h morphine
- *Type of surgery*: major elective gynaecological surgery

Ondansetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 46 (19 to 65)
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 24
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 136
- *Use of perioperative opioids (if yes, which?)*: 5.6 ± 0.6 µg/kg fentanyl, 38 ± 24.6 mg/48 h morphine
- *Type of surgery*: major elective gynaecological surgery

Included criteria: ASA I or II, women 18 to 65 years of age, weighing 45 to 90 kg, undergoing major elective gynaecological surgery

Excluded criteria: had received opioids, NSAIDs, steroids, or antiemetic agents during the previous month; had hypersensitivity to either ondansetron or steroids

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 0.9% saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 68% (metoclopramide 10 mg) Ondansetron

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Lopez Olaondo 1996 *(Continued)*

- *Dose*: ondansetron: 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 36% (metoclopramide 10 mg)

Dexamethasone

- *Dose*: dexamethasone: 8 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 28% (metoclopramide 10 mg)

Ondansetron + dexamethasone

- *Dose*: ondansetron 4 mg, dexamethasone 8 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 8% (metoclopramide 10 mg)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 2 hours, 12 hours, 24 hours, 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Spain **Setting:** inpatient, single-centre **Author's name:** L. López-Olaondo **Institution:** Department of Anaesthesiology and Critical Care, University Clinic, School of Medicine, University of Navarra, Pamplona, Spain **Email:** NA **Address:** Departamento de Anestesiología, Clínica Universitaria, Apartado 192, 31080 Pamplona, Spain **Language:** English **Duration of study:** NA **Trial registry number:** NA

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Lopez Olaondo 1996 *(Continued)*

	Study's primary outcome: complete response, as defined by no nausea or emetic episodes during the 48-hour postoperative period
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the study was prospective, conducted in a double-blind manner, with a stratified randomization to ensure an equal number of patients of the same age and weight undergoing the same type of surgery in each group..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "both the nurses and the anaesthetist were unaware of which antiemetic the patient had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Lutz 1969

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Benzquinamid • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 117 • *Received treatment (n)*: NA • *Analysed (n)*: 117 • *Age (mean ± SD, median (IQR), median (range))*: 49.7 (14 to 93)

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Lutz 1969 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 52.14
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: intra-abdominal, intrapelvic, tegmental, intrathoracic, neck, and/ or ocular surgery

Thiethylperazine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 111
- *Received treatment (n)*: NA
- *Analysed (n)*: 111
- *Age (mean ± SD, median (IQR), median (range))*: 49.7 (16 to 86)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 63.06
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: intra-abdominal, intrapelvic, tegmental, intrathoracic, neck, and/ or ocular surgery

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 100
- *Received treatment (n)*: NA
- *Analysed (n)*: 100
- *Age (mean ± SD, median (IQR), median (range))*: 51.8 (24 to 82)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 64
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: intra-abdominal, intrapelvic, tegmental, intrathoracic, neck, and/ or ocular surgery

Included criteria: male and female, scheduled for surgery under general anaesthesia

Excluded criteria: NA

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Lutz 1969 *(Continued)*

	Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear
Interventions	**Intervention characteristics** Benzquinamid • *Dose*: 50 mg • *Time point of administration*: upon closure of the skin • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA Thiethylperazine • *Dose*: 10 mg • *Time point of administration*: upon closure of the skin • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** H. Lutz **Institution:** Anaesthesieabteilung Klinikum Mannheim der Universität Heidelberg, Mannheim, Theodor-Kurzer-Ufer, Deutschland **Email:** NA **Address:** Anaesthesieabteilung Klinikum Mannheim der Universität Heidelberg, BRD-6800 Mannheim, Theodor-Kurzer-Ufer, Deutschland **Duration of study:** NA **Language:** German (2 German reviewers), English (secondary publication) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None
Risk of bias	

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Lutz 1969 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly assigned" (translated). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind manner"). The control group received no placebo treatment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind manner")
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Maddali 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 30.54 ± 7.62 • *Weight (mean ± SD, median (IQR), median (range))*: 63.43 ± 11.59 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 61.75 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction

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Maddali 2003 *(Continued)*

- *Type of surgery*: diagnostic gynaecological laparoscopic procedures

Dexamethasone + metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 29.3 ± 7.41
- *Weight (mean ± SD, median (IQR), median (range))*: 63.75 ± 16.14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 63.08
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction
- *Type of surgery*: diagnostic gynaecological laparoscopic procedures

Dexamethasone + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 27.67 ± 6.31
- *Weight (mean ± SD, median (IQR), median (range))*: 61.25 ± 8.96
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 64
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction
- *Type of surgery*: diagnostic gynaecological laparoscopic procedures

Included criteria: women posted for diagnostic gynaecological laparoscopic procedure

Excluded criteria: women over 60 years of age, ASA higher than II, significant medical disease, received antiemetics 24 hours before surgery, history of motion sickness or PONV

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 2 to 3 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 15% (ondansetron 1 mg)

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Maddali 2003 *(Continued)*

	Dexamethasone + metoclopramide • *Dose*: dexamethasone 8 mg, metoclopramide 10 mg • *Time point of administration*: 2 to 3 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2.5% (ondansetron 1 mg) Dexamethasone + ondansetron • *Dose*: dexamethasone 8 mg, ondansetron 4 mg • *Time point of administration*: 2 to 3 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2.5% (ondansetron 1 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Oman **Setting:** inpatient, single-centre **Author's name:** Madan Mohan Maddali **Institution:** Department of Anaesthesia, Royal Hospital, Muscat, Oman **Email:** madan@omantel.net.om **Address:** Department of Anaesthesia, Royal Hospital, PB 1331, PC 111, Seeb, Muscat, Sultanate of Oman **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV in the first 24 hours and its amelioration with the 2-drug combination. **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Maddali 2003 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "were randomised into 3 groups using the table of random sampling numbers. Those administering the interventions..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...containing the drugs were coded. The anaesthetist and the investigator were blinded to the drugs administered. All 120 women were premedicated"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "those assessing the outcomes were blinded to group assignment for the duration of the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Madej 1986a

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 51 • *Received treatment (n)*: NA • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range))*: 35.7 ± 1.6 • *Weight (mean ± SD, median (IQR), median (range))*: 59.0 ± 1.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 0.05 mg if < 50 kg, 0.1 mg if > 50 kg (for induction) • *Type of surgery*: minor gynaecological surgery (dilatation, curettage, other)

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Madej 1986a *(Continued)*

Domperidone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 35.8 ± 1.6
- *Weight (mean ± SD, median (IQR), median (range))*: 60.8 ± 1.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0.05 mg if < 50 kg, 0.1 mg if > 50 kg (for induction)
- *Type of surgery*: minor gynaecological surgery (dilatation, curettage, other)

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 48
- *Age (mean ± SD, median (IQR), median (range))*: 34.7 ± 2.1
- *Weight (mean ± SD, median (IQR), median (range))*: 61.5 ± 2.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0.05 mg if < 50 kg, 0.1 mg if > 50 kg (for induction)
- *Type of surgery*: minor gynaecological surgery (dilatation, curettage, other)

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 36.8 ± 2.0
- *Weight (mean ± SD, median (IQR), median (range))*: 59.1 ± 2.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA

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Madej 1986a *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 0.05 mg if < 50 kg, 0.1 mg if > 50 kg (for induction)
- *Type of surgery*: minor gynaecological surgery (dilatation, curettage, other)

Included criteria: women, ASA grade I or II, 16 to 70 years of age, undergoing minor gynaecological surgery as day-cases in the same unit

Excluded criteria: already receiving medication with antiemetic properties, would receive ergometrine during the procedure

Pretreatment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Domperidone • *Dose*: 20 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Droperidol • *Dose*: 2.5 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Metoclopramide • *Dose*: 10 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 4 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 4 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 4 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** England

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Madej 1986a *(Continued)*

Setting: outpatient, single-centre

Author's name: T.H. Madej

Institution: University Department of Anaesthesia, St James' s University Hospital

Email: NA

Address: University Department of Anaesthesia, St James's University Hospital, Beckett Street, Leeds LS9 7TF

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "immediately before the induction of anaesthesia, each patient received one of the study drugs, chosen in a double-blind, randomized fashion, i.v." Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the drugs were presented in numbered, identical 4-ml ampoules containing one of the following: domperidone 20 mg, droperidol 2.5 mg, metoclopramide 10 mg or placebo (saline)" Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...of etomidate i.v., as necessary. After operation the patients were assessed by trained members of the nursing staff. They were observed..." Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "two hundred and one patients were involved in the study initially; two were excluded from the droperidol group because ergometrine was given"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear

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Madej 1986b

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 40.3 ± 1.9 • *Weight (mean ± SD, median (IQR), median (range))*: 63.6 ± 1.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 8 patients not requiring opioid analgesia within 6 hours of surgery • *Type of surgery*: major gynaecological surgery Domperidone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 39.9 ± 1.7 • *Weight (mean ± SD, median (IQR), median (range))*: 61.2 ± 1.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 5 patients not requiring opioid analgesia within 6 hours of surgery • *Type of surgery*: major gynaecological surgery Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 49

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Madej 1986b *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 38.4 ± 1.5
- *Weight (mean ± SD, median (IQR), median (range))*: 60.3 ± 1.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 17 patients not requiring opioid analgesia within 6 hours of surgery
- *Type of surgery*: major gynaecological surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 48
- *Age (mean ± SD, median (IQR), median (range))*: 38.1 ± 1.7
- *Weight (mean ± SD, median (IQR), median (range))*: 60.5 ± 1.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 6 patients not requiring opioid analgesia within 6 hours of surgery
- *Type of surgery*: major gynaecological surgery

Included criteria: 200 women undergoing major gynaecological surgery, ASA class I or II, between 16 and 70 years of age

Excluded criteria: taking drugs with antiemetic effects

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 10 minutes before end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Domperidone • *Dose*: 20 mg • *Time point of administration*: 10 minutes before end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM

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Madej 1986b *(Continued)*

	Droperidol • *Dose*: 2.5 mg • *Time point of administration*: 10 minutes before end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Metoclopramide • *Dose*: 10 mg • *Time point of administration*: 10 minutes before end of procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Extrapyramidal symptoms (0 to 6 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** inpatient, single-centre **Author's name:** T.H. Madej **Institution:** Department of Anaesthesia, St. James´s University Hospital, Bradford **Email:** NA **Address:** Beckett Street, Leeds LS9 7TF **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the appropriate drug was chosen in a double-blind, randomized fashion" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "...i.v. The appropriate drug was chosen in a double-blind, randomized fashion, the drugs being presented in numbered, identical 4-ml ampoules containing one of the following..."

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Madej 1986b *(Continued)*

		Judgement comment: time point of randomization unclear
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "two hundred patients were involved in the study initially; one patient in the droperidol group and two patients in the metoclopramide group were excluded, because supplementary doses of atropine were given in the recovery room"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker): unclear; (perioperative opioids): yes

Manaa 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 52 • *Received treatment (n)*: NA • *Analysed (n)*: 52 • *Age (mean ± SD, median (IQR), median (range))*: 32 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 3 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 46 • *Non-smoker (%)*: 71.2 • *History of PONV/motion sickness (%)*: 9.6/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 125 • *Use of perioperative opioids (if yes, which?)*: 156 mg fentanyl, morphine • *Type of surgery*: maxillofacial surgical procedure Dexamethasone • *Assessed for eligibility (n)*: -

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Manaa 2012 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 52
- *Received treatment (n)*: NA
- *Analysed (n)*: 52
- *Age (mean ± SD, median (IQR), median (range))*: 30 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 3
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: 71.2
- *History of PONV/motion sickness (%)*: 5.8/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 121
- *Use of perioperative opioids (if yes, which?)*: 156 mg fentanyl, morphine
- *Type of surgery*: maxillofacial surgical procedure

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 52
- *Received treatment (n)*: NA
- *Analysed (n)*: 52
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 3
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 42
- *Non-smoker (%)*: 78.8
- *History of PONV/motion sickness (%)*: 19.2/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 131
- *Use of perioperative opioids (if yes, which?)*: 169 mg fentanyl, morphine
- *Type of surgery*: maxillofacial surgical procedure

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 52
- *Received treatment (n)*: NA
- *Analysed (n)*: 52
- *Age (mean ± SD, median (IQR), median (range))*: 32 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23 ± 3
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 40
- *Non-smoker (%)*: 67.3
- *History of PONV/motion sickness (%)*: 7.7/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 137
- *Use of perioperative opioids (if yes, which?)*: 158 mg fentanyl, morphine
- *Type of surgery*: maxillofacial surgical procedure

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Manaa 2012 *(Continued)*

	Included criteria: written informed consent, scheduled electively for maxillofacial surgical procedure (e.g. impacted tooth extraction, jaw reconstruction, removal of cyst or tumour), willing to be enrolled in this randomized clinical, double-blind, placebo-controlled trial **Excluded criteria:** had received any antiemetic medication, had experienced emesis or nausea during a period of 24 hours before surgery, pregnant, had consumed psychoactive substances for 24 hours before surgery, had received steroids over a period of 6 months before surgery, known allergy to study drugs, ASA class III or higher, any condition that contraindicated steroid administration: hypertension, heart disease, renal failure, peptic ulcer disease, diabetes, Cushing disease, adrenal insufficiency, immunosuppression, recent tuberculosis, and cataracts **Pretreatment:** baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV): no; (history of motion sickness, perioperative opioids): unclear
Interventions	**Intervention characteristics** Dexamethasone + metoclopramide • *Dose*: dexamethasone 8 mg, metoclopramide 10 mg • *Time point of administration*: dexamethasone before anaesthesia induction, metoclopramide at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 5.8% (promethazine) Dexamethasone • *Dose*: 8 mg • *Time point of administration*: dexamethasone before anaesthesia induction, placebo at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 3.8% (promethazine) Metoclopramide • *Dose*: 10 mg • *Time point of administration*: placebo before anaesthesia induction, metoclopramide at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 25% (promethazine) Placebo • *Dose*: 0.9% normal saline • *Time point of administration*: placebo before anaesthesia induction, placebo at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 36.5% (promethazine)
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Postoperative wound infection (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Saudi Arabia

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Manaa 2012 *(Continued)*

Setting: outpatient, single-centre

Author's name: Essam M. Manaa

Institution: Anesthesia Department, Faculty of Medicine, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia

Email: e_manaa@yahoo.com

Address: Anesthesia Department, Faculty of Medicine, King Khalid University Hospital, King Saud University, PO Box 7805, Riyadh 11472, Saudi Arabia.

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: complete response to antiemetic prophylaxis

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "clinical, double-blind, placebo controlled trial. Patients between the ages of 20 and 52 years were randomly assigned to one of four treatment groups using a table of computer-generated random numbers: (A) dexamethasone–metoclopramide group who received..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the medications were prepared to the study by the head nurse of operating room in two numbered 5 ml syringes, which were identical in appearance" Judgement comment: no statement on blinding of anaesthesiologists and participants. No statement on further involvement in the study of the head nurse who prepared the medication
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "one of the investigators blinded to the antiemetic treatment group recorded all intraoperative and recovery variables, including the incidence of PONV and the need for rescue antiemetic medication"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data (outcome of interest: vomiting in PACU)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the four treatment groups were comparable with respect to sex, age, BMI, menstrual cycle period, prior use of cigarettes" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV): no; (history of motion sickness, perioperative opioids): unclear

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Mansour 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 33.4 ± 8.6 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.6 ± 6.4 • *ASA I/II/III/IV (n)*: 30/20/0/0 • *Gender (female in %)*: 58 • *Non-smoker (%)*: 86 • *History of PONV/motion sickness (%)*: 34 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 92.6 • *Use of perioperative opioids (if yes, which?)*: 0.46 mg fentanyl PCA • *Type of surgery*: laparoscopic surgical procedure (cholecystectomy, herniorrhaphy, gynaecological procedure) Dexamethasone + metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 35.7 ± 9.2 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26.9 ± 7.1 • *ASA I/II/III/IV (n)*: 23/27/0/0 • *Gender (female in %)*: 46 • *Non-smoker (%)*: 84 • *History of PONV/motion sickness (%)*: 38 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 99.8 • *Use of perioperative opioids (if yes, which?)*: 0.50 mg fentanyl PCA • *Type of surgery*: laparoscopic surgical procedure (cholecystectomy, herniorrhaphy, gynaecological procedure) Dexamethasone + palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50

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Mansour 2013 *(Continued)*

- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 34.9 ± 9.5
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 27.1 ± 6.2
- *ASA I/II/III/IV (n)*: 26/24/0/0
- *Gender (female in %)*: 56
- *Non-smoker (%)*: 76
- *History of PONV/motion sickness (%)*: 30
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 98.7
- *Use of perioperative opioids (if yes, which?)*: 0.49 mg fentanyl PCA
- *Type of surgery*: laparoscopic surgical procedure (cholecystectomy, herniorrhaphy, gynaecological procedure)

Included criteria: 20 to 55 years of age, ASA I or II, scheduled for elective laparoscopic surgical procedure with known high risk of PONV. Risk factors were female gender, non-smoking status, history of PONV or motion sickness, and postoperative opioids. Each risk factor was given a score of 1. Only patients who had at least 2 risk factors (risk score 2 to 4) were enrolled

Excluded criteria: over 60 years of age, ASA > III, body mass index (BMI) > 35 kg/m^2, received a prophylactic antiemetic within 24 hours of surgery, concomitant administration of steroids or psychotropic drugs, contraindication to the use of corticosteroids (glaucoma, severe hypertension, heart disease, renal failure, peptic ulcer disease, diabetes mellitus, adrenal insufficiency, immunosuppression, recent tuberculosis), pregnant or lactating women, a condition requiring long-term opioid use, allergic to any of the study drugs (excluded and replaced by other patients)

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8mg • *Time point of administration*: dexamethasone before anaesthesia induction, saline 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 30% (4 mg ondansetron) Dexamethasone + metoclopramide • *Dose*: dexamethasone 8 mg, metoclopramide 25 mg • *Time point of administration*: dexamethasone before anaesthesia induction, metoclopramide 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 24% (4 mg ondansetron) Dexamethasone + palonosetron • *Dose*: dexamethasone 8 mg, palonosetron 0.075 mg • *Time point of administration*: dexamethasone + palonosetron before anaesthesia induction, saline 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4% (4 mg ondansetron)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome

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Mansour 2013 *(Continued)*

Vomiting (0 to 6 hours)

- Outcome type: dichotomous outcome

Vomiting (12 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Constipation (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Saudi Arabia **Setting:** inpatient, single-centre **Author's name:** Emad E. Mansour **Institution:** Department of Anesthesia, Ain Shams University, Egypt **Email:** emad.mansour@gmail.com **Address:** King Fahd Military Medical Complex, PO Box 946, Dhahran 31932, Saudi Arabia **Language:** English **Duration of study:** April 2012 to August 2012 **Trial registry number:** NA **Study's primary outcome:** incidence of PONV 24 hours after surgery
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated into three equal groups (randomization was performed with the use of sealed envelopes) to receive one of three prophylactic regimens"

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Mansour 2013 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "patients were randomly allocated into three equal groups (randomization was performed with the use of sealed envelopes) to receive one of three prophylactic regimens" Judgement comment: SNOSE not explicitly stated (sequentially numbered and opaque?)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "for proper blinding, the study drugs were prepared by the operating room (OR) pharmacy in the morning of operation. They were prepared in two identical 5 ml syringes and labeled; study drug 1 and 2. Study drug 1 was given immediately before induction of anesthesia (dexamethasone in groups D + S and D + M, and combination of dexamethasone and palonosetron in group D + P) and study drug 2 was given 30 min before the expected end of surgery (metoclopramide in group D + M, and normal saline in groups D + S and D + P) by the attending anesthesiologist who was blinded to the study"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the total opioid analgesic consumption was recorded by the acute pain service nurse in charge who was blinded to the study" Judgement comment: no statement on blinding of personnel for assessment of other outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "groups were comparable with regard to demographic data (age, gender, BMI, ASA physical status), risk factors for PONV, and times of anesthesia; recovery; and PACU stay (Table 1)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Martins 1995

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 43.3 ± 10.2 • *Weight (mean ± SD, median (IQR), median (range))*: 66.0 ± 13.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Martins 1995 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 86
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 168
- *Use of perioperative opioids (if yes, which?)*: postoperative analgesia with 30 mg meperidine IV (every 3 hours)
- *Type of surgery*: gynaecological or urological surgery

Promethazine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 47.5 ± 9.5
- *Weight (mean ± SD, median (IQR), median (range))*: 66.2 ± 9.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 86
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 180
- *Use of perioperative opioids (if yes, which?)*: postoperative analgesia with 30 mg meperidine IV (every 3 hours)
- *Type of surgery*: gynaecological or urological surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 44.7 ± 9.7
- *Weight (mean ± SD, median (IQR), median (range))*: 63.5 ± 10.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 91
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 162
- *Use of perioperative opioids (if yes, which?)*: postoperative analgesia with 30 mg meperidine IV (every 3 hours)
- *Type of surgery*: gynaecological or urological surgery

Included criteria: both sexes, 18 to 65 years of age, ASA I to III, underwent urological or gynaecological surgery under general anaesthesia

Excluded criteria: kidney, hepatic, or endocrine-metabolic disorder; used antiemetic medication in the 24 hours before surgery

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Martins 1995 *(Continued)*

	Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: if needed, metoclopramide 10 mg IV (every 6 hours) Promethazine • *Dose*: 25 mg promethazine • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: if needed, metoclopramide 10 mg IV (every 6 hours) Ondansetron • *Dose*: 4 mg ondansetron • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: if needed, metoclopramide 10 mg IV (every 6 hours)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Brazil **Setting:** inpatient, single-centre **Author's name:** Carmen Regina Bortolozzo **Institution:** Hospital de Clinicas de Porto Alegre **Email:** NA **Address:** Rua Joao Alfredo 683/401, 90050-230 Porto Alegre - RS **Duration of study:** NA **Language:** Portuguese (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement

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Martins 1995 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided" (translated). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no statement but different interventions make blinding of the anaesthetist impossible
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Mathia 1988

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 31.6 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 60.33 ± 9.66 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 48.3 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: minor obstetrical/gynaecological procedure

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Mathia 1988 *(Continued)*

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 18
- *Received treatment (n)*: NA
- *Analysed (n)*: 18
- *Age (mean ± SD, median (IQR), median (range))*: 30.6 ± 7.6
- *Weight (mean ± SD, median (IQR), median (range))*: 59.51 ± 14.06
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 42.78
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: minor obstetrical/gynaecological procedure

Metoclopramide + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 19
- *Received treatment (n)*: NA
- *Analysed (n)*: 19
- *Age (mean ± SD, median (IQR), median (range))*: 30.6 ± 6.8
- *Weight (mean ± SD, median (IQR), median (range))*: 67.59 ± 13.70
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 50.4
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: minor obstetrical/gynaecological procedure

Included criteria: female, 19 to 45 years of age, free of disease or with asymptomatic disease, ASA I or II, minor obstetrical/gynaecological procedure

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: placebo tablets
- *Time point of administration*: evening before and morning of surgery
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide

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Mathia 1988 *(Continued)*

- *Dose*: 20 mg
- *Time point of administration*: evening before and morning of surgery
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide + droperidol

- *Dose*: metoclopramide 20 mg, droperidol 0.25 mg
- *Time point of administration*: metoclopramide evening before and morning of surgery, droperidol on arrival to the surgery site on the day of surgery
- *Route of administration*: metoclopramide IV, droperidol IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, NA **Author's name:** Maj. William J. Mathia **Institution:** Darnell Army Hospital in Fort Hood, Texas **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized into...". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement comment: different treatment procedures in the groups. Unclear whether anaesthesiologists were blinded

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Mathia 1988 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Mathiesen 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 43 • *Received treatment (n)*: NA • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 46 (43 to 50) • *Weight (mean ± SD, median (IQR), median (range))*: 67 (61 to 74) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 75 • *Use of perioperative opioids (if yes, which?)*: 3300 µg remifentanil, 40 mg morphine via PCA • *Type of surgery*: abdominal hysterectomy ± salpingo-oophorectomy Dexamethasone (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 42 • *Received treatment (n)*: NA • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 46 (42 to 51) • *Weight (mean ± SD, median (IQR), median (range))*: 67 (61 to 71)

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Mathiesen 2009 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 67
- *Use of perioperative opioids (if yes, which?)*: 3018 µg remifentanil, 38 mg morphine via PCA
- *Type of surgery*: abdominal hysterectomy ± salpingo-oophorectomy

Included criteria: scheduled for abdominal hysterectomy (salpingo-oophorectomy), 18 to 75 years of age, BMI 18 to 32, ASA I or II

Excluded criteria: inability to cooperate, allergy to any drugs in the study, diagnosis of ovarian cancer, alcohol and/or drug abuse, treatment with antacids or antidepressants, history of diabetes or epilepsy, daily intake of analgesics or intake of any analgesic within 24 hours before surgery, treatment with systemic glucocorticoids within 4 weeks before surgery, known impaired kidney function

Pretreatment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo (group B) • *Dose*: placebo • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 78.95% (ondansetron 4 mg + 1 mg supplemental doses IV) Dexamethasone (group C) • *Dose*: 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 62.16% (ondansetron 4 mg + 1 mg supplemental doses IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 2 hours, 2 to 4 hours, 4 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Astra Tech, Taastrup, Denmark: Supplier of CADD-Legacy PCA devices. Conflict of interest: Dr Dahl has received an unrestricted research grant from Pfizer, Denmark **Country:** Denmark **Setting:** inpatient, multi-centre (2) **Author's name:** Ole Mathiesen **Institution:** Department of Anaesthesia, Copenhagen University Hospital, Glostrup, Denmark **Email:** olemat@dadlnet.dk

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Mathiesen 2009 *(Continued)*

Address: Department of Anaesthesia, Copenhagen University Hospital, Ndr. Ringvej, DK-2600 Glostrup, Denmark

Duration of study: June 2005 to November 2007

Language: English

Study's primary outcome: patient-controlled morphine consumption from 0 to 4 to 0 to 24 hours after operation

Trial registry number: NCT00209495

Notes	Two out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a computer-generated block randomization schedule prepared by the hospital pharmacy"
Allocation concealment (selection bias)	Low risk	Quote: "study medication was prepared by the hospital pharmacy into identical capsules of either 300 mg pregabalin or placebo. A separate package containing either dexamethasone or isotonic sodium chloride was opened and prepared into a neutral syringe by a nurse, who was not part..." Quote: "...of the study or any handling of the patient. All medications were given to the patient by one of the investigators. Study medication was marked with the name of the project, the investigator's name and consecutive numbers according to a computer-generated block randomization schedule prepared by the hospital pharmacy..."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "no person was aware of group assignment until all patients had been included and assessments were completed"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "no person was aware of group assignment until all patients had been included and assessments were completed"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...for inclusion in the study. One hundred and twenty-eight patients, aged 30 to 70 years, were included (Regional Hospital Herning: n 5 80, and Glostrup Hospital: n 5 48) and randomly assigned to their treatment group. However, 12 of these patients were subsequently excluded, resulting in data from 116 patients in the final analyses (Fig. 1). For seven of these patients, we only have data for the first 4 h postoperatively: four patients were re-operated and were excluded from further analyses, two patients wanted to drop out and have different analgesic medication (NSAID) and one patient's 24-h data were not obtained because of logistic problems. There were no significant differences..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00209495 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

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Mathiesen 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 49 • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 26 (21 to 32) • *Weight (mean ± SD, median (IQR), median (range))*: 74 (63 to 92) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 35.56 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 39 • *Use of perioperative opioids (if yes, which?)*: 1 mg alfentanil, 28 µg sufentanil, postoperative morphine • *Type of surgery*: bilateral tonsillectomy Dexamethasone (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 48 • *Received treatment (n)*: NA • *Analysed (n)*: 43 • *Age (mean ± SD, median (IQR), median (range))*: 27 (21 to 31) • *Weight (mean ± SD, median (IQR), median (range))*: 70 (63 to 80) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 34.88 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 37 • *Use of perioperative opioids (if yes, which?)*: 1 mg alfentanil, 26 µg sufentanil, postoperative morphine • *Type of surgery*: bilateral tonsillectomy **Included criteria:** scheduled for bilateral tonsillectomy a.m. Boyle-Davis, 18 to 50 years of age, ASA I or II, standardized surgical technique using cold dissection and bipolar diathermia for haemostasis **Excluded criteria:** inability to cooperate or speak Danish; allergy to drugs in the study; alcohol or drug abuse; treatment with antidepressant-, antiepileptic-, or antidiabetic medication or with glucocorticoids within 4 weeks before the operation, pregnant or breastfeeding, tonsillar malignancy, impaired kidney function, daily intake of analgesics or intake of any analgesic within 24 hours before surgery

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Mathiesen 2011 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Placebo (group B) • *Dose*: placebo • *Time point of administration*: placebo, paracetamol, and pregabalin before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg IV Dexamethasone (group C) • *Dose*: 8 mg • *Time point of administration*: dexamethasone, paracetamol, and pregabalin before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 2 hours, 2 to 4 hours, 4 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Denmark **Setting:** outpatient, single-centre **Author's name:** Ole Mathiesen **Institution:** Section of Acute Pain Management and Palliative Medicine 4114, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark **Email:** olemat@dadlnet.dk **Address:** Section of Acute Pain Management and Palliative Medicine 4114, Department of Anaesthesia Centre of Head and Orthopaedics, Blegdamsvej 9, 2100 Copenhagen, Denmark **Duration of study:** January 2006 to December 2009 **Language:** English **Study's primary outcome:** pain during swallowing at 2 hours postoperatively **Trial registry number:** NCT00378547
Notes	Two out of 3 groups relevant (paracetamol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "study medication was marked with the name of the project, the investigator's name and consecutive numbers according to a computer-generated block randomization schedule prepared by the hospital pharmacy"

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Mathiesen 2011 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "a separate package containing either dexamethasone or isotonic sodium chloride was opened and prepared in a neutral syringe by a nurse, who was not a part of the study or involved in any handling of the patient. Two project nurses involved in research at the Department of Day Case Surgery were in charge of all medications given to the patient. Study medication was marked with the name of the project, the investigator's name and consecutive numbers according to a computer-generated block randomization schedule prepared by the hospital pharmacy. Each block contained nine numbers and the patients were assigned consecutively to their group according to their number"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "no person was aware of group assignment until all patients had been included and assessments were completed"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the project nurses conducted all assessments. No person was aware of group assignment until all patients had been included and assessments were completed"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred and forty-seven patients were included and randomly assigned to their treatment group. Sixteen patients were later excluded and consequently 131 patients were included in the final analyses..." Judgement comment: reasons for missing outcome data described and unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00378547 (retrospective registration)
Other bias	Unclear risk	Quote: "there were no significant differences between groups for patient characteristics and perioperative data" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Matsota 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Droperidol (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 50.73 ± 14.02 • *Weight (mean ± SD, median (IQR), median (range))*: 75.63 ± 11.58 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Matsota 2015 *(Continued)*

- *ASA I/II/III/IV (n)*: 27/13/0/0
- *Gender (female in %)*: 55
- *Non-smoker (%)*: 50
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93.38
- *Use of perioperative opioids (if yes, which?)*: 100 µg fentanyl for induction, intraoperative remifentanil, meperidine (significant difference in meperidine consumption during PACU -> significantly less in group D + O compared to group D)
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron (group O)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 53.8 ± 16.07
- *Weight (mean ± SD, median (IQR), median (range))*: 74.83 ± 8.96
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 26/14/0/0
- *Gender (female in %)*: 55
- *Non-smoker (%)*: 52.5
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93.45
- *Use of perioperative opioids (if yes, which?)*: 100 µg fentanyl for induction, intraoperative remifentanil, meperidine (significant difference in meperidine consumption during PACU -> significantly less in group D + O compared to group D)
- *Type of surgery*: laparoscopic cholecystectomy

Droperidol + ondansetron (group D + O)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 47
- *Age (mean ± SD, median (IQR), median (range))*: 50.19 ± 16.07
- *Weight (mean ± SD, median (IQR), median (range))*: 76.13 ± 8.01
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 30/17/0/0
- *Gender (female in %)*: 55.3
- *Non-smoker (%)*: 48.9
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 92.02
- *Use of perioperative opioids (if yes, which?)*: 100 µg fentanyl for induction, intraoperative remifentanil, meperidine (significant difference in meperidine consumption during PACU -> significantly less in group D + O compared to group D)
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, over 18 years of age, weighing less than 95 kg, undergoing elective laparoscopic cholecystectomy

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Matsota 2015 *(Continued)*

	Excluded criteria: obesity class III (body mass index ≥ 40 kg/m^2), medical history of motion sickness, diabetes mellitus, intake of opioids and antiemetics during the previous month, episodes of emesis 24 hours preoperatively **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker): unclear; (perioperative opioids): yes
Interventions	**Intervention characteristics** Droperidol (group D) • *Dose*: 1.25 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Droperidol + ondansetron (group D + O) • *Dose*: droperidol 1.25 mg, ondansetron 4 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 6 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Arrhythmia (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Greece **Setting:** inpatient, single-centre **Author's name:** Paraskevi Matsota

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Matsota 2015 *(Continued)*

Institution: 2nd Department of Anesthesiology, University Hospital "Attikon", Athens, Greece

Email: matsota@yahoo.gr

Address: University Hospital, 1 Rimini St, Chaidari 12462, Greece

Duration of study: August 2007 to August 2010

Language: English

Study's primary outcome: number of patients experiencing PONV, percentage of patients with a complete response (no nausea and no vomiting) during the 24-hour postoperative period, number of patients who required rescue antiemetic medication

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "participants were randomized with the closed envelope method to one of the following three study groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "closed envelope method" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients at the PACU and ward were attended and interviewed by a different team of investigators unaware of the study protocol"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "patients, with an ASA physical status I or II, aged over 18 years, weighing less than 95 kg, were initially enrolled in the study. In 10 cases a protocol deviation was recorded during their stay in the PACU (in 6 patients morphine was administered instead of meperidine and in 4 patients clonidine for the treatment of hypertension), in 8 individuals the operation was cancelled, and in 5 the procedure was converted to open cholecystectomy, and therefore all were excluded from the study; thus, 127 patients completed the protocol and were finally included: 40 in group D..." Judgement comment: rate of missing outcome data > 15%. However, reasons described and unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "groups were similar and no statistically significant differences were detected regarding age, gender, weight, smoking status, duration of operation, intraoperative fluid administration and intraoperative meperidine dose (Table I)"

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Matsota 2015 *(Continued)*

Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker): unclear; (perioperative opioids): yes

Mazzarella 1988

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 7 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** L-sulpiride (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 30.1 ± 1.1 • *Weight (mean ± SD, median (IQR), median (range))*: 54.3 ± 4.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, thiopentone) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 0.05 mg for premedication • *Type of surgery*: diagnostic curettage or spontaneous or voluntary abortion L-sulpiride (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 27.0 ± 1.5 • *Weight (mean ± SD, median (IQR), median (range))*: 48.2 ± 2.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, thiopentone) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 0.05 mg for premedication • *Type of surgery*: diagnostic curettage or spontaneous or voluntary abortion Droperidol (group C)

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Mazzarella 1988 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 27.5 ± 2.7
- *Weight (mean ± SD, median (IQR), median (range))*: 47.4 ± 1.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, thiopentone)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl 0.05 mg for premedication
- *Type of surgery*: diagnostic curettage or spontaneous or voluntary abortion

Droperidol (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 26.4 ± 2.1
- *Weight (mean ± SD, median (IQR), median (range))*: 52.3 ± 4.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, thiopentone)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl 0.05 mg for premedication
- *Type of surgery*: diagnostic curettage or spontaneous or voluntary abortion

Metoclopramide (group E)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 29.2 ± 1.8
- *Weight (mean ± SD, median (IQR), median (range))*: 55.2 ± 3.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, thiopentone)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl 0.05 mg for premedication

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Mazzarella 1988 *(Continued)*

- *Type of surgery*: diagnostic curettage or spontaneous or voluntary abortion

Metoclopramide (group F)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 28.6 ± 1.4
- *Weight (mean ± SD, median (IQR), median (range))*: 55.1 ± 4.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, thiopentone)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl 0.05 mg for premedication
- *Type of surgery*: diagnostic curettage or spontaneous or voluntary abortion

Placebo (group G)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 29.1 ± 2.2
- *Weight (mean ± SD, median (IQR), median (range))*: 51.3 ± 2.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, thiopentone)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl 0.05 mg for premedication
- *Type of surgery*: diagnostic curettage or spontaneous or voluntary abortion

Included criteria: ASA class I or II, undergoing diagnostic curettage or spontaneous or voluntary abortion

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics**

L-sulpiride(group A)

- *Dose*: 50 mg
- *Time point of administration*: 15 minutes before induction of anaesthesia
- *Route of administration*: IV

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Mazzarella 1988 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: NA

L-sulpiride (group B)

- *Dose*: 100 mg
- *Time point of administration*: 15 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (group C)

- *Dose*: 2.5 mg
- *Time point of administration*: 15 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (group D)

- *Dose*: 5.0 mg
- *Time point of administration*: 15 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide (group E)

- *Dose*: 10 mg
- *Time point of administration*: 15 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide (group F)

- *Dose*: 20 mg
- *Time point of administration*: 15 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo (group G)

- *Dose*: saline
- *Time point of administration*: 15 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes

Vomiting (0 to 3 hours)

- Outcome type: dichotomous outcome

Headache (time point unknown)

- Outcome type: dichotomous outcome

Sedation/drowsiness (time point unknown)

- Outcome type: dichotomous outcome

Visual disturbances (e.g. blurred vision) (time point unknown)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

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Mazzarella 1988 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** single-centre **Author's name:** Angelo Forgione **Institution:** Department of Research Development, RAZIZZA S.P.A. **Email:** NA **Address:** Ravizza S.P.A., Via Europa 35, 20053 Muggio (Milan) Italy **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly given". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind fashion")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind fashion")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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McKay 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Chlorpromazine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 72 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 98 • *Non-smoker (%)*: 65 • *History of PONV/motion sickness (%)*: 33/NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl or sufentanil administered during the operation at the anaesthesiologist's discretion, morphine as needed or requested • *Type of surgery*: elective laparoscopic abdominal procedure Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 37 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 90 • *Non-smoker (%)*: 58 • *History of PONV/motion sickness (%)*: 43/NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl or sufentanil administered during the operation at the anaesthesiologist's discretion, morphine as needed or requested • *Type of surgery*: elective laparoscopic abdominal procedure **Included criteria:** 18 years and over, requiring general anaesthesia for elective laparoscopic abdominal procedures **Excluded criteria:** pregnant; liver or renal dysfunction; vestibular disease; cardiac arrhythmias; prolonged QTc (> 440 ms); seizure disorder; Parkinson's disease; hyperthyroidism; dyskinesia, nausea, or vomiting within 24 hours; currently (within 24 hours of admission) receiving antiemetic therapy or long-term steroid therapy or lithium, or drugs for depression; allergic to chlorpromazine or any of the

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McKay 2009 *(Continued)*

	anaesthetic or analgesic drugs; obese (BMI > 35); used an investigational drug within 30 days before surgery; unwilling or unable to give informed consent **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV): no; (duration of anaesthesia, history of motion sickness, peri-operative opioids): unclear
Interventions	**Intervention characteristics** Chlorpromazine • *Dose*: 10 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 18% dimenhydrinate (25 to 50 mg IV) Placebo • *Dose*: 0.9 % saline • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 33% dimenhydrinate (25 to 50 mg IV)
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Sedation/drowsiness (PACU)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** The Royal University Hospital Foundation. No author has any commercial or other affiliation that might constitute a conflict of interest **Country:** Canada **Setting:** inpatients and outpatients, single-centre **Author's name:** William P McKay **Institution:** Dept of Anesthesia, University of Saskatchewan **Email:** NA **Address:** NA **Language:** English **Duration of study:** October 2003 to October 2006 **Trial registry number:** NA **Study's primary outcome:** incidence of PONV during the first 24 hours after surgery
Notes	None
Risk of bias	

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McKay 2009 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "subjects were randomised with a computer-generated random number table"
Allocation concealment (selection bias)	Low risk	Quote: "October, 2006. Randomisation and blinding. Subjects were randomised with a computer-generated random number table using opaque sealed triple-folded cards containing the study assignment. These were opened in a closed..." Judgement comment: "all investigators, the patient, and all personnel involved in patient care were blinded as to treatment, with concealment of allocation" Statement on concealed allocation included
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...containing the study assignment. These were opened in a closed room by a nurse not involved in the subject's clinical care, and with no knowledge of the subject, and only after inclusion of the patient in the study. The nurse prepared the study drug. The study drug was diluted to 10mg/ml and 1ml of study drug or saline was provided. All investigators, the patient, and all personnel involved in patient care were blinded as to treatment, with concealment of allocation. Electrocardiograph (ECG) strips were de-identified and randomised. ECG measurement and data entry was blinded. Procedures. Patients were randomly assigned..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...drug or saline was provided. All investigators, the patient, and all personnel involved in patient care were blinded as to treatment, with concealment of allocation. Electrocardiograph (ECG) strips were de-identified and randomised. ECG measurement and data entry was blinded. Procedures. Patients were randomly assigned to..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...is presented in Table 1. Sixty subjects were recruited to each group. All but one subject, who had an unplanned admission to the intensive care unit (placebo group) completed the study until leaving PACU, with no protocol violations. One subject in the placebo group could not be contacted subsequently. She had no nausea or vomiting up to discharge from PACU and was analysed in the placebo group as intent-to-treat. Significantly more subjects smoked than..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV): no; (duration of anaesthesia, history of motion sickness, perioperative opioids): unclear

McKean 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics**

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McKean 2006 *(Continued)*

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 22
- *Age (mean ± SD, median (IQR), median (range))*: 26 (16 to 47)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/0/0/0
- *Gender (female in %)*: 77
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: morphine, hydrocodone
- *Type of surgery*: tonsillectomy

Dexamethasone + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 37
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: 23 (16 to 42)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/0/0/0
- *Gender (female in %)*: 91
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: morphine, hydrocodone
- *Type of surgery*: tonsillectomy

Included criteria: scheduled to undergo elective tonsillectomy, 16 to 70 years of age, ASA I, weight 50 to 100 kg

Excluded criteria: suspected diagnosis of malignancy, unilateral tonsillectomy, contraindications to the use of non-steroidal anti-inflammatory drugs

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender): no; (duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: placebo at induction of anaesthesia, ondansetron during anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: cyclizine 50 mg IM

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McKean 2006 *(Continued)*

	Dexamethasone + ondansetron • *Dose*: dexamethasone 10 mg, ondansetron 4 mg • *Time point of administration*: dexamethasone at induction of anaesthesia, ondansetron during anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: cyclizine 50 mg IM
Outcomes	*Adverse events (general notes in the publication, 7 days' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Scotland **Setting:** inpatient, single-centre **Author's name:** S. McKean **Institution:** Departments of Otorhinolaryngology and Anaesthetics, Victoria Hospital, Kirkcaldy, Scotland **Email:** simon@jazzle.co.uk **Address:** 46 Wilson Street, Perth, PH2 0EY, Scotland, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** pain scores **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly generated number sequence" Judgement comment: no information on how this number sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "use of non-steroidal anti-inflammatory drugs. Randomization Patients were allocated according to a randomly generated number sequence to the control group who received 2 mL of normal saline intravenously at induction of anaesthesia and the trial group who received 10 mg (2 mL) of dexamethasone intravenously at induction of anaesthesia. The instructions regarding each patient..." Quote: "...at induction of anaesthesia. The instructions regarding each patient were placed in a sealed opaque envelope, which was opened by the anaesthetist once the patient was in the anaesthetic room. Neither patient, nor surgeon, nor..." Judgement comment: it is unclear which person placed the instructions in the envelopes. It is unclear whether the person who decided on enrolment of patients was aware of the allocation

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McKean 2006 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "...at induction of anaesthesia. The instructions regarding each patient were placed in a sealed opaque envelope, which was opened by the anaesthetist once the patient was in the anaesthetic room. Neither patient, nor surgeon, nor researcher knew whether the patient had received dexamethasone. Anaesthetic and operative technique..." Judgement comment: anaesthetists were aware of group assignment
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...was in the anaesthetic room. Neither patient, nor surgeon, nor researcher knew whether the patient had received dexamethasone. Anaesthetic and operative technique..."
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "seventy-two patients were enrolled in the study. Two patients were excluded because the anaesthetist was compelled to deviate from the anaesthetic protocol in the interest of patient care. A further 24 patients dropped out of the study. Of these 16 were not contactable, six had forgotten to fill in the form and two had lost their form. The non-responders were equally divided between the two groups. Therefore, from a possible 72 patients, 46 (64%) returned their symptom sheets" Judgement comment: large dropout rate (> 15%)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender): no; (duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

McKenzie 1993

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 139 • *Age (mean ± SD, median (IQR), median (range))*: 30.2 ± 0.5 • *Weight (mean ± SD, median (IQR), median (range))*: 64.2 ± 1.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 32/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 40.7

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McKenzie 1993 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 57% of patients received fentanyl or alfentanil
- *Type of surgery*: ambulant gynaecological laparoscopy

Ondansetron (1 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 133
- *Age (mean ± SD, median (IQR), median (range))*: 30.2 ± 0.5
- *Weight (mean ± SD, median (IQR), median (range))*: 64.4 ± 1.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 32/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 39.1
- *Use of perioperative opioids (if yes, which?)*: 54% of patients received fentanyl or alfentanil
- *Type of surgery*: ambulant gynaecological laparoscopy

Ondansetron (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 136
- *Age (mean ± SD, median (IQR), median (range))*: 31.0 ± 0.5
- *Weight (mean ± SD, median (IQR), median (range))*: 65.3 ± 1.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 32/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 39.4
- *Use of perioperative opioids (if yes, which?)*: 61% of patients received fentanyl or alfentanil
- *Type of surgery*: ambulant gynaecological laparoscopy

Ondansetron (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 136
- *Age (mean ± SD, median (IQR), median (range))*: 30.3 ± 0.5
- *Weight (mean ± SD, median (IQR), median (range))*: 66.0 ± 1.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA

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McKenzie 1993 *(Continued)*

- *History of PONV/motion sickness (%)*: 34/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 39.7
- *Use of perioperative opioids (if yes, which?)*: 55% of patients received fentanyl or alfentanil
- *Type of surgery*: ambulant gynaecological laparoscopy

Included criteria: non-pregnant, ASA I to II, women between 18 and 70 years of age, scheduled for gynaecological laparoscopy

Excluded criteria: any prophylactic antiemetics preceding surgery, > 75% over ideal body weight, scheduled to have gastric suction during or after surgery, abnormalities in clinical laboratory tests of liver function, scheduled to undergo a liver biopsy during surgery, pregnancy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline 0.9% • *Time point of administration*: immediately before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: yes (discretion of investigator) Ondansetron (1 mg group) • *Dose*: 1 mg • *Time point of administration*: immediately before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: yes (discretion of investigator) Ondansetron (4 mg group) • *Dose*: 4 mg • *Time point of administration*: immediately before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: yes (discretion of investigator) Ondansetron (8 mg group) • *Dose*: 8 mg • *Time point of administration*: immediately before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: yes (discretion of investigator)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)*

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McKenzie 1993 *(Continued)*

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, multi-centre (8) **Author's name:** Ray McKenzie **Institution:** Department of Anesthesiology, Magee-Women's Hospital, Pittsburgh, Pennsylvania, USA **Email:** NA **Address:** Department of Anesthesiology, Magee-Women's Hospital, 300 Halket Street, Pittsburgh, Pennsylvania 15213-3180, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "... patients were randomized...". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "placebo (8 ml) or the appropriate volume of ondansetron (2 mg/ml) was admixed with normal saline to a final volume of 20 ml [...] in a double-blind fashion" It is not clear from the description if blinding was adequate (identical appearance of syringes, sequentially numbered)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "a total of 580 patients were enrolled in this study. Table 1 lists those patients in each treatment group who were not included in the analysis of efficacy because of protocol violations [...]. A total of 36 patients in the study had protocol violations [...] [which] affect either the incidence of [PONV] or the effectiveness of ondansetron"

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McKenzie 1993 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

McKenzie 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 89 • *Received treatment (n)*: 89 • *Analysed (n)*: 89 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine PCA • *Type of surgery*: major gynaecological surgery Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 91 • *Received treatment (n)*: 91 • *Analysed (n)*: 91 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine PCA

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McKenzie 1994 *(Continued)*

- *Type of surgery*: major gynaecological surgery

Included criteria: after approval of our institutional review board, 180 women, ASA I or II, 18 to 70 years of age, scheduled for major gynaecological surgery gave written informed consent

Excluded criteria: recent (within 24 hours) or chronic ingestion of any other medicine with potential antiemetic properties, hypersensitivity to ondansetron or corticoids, if continuous gastric suction was ordered during the 24-hour postoperative period

Pretreatment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids; data not provided): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: ondansetron with saline during operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA (droperidol 0.625 mg IV, prochlorperazine IM) Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: during operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA (droperidol 0.625 mg IV, prochlorperazine IM)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Ray McKenzie **Institution:** Department of Anesthesiology and Critical Care Medicine, Magee-Womens Hospital and University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA **Email:** NA **Address:** 300 Halket Street, Pittsburgh, PA 15213-3180, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response, defined as no emesis and no administration of rescue antiemetic medication during the 24-hour postoperative period
Notes	None

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McKenzie 1994 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "pump for self-administration of morphine. After induction of anesthesia, patients were randomized in a double-blind fashion to receive either IV ondansetron, 4 mg, plus saline (Group l), or IV ondansetron 4 mg, plus dexamethasone, 8 mg (Group 2). Preoperative data collected included age..." Judgement comment: no details on the randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: statement: "double-blind" is insufficient for judgement on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: statement: "double-blind" is insufficient for judgement on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no significant difference between groups in age, weight, height, amount of intraoperative fentanyl, duration of surgery, estimated blood loss, or postoperative morphine consumption. The history of preoperative nausea, vomiting after previous anesthesia, or motion sickness was not different between groups" Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids; data not provided): unclear

McKenzie 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40

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McKenzie 1997 *(Continued)*

- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range), mean (CI low, high))*: 40 (37.0 to 42.3)
- *Weight (mean ± SD, median (IQR), median (range))*: 67 (62.7 to 71.5)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 50/25
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O + isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 107
- *Use of perioperative opioids (if yes, which?)*: 393 µg fentanyl, 47 mg morphine via PCA in 24 hours
- *Type of surgery*: major gynaecological surgery

Ondansetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range), mean (CI low, high))*: 41 (38.5 to 43.8)
- *Weight (mean ± SD, median (IQR), median (range))*: 70 (66.5 to 73.9)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 50/36
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O + isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100
- *Use of perioperative opioids (if yes, which?)*: 436 µg fentanyl, 50 mg morphine via PCA in 24 hours
- *Type of surgery*: major gynaecological surgery

Included criteria: after approval of the Magee-Women's Hospital Institutional Review Board, informed consent was obtained from 80 women 18 to 65 years of age, who were scheduled for major gynaecological surgery. All women were ASA I, II, or III

Excluded criteria: diabetes; had recently (within 24 hours) ingested any other medicine with potential antiemetic properties; had hypersensitivity to soybean, ondansetron, or corticoids; if continuous gastric suction was ordered during the 24-hour postoperative period

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: ondansetron with saline after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 57.5% (droperidol 0.625 mg IV, prochlorperazine IM)

Ondansetron + dexamethasone

- *Dose*: ondansetron 4 mg, dexamethasone 20 mg
- *Time point of administration*: after induction of anaesthesia

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McKenzie 1997 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 47,5% (droperidol 0.625 mg IV, prochlorperazine IM)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** US **Setting:** inpatient, single-centre **Author's name:** Ray McKenzie **Institution:** Department of Anesthesiology, Magee-Womens Hospital, Pittsburgh, PA, USA **Email:** NA **Address:** 300 Halket Street, Pittsburgh, PA 15213, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response, defined as no emesis and no administration of rescue antiemetic medication during the 24-hour postoperative period
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...each ml of blood lost. The patients were stratified by a positive or negative history of PONV with previous surgery to assure an equal number of patients (n = 20) in each subgroup. After induction of anesthesia and when the patient was stable, ondansetron 4 mg IV was given. Identical syringes of saline (Group 1) or dexamethasone 20 mg (Group 2) were prepared via random number table assignment by personnel not involved in the study. The unknown study drug was administered..."
Allocation concealment (selection bias)	Low risk	Quote: "...4 mg IV was given. Identical syringes of saline (Group 1) or dexamethasone 20 mg (Group 2) were prepared via random number table assignment by personnel not involved in the study. The unknown study drug was administered IV..."

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McKenzie 1997 *(Continued)*

		Judgement comment: participants and investigators could not foresee assignment (random number table and syringes generated by personnel not involved in the study)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "after induction of anesthesia and when the patient was stable, ondansetron 4 mg IV was given. Identical syringes of saline (Group 1) or dexamethasone 20 mg (Group 2) were prepared via random number table assignment by personnel not involved in the study. The unknown study drug was administered IV after confirming no change in vital signs. The 24hour study duration began..."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Metaxari 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 62 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 50 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 34/16/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 80 • *History of PONV/motion sickness (%)*: 10 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 113 • *Use of perioperative opioids (if yes, which?)*: 250 µg fentanyl intraoperative, 17 patients received pethidine postoperative • *Type of surgery*: partial or total thyroidectomy

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Metaxari 2011 *(Continued)*

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 61
- *Received treatment (n)*: NA
- *Analysed (n)*: 51
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 32/18/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 64
- *History of PONV/motion sickness (%)*: 6
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl intraoperative, 18 patients received pethidine postoperative
- *Type of surgery*: partial or total thyroidectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 61
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 35/16/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 52
- *History of PONV/motion sickness (%)*: 3.92
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: 250 µg fentanyl intraoperative, 16 patients received pethidine postoperative
- *Type of surgery*: partial or total thyroidectomy

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 61
- *Received treatment (n)*: NA
- *Analysed (n)*: 52
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 33/18/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 69.23
- *History of PONV/motion sickness (%)*: 13.46

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Metaxari 2011 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 125
- *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl intraoperative, 15 patients received pethidine postoperative
- *Type of surgery*: partial or total thyroidectomy

Included criteria: female, euthyroid, ASA I or II, 20 to 65 years of age, scheduled to undergo elective partial or total thyroidectomy

Excluded criteria: administration of antiemetic medication within 24 hours before surgery; gastrointestinal disorder; significant cardiovascular, respiratory, renal, hepatic, or endocrine disease; pregnant; menstruating at the time of surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (perioperative opioids, non-smoker): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: 0.9% saline • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Granisetron • *Dose*: 3 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Tropisetron • *Dose*: 5 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Greece **Setting:** inpatient, single-centre **Author's name:** A. Papaioannou

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Metaxari 2011 *(Continued)*

Institution: Medical School, University of Crete

Email: alpapa@med.uoc.gr

Address: University of Crete, P.O. Box 2208,71003 Heraklion, Crete, Greece

Duration of study: March 2006 to March 2009

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...and surgeons. Patients were randomly assigned by an electronic randomization table to one of four groups to receive, in a blind..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("in a blind manner")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperative nausea was assessed subjectively using a visual analogue scale (VAS) ruler by a doctor blind to the antiemetic/placebo administered to the patient"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "a total of 245 female patients were initially randomized into the four groups, namely, the placebo group (n = 62 patients, ondansetron group (n = 61), granisetron group (n = 61), and tropisetron group (n = 61). Data were lost for four, three and one patient in the placebo, ondansetron, and granisetron group, respectively. Four patients refused to continue with the study after randomization, and four patients were excluded because of inadvertent propofol administration. Twenty-five patients (Fig. 1) were not included in the final analysis due to the administration of a serotonin antagonist as rescue medication for PONV during the study period" Judgement comment: rate of missing outcome data over 15%; reasons for missing outcome data were reported and were unrelated to the outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there were no differences among groups in terms of age, weight, height, ASA physical status, duration of anesthesia, total dose of fentanyl and volume of Ringer's lactate solution infused, days from last menstruation, and history of PONV or motion sickness" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (perioperative opioids, non-smoker): yes

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Mikawa 1995

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 53 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 40/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 8/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 152 • *Use of perioperative opioids (if yes, which?)*: buprenorphine (epidural catheter) • *Type of surgery*: gynaecological surgery Granisetron (20 µg/kg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 40/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 10/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 159 • *Use of perioperative opioids (if yes, which?)*: buprenorphine (epidural catheter) • *Type of surgery*: gynaecological surgery Granisetron (40 µg/kg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40

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Mikawa 1995 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 40/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 5/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 155
- *Use of perioperative opioids (if yes, which?)*: buprenorphine (epidural catheter)
- *Type of surgery*: gynaecological surgery

Included criteria: inpatient, ASA I, 22 to 65 years of age, undergoing elective gynaecological surgery

Excluded criteria: had taken an antiemetic medication within 24 hours before surgery, gastrointestinal disease, pregnant, more than 25% heavier than ideal body weight, abnormalities in clinical laboratory tests of liver and renal function, presence of vomiting in the 24 hours preceding study drug administration, need for a nasogastric tube postoperatively .

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: NA • *Time point of administration*: 30 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 43% (metoclopramide) Granisetron (20 µg/kg group) • *Dose*: 20 µg/kg • *Time point of administration*: 30 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (metoclopramide) Granisetron (40 µg/kg group) • *Dose*: 40 µg/kg • *Time point of administration*: 30 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (metoclopramide)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA

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Mikawa 1995 *(Continued)*

Country: Japan

Setting: inpatient, single-centre

Author's name: Katsuya Mikawa

Institution: Departments of Anaesthesiology and Intensive Care Unit, Kobe University School of Medicine, Kobe, Japan

Email: NA

Address: Kusunoki-cho 7, Chuo-ku, Kobe, 650, Japan.

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned to one of three groups (n = 40 for each group) to receive pretreatment" Judgement comment: no statement on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "...with the preoperative blood samples. All observations were made without knowledge of which treatment each patient received. For the purpose of data..." Judgement comment: no statement on blinding of participants and anaesthesiologist
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all observations were made without knowledge of which treatment each patient received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

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Mikawa 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline Characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 40/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 7.5/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 159 • *Use of perioperative opioids (if yes, which?)*: buprenorphine (epidural catheter) • *Type of surgery*: gynaecological surgery Granisetron (2 µg/kg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 55 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: I • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 5/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 151 • *Use of perioperative opioids (if yes, which?)*: buprenorphine (epidural catheter) • *Type of surgery*: gynaecological surgery Granisetron (5 µg/kg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 9

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Mikawa 1997 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 40/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 10/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 147
- *Use of perioperative opioids (if yes, which?)*: buprenorphine (epidural catheter)
- *Type of surgery*: gynaecological surgery

Granisetron (10 µg/kg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 48 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 40/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 8/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 161
- *Use of perioperative opioids (if yes, which?)*: buprenorphine (epidural catheter)
- *Type of surgery*: gynaecological surgery

Granisetron (20 µg/kg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 40/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 5
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 156
- *Use of perioperative opioids (if yes, which?)*: buprenorphine (epidural catheter)
- *Type of surgery*: gynaecological surgery

Included criteria: 200 otherwise healthy inpatients, ASA I, 20 to 67 years of age, undergoing elective gynaecological surgery after obtaining institutional approval and informed consent of all patients

Excluded criteria: antiemetic medication within 24 hours before surgery, gastrointestinal disease, pregnancy, obesity (> 25% heavier than ideal body weight), liver and/or renal dysfunction, vomiting in the 24 hours preceding surgery, need for postoperative nasogastric tube

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Mikawa 1997 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: NA • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 48% (metoclopramide 10 mg/kg IV) Granisetron (2 µg/kg group) • *Dose*: 2 µg/kg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 40% (metoclopramide 10 mg/kg IV) Granisetron (5 µg/kg group) • *Dose*: 5 µg/kg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 18% (metoclopramide 10 mg/kg IV) Granisetron (10 µg/kg group) • *Dose*: 10 µg/kg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 13% (metoclopramide 10 mg/kg IV) Granisetron (20 µg/kg group) • *Dose*: 20 µg/kg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (metoclopramide 10 mg/kg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Katsuya Mikawa

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Mikawa 1997 *(Continued)*

Institution: Departments of Anaesthesiology and Intensive Care, Kobe University School of Medicine, Chuo-ku, Kobe, Japan

Email: NA

Address: Kusunoki-cho 7, Chuo-ku, Kobe 650, Japan.

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: antiemetic effects

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly assigned to one of five groups (n = 40 for each group) to receive saline (control) or granisetron (Kytril"; SmithKline Beecham Seiyaku, Tokyo, Japan) at four different doses (2 pg/kg, 5 pg/kg, 10 pg/kg, or 20 pg/kg)" Judgement comment: no details on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "...10 pg/kg, or 20 pg/kg). Saline or granisetron was administered intravenously over 5 min immediately after the induction of anesthesia (immediately before surgery) by anesthetists who were blinded to the nature of treatment. These medications had been prepared beforehand in equivalent volume by an assistant. Vital signs (arterial blood pressure..." Judgement Comment: anaesthetists were blinded, but no indication is given on whether other personnel and participants were blinded to the intervention.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...received a diclofenac suppository. Blind observers monitored patients for emetic episodes, severity of nausea, and vital signs for a 24 hour period that began when patients responded to a vocal command after surgery. Adverse events (rash, headache, and diarrhea) within 24 hours after surgery were assessed by questionnaire. At the completion..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

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Millar 1987

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 24 ± 0.9 • *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 1.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 29/NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 8 • *Use of perioperative opioids (if yes, which?)*: none • *Type of surgery*: day-case termination of pregnancy Droperidol (0.25 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 48 • *Age (mean ± SD, median (IQR), median (range))*: 23 ± 0.8 • *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 1.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 47/NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 8 • *Use of perioperative opioids (if yes, which?)*: none • *Type of surgery*: day-case termination of pregnancy Droperidol (0.5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 47 • *Age (mean ± SD, median (IQR), median (range))*: 25 ± 1.0 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 1.9

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Millar 1987 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 64/NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 8
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: day-case termination of pregnancy

Included criteria: 150 patients who presented for day-case termination of pregnancy, over 16 years of age, assessed preoperatively as ASA I or II, not taking antiemetics or drugs with a possible interaction with droperidol

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of motion sickness, non-smoker): unclear; (history of PONV): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: sterile water • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (metoclopramide 10 mg) Droperidol (0.25 mg group) • *Dose*: 0.25 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8% (metoclopramide 10 mg) Droperidol (0.5 mg group) • *Dose*: 0.5 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)*

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Millar 1987 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Australia **Setting:** outpatient, single-centre **Author's name:** J.M. Millar **Institution:** Nuffield Department of Anaesthetics and Radcliffe Infirmary, Victoria **Email:** NA **Address:** Radcliff Infirmary, Oxford OX2 6HE **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were assigned randomly to one of three groups to receive intravenously either sterile water, droperidol 0.25 mg or droperidol 0.5 mg" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "pharmacy prepared identical, randomly numbered ampoules that contained the test dose in 0.5 ml"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "a direct enquiry about postoperative nausea and vomiting was made al this time, and questionnaires and prepaid envelopes were given to the patients with instructions that these should be completed 24 hours after discharge" Quote: "the patients were assessed by an experienced anaesthetist and deemed fit for discharge if they were free from significant pain, sedation and nausea, had no surgical complications such as continued blood loss. and could dress themselves and walk steadily" Judgement comment: insufficient information on blinding of recovery staff and anaesthetist who assessed the outcomes. For the 24 hour time point questionnaires were used
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "there was a 76% response to the questionnaire (Table 4)..." Quote: "test for nonparametric data. The results of six patients were excluded from the trial due to noncompliance with the protocol. Thc characteristics..."

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Millar 1987 *(Continued)*

		Judgement comment: all missing data before discharge with reasons explained. High rate of loss of response to the questionnaire at 24 hours (24%)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the characteristics of the three groups were similar. There were no significant differences in age, weight or gestation. Significantly fewer patients in the group that received droperidol 0.5 mg had had a previous anaesthetic, and a significantly greater proportion of patients in both droperidol groups gave a history of nausea and vomiting after general anaesthesia" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of motion sickness, non-smoker): unclear; (history of PONV): yes

Misra 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 34.47 ± 10.08 • *Weight (mean ± SD, median (IQR), median (range))*: 57.2 ± 14.02 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 65 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 7.5/12.5 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 175.46 • *Use of perioperative opioids (if yes, which?)*: "a willful effort was made to avoid opioids" • *Type of surgery*: mastoidectomy, tympanoplasty Ondansetron (group III) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 35.77 ± 9.01 • *Weight (mean ± SD, median (IQR), median (range))*: 58.25 ± 13.53 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Misra 2005 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 69.23
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 5.1/ 7.7
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 178.52
- *Use of perioperative opioids (if yes, which?)*: "a willful effort was made to avoid opioids"
- *Type of surgery*: mastoidectomy, tympanoplasty

Included criteria: either sex, 18 to 52 years of age, ASA I or II, undergoing middle ear surgery

Excluded criteria: pregnant; obesity; diabetes mellitus; impaired renal or liver function; had taken H2 antagonist, antiemetic, or psychoactive medication; nausea, retching, or vomiting within 48 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Control (group I) • *Dose*: saline, placebo plaster • *Time point of administration*: at end of surgical procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Ondansetron (group III) • *Dose*: ondansetron 4 mg, placebo plaster • *Time point of administration*: at end of surgical procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** the study was supported financially by the study authors **Country:** India **Setting:** inpatient, single-centre **Author's name:** Asok Jayaraj Pullani **Institution:** Department of Anesthesioogy, M.L.N. Medical College and Associated Hospitals, Allahabad, India **Email:** ashokjayaraj@yahoo.com

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Misra 2005 *(Continued)*

	Address: 103, New PG Hostel, SRN Hospital, Allahabad, UP, India, PIN 211001 **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	Two out of 3 groups relevant (acustimulation)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "anesthesia was standardized and given by an anesthesiologist blinded to group assignment" Judgement comment: study design ensures blinding of participants (placebo treatment)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the incidence of PONV was evaluated within six hours and 24 hours after transfer to the postoperative unit by a blinded observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 120 patients enrolled, three were subsequently excluded because they required administration of dexamethasone in the postoperative period for bronchospasm in two cases and facial nerve injury in one case"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the demographic characteristics of the three groups were similar, as were history of previous PONV and motion sickness. None of the women included in the study were in their menstrual phase. There were no significant differences between the three groups with respect to duration of surgery or anesthesia, or the amount of iv fluids administered (Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Mitra 1998

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics**

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Mitra 1998 *(Continued)*

Ondansetron (group A)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 27 ± 4.9
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 14.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 10/0
- *Type of general anaesthesia*: general anaesthesia (N_2O, pethidine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 45
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg pethidine intraoperative
- *Type of surgery*: caesarean section

Dexamethasone (group B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 23 ± 3.9
- *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 6.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 5/5
- *Type of general anaesthesia*: general anaesthesia (N_2O, pethidine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 46
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg pethidine intraoperative
- *Type of surgery*: caesarean section

Ondansetron + dexamethasone (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 24 ± 4.2
- *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 7.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 5/15
- *Type of general anaesthesia*: general anaesthesia (N_2O, pethidine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 46

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Mitra 1998 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg pethidine intraoperative
- *Type of surgery*: caesarean section

Placebo (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 26 ± 3.6
- *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 6.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/15
- *Type of general anaesthesia*: general anaesthesia (N_2O, pethidine)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 45
- *Use of perioperative opioids (if yes, which?)*: 0.5 mg/kg pethidine intraoperative
- *Type of surgery*: caesarean section

Included criteria: obstetric patients scheduled for lower segment caesarean section

Excluded criteria: had received opioids, steroids, or antiemetic agents during the previous 3 months

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron (group A) • *Dose*: 4 mg • *Time point of administration*: after delivery of the baby • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone (group B) • *Dose*: 8 mg • *Time point of administration*: after delivery of the baby • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron + dexamethasone (group C) • *Dose*: 4 mg ondansetron, 8 mg dexamethasone • *Time point of administration*: after delivery of the baby • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo (group D) • *Dose*: saline • *Time point of administration*: after delivery of the baby • *Route of administration*: IV

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Mitra 1998 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Manjushree Ray **Institution:** Department of Anaesthesiology, Nilratan Sircar Medical College, Calcutta **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "patients were randomly allocated to 4 groups..." No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Mitra 1998 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: quote: "all groups were comparable in regard to demographic profile, previous surgical experience, previous history of postoperative nausea vomiting, motion sickness and duration of anaesthesia" Baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Mitsunari 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 23 • *Received treatment (n)*: 23 • *Analysed (n)*: 23 • *Age (mean ± SD, median (IQR), median (range))*: 32.4 ± 8.9 • *Weight (mean ± SD, median (IQR), median (range))*: 53.9 ± 8.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 142.2 • *Use of perioperative opioids (if yes, which?)*: 4.9 µg/kg fentanyl intraoperative • *Type of surgery*: gynaecological laparoscopic surgery Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 29 • *Received treatment (n)*: 29 • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 29.5 ± 4.6 • *Weight (mean ± SD, median (IQR), median (range))*: 52.4 ± 6.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Mitsunari 2007 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138.1
- *Use of perioperative opioids (if yes, which?)*: 3.8 µg/kg fentanyl intraoperative
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: scheduled for elective gynaecological laparoscopic surgery requiring general anaesthesia

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (non-smoker, history of PONV/motion sickness): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Droperidol • *Dose*: 2.5 mg • *Time point of administration*: when the surgery was started • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Control • *Dose*: none • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (until the next morning after surgery)* • Outcome type: dichotomous outcome *Nausea (until the next morning after surgery)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (until the next morning after surgery)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, observation until the next morning after surgery)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Hiroaki Mitsunari **Institution:** Department of Anesthesiology, Tachikawa General Hospital, Niigata, Japan **Email:** NA **Address:** Department of Anesthesiology, Tachikawa General Hospital, 3-2-11 Kanda-cho, Nagaoka, Niigata 940-8621, Japan **Duration of study:** January 2003 to December 2004

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Mitsunari 2007 *(Continued)*

	Language: English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized to one of two groups: group 1 patients (n = 23) received 2.5 mg droperidol intravenously when the surgery was started, while group 2 patients (n = 29) did not receive any droperidol" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "patients were randomized to one of two groups: group 1 patients (n = 23) received 2.5 mg droperidol intravenously when the surgery was started, while group 2 patients (n = 29) did not receive any droperidol..." Judgement comment: no placebo intervention in the control arm. No blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "any episodes of nausea and vomiting, rescue medications, and adverse effects were recorded until the next morning after the surgery by nurses who had not been informed of this study" Quote: "both patients and nurses were unaware of the anaesthetic technique"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "...but the total fentanyl dose in group 1 was higher than that in group 2" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (non-smoker, history of PONV/motion sickness): unclear; (perioperative opioids): yes

Moens 1997

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics**

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Moens 1997 *(Continued)*

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 104
- *Received treatment (n)*: 104
- *Analysed (n)*: 104
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 14.2
- *Weight (mean ± SD, median (IQR), median (range))*: male: 78 ± 8.3, female: 66 ± 11.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 72
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31/NA
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 54% longer than 90 minutes
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major gynaecological or elective abdominal surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 104
- *Received treatment (n)*: 102
- *Analysed (n)*: 102 (efficacy analysis), 104 (safety analysis)
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 15.1
- *Weight (mean ± SD, median (IQR), median (range))*: male: 76 ± 12.4, female: 65 ± 10.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 66
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 27/NA
- *Type of general anaesthesia*: inhalational anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 47% longer than 90 minutes
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major gynaecological or elective abdominal surgery

Included criteria: between 18 and 75 years of age, major gynaecological or elective abdominal surgery performed under general anaesthesia by laparoscopy, female, not at risk of pregnancy, not breastfeeding

Excluded criteria: had taken an antiemetic medication or experienced retching or vomiting the 24 hours before surgery, would have an intragastric tube in the site postoperatively, weighing less than 45 kg or more than 100 kg

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia

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Moens 1997 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: placebo • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Belgium **Setting:** inpatient, multi-centre (15) **Author's name:** Ph. Moens **Institution:** St-Vincentiusziekenhuis, 2018 Antwerpen **Email:** NA **Address:** St-Vincentiusziekenhuis, St-Vincentiusstraat 20, 2018 Antwerpen **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of emesis during the first 24 hours after surgery **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Moens 1997 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "the patients were randomized to receive [...] either ondansetron 4 mg or placebo"; "randomization was in groups of twelve patients, with six patients in each group receiving the active medication" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "the intent-to-treat population consists of 208 patients who entered the study. All patients were included in the safety analysis and efficacy data, i.e. PONV assessment, were available from 206 patients of whom 102 received placebo and 104 received ondansetron 4 mg''
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Mohammadi 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 16 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 36/14/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Mohammadi 2007 *(Continued)*

- *Type of general anaesthesia*: TIVA (propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 45
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl preoperative, 10 patients required post-operative opioid
- *Type of surgery*: laparoscopic surgery

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 36 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 80 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 38/12/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 46
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl preoperative; 1 patient required postoperative opioid
- *Type of surgery*: laparoscopic surgery

Included criteria: ASA I or II, women, 20 to 45 years of age, scheduled for outpatient laparoscopic surgery under general anaesthesia for assisted reproductive technologies (ART)

Excluded criteria: sensitivity to non-steroidal anti-inflammatory drugs (NSAIDs), gastrointestinal bleeding, known allergy to any study drug, receiving long-term steroid therapy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone • *Dose*: 8 mg • *Time point of administration*: before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Adverse events (general notes in the publication, observation until discharge)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was supported by a grant from Tehran University of Medical Sciences

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Mohammadi 2007 *(Continued)*

Country: Iran

Setting: outpatient, single-centre

Author's name: Sussan Soltani Mohammadi

Institution: Department of Anesthesology, Dr Shariati Hospital, Al-e-Ahmad High way, North Kargar Street, Tehran, Iran

Email: NA

Address: Department of Anesthesology, Dr Shariati Hospital, Al-e-Ahmad High way, North Kargar Street, Tehran 1411713135, Iran

Duration of study: November 2006 to February 2007

Language: English

Study's primary outcome: incidence of postoperative nausea and vomiting and/or pain

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "randomization was based on computer-generated codes"
Allocation concealment (selection bias)	Low risk	Judgement comment: quote: "codes were concealed until interactions were assigned. The coded syringes were prepared by an independent anesthetist in equal volume and shape..."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the coded syringes were prepared by an independent anesthetist in equal volume (2 ml) and shape, therefore both the anesthesiologist and the patient was blinded to the group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "by a blinded observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: quote: "the patients' characteristics (e.g., age, weight) and the durations of anesthesia and surgery were similar between the two groups (table 1)" Baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

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Monohar 2017

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Palonosetron (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 37.68 ± 11.15 • *Weight (mean ± SD, median (IQR), median (range))*: 57.92 ± 9.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 42/8/0/0 • *Gender (female in %)*: 84 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 70.30 • *Use of perioperative opioids (if yes, which?)*: intraoperative tramadol • *Type of surgery*: laparoscopic cholecystectomy Granisetron (group G) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 38.02 ± 11.45 • *Weight (mean ± SD, median (IQR), median (range))*: 57.4 ± 10.92 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 39/11/0/0 • *Gender (female in %)*: 80 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 72.34 • *Use of perioperative opioids (if yes, which?)*: intraoperative tramadol • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** adult, 18 to 65 years of age, ASA I and II, both sexes, scheduled for elective laparoscopic cholecystectomy under general anaesthesia **Excluded criteria:** history of any renal, liver, or gastrointestinal disease; motion sickness; PONV; history of smoking or alcoholism; pregnant; lactating; menstruating; hypersensitivity to `5-HT3` antagonists, had taken antiemetic medication within the last 24 hours, suffered from difficult intubation during induction of anaesthesia

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Monohar 2017 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear
Interventions	**Intervention characteristics** Palonosetron (group P) • *Dose*: 0.075 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 30% (metoclopramide 10 mg IV) Granisetron (group G) • *Dose*: 40 µg/kg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 40% (metoclopramide 10 mg IV)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 4 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** nil **Country:** India **Setting:** inpatient, single-centre **Author's name:** Longjam Eshori **Institution:** Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India **Email:** eshoridr@gmail.com **Address:** Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal – 795 004, Manipur, India **Duration of study:** September 2013 to August 2015 **Language:** English **Study's primary outcome:** complete response **Trial registry number:** NA

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Monohar 2017 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using simple randomization by a computer-generated random number chart"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the test drug, prepared by personnel blinded to the study, was administered 10 min before the induction of anesthesia"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "deviation and number (%). The two groups were comparable with respect to their demographic profile as shown in Table 1. The incidence of nausea, vomiting" Quote: "there was no statistical difference between the two groups, palonosetron and granisetron, with respect to their demographic profiles such as age, weight, height, sex, duration of anesthesia and surgery, presence of comorbidities, and ASA status" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Moon 2010

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Haloperidol + dexamethasone (group H) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA

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Moon 2010 *(Continued)*

- *Analysed (n)*: 46
- *Age (mean ± SD, median (IQR), median (range))*: 38.6 ± 9.60
- *Weight (mean ± SD, median (IQR), median (range))*: 55.7 ± 7.50
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 42/4/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 93
- *History of PONV/motion sickness (%)NA*: 54
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 124.6
- *Use of perioperative opioids (if yes, which?)*: PCA with fentanyl 1000 µg (mean amount of fentanyl per group not reported), pethidine injection 0 to 2 hours (11) and 2 to 24 hours (0)
- *Type of surgery*: gynaecological laparoscopic surgery

Dexamethasone (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 48
- *Age (mean ± SD, median (IQR), median (range))*: 39.2 ± 11.1
- *Weight (mean ± SD, median (IQR), median (range))*: 56.1 ± 8.10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 40/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 92
- *History of PONV/motion sickness (%)NA*: 50
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 121.4
- *Use of perioperative opioids (if yes, which?)*: PCA with fentanyl 1000 µg (mean amount of fentanyl per group not reported), pethidine injection 0 to 2 hours (18) and 2 to 24 hours (1)
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: ASA I or II, 20 to 65 years of age

Excluded criteria: BMI > 30 kg/m^2, deep vein thrombosis, history of psychiatric disease, intake of dopamine antagonists, drug abuse, drug intolerance, gastrointestinal disease, cardiovascular disease, respiratory disease, cerebral disease, renal disease, hepatological disease intake of antiemetics within 24 hours before surgery, pregnancy, breastfeeding

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Haloperidol + dexamethasone (group H) • *Dose*: haloperidol 1 mg/mL, dexamethasone 5 mg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg Dexamethasone (group C) • *Dose*: NaCl 1 mL, dexamethasone 5 mg • *Time point of administration*: 30 minutes before end of surgery

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Moon 2010 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *QT prolongation (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Drong Eon Moon **Institution:** Department of Anaesthesiology and Pain Medicine, The Catholic University of Korea College of Medicine **Email:** demoon@catholic.ac.kr **Address:** Department of Anaesthesiology and Pain Medicine, The CatholicUniversity of Korea College of Medicine, 505, Banpo – dong, Seocho-gu, Seoul 137-701, Korea **Duration of study:** NA **Language:** Korean (translated by Woocheol Sim) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "a nurse not involved in the study prepared the study medications, in order to keep the anaesthesiologists blinded" (translated)
Blinding of outcome assessment (detection bias)	Low risk	Judgement comment: quote: "investigator who was collecting the data was blinded" (translated)

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Moon 2010 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: 2 participants were missing from group H without reasons
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Morin 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 33 (23 to 42) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 22 (19 to 26) • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 75 • *History of PONV/motion sickness (%)*: 22.2/13.3 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 85 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction • *Type of surgery*: diagnostic or therapeutic gynaecological laparoscopy Droperidol (0.625 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 46 • *Age (mean ± SD, median (IQR), median (range))*: 36 (25 to 60) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26 (20 to 30) • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Morin 1999 *(Continued)*

- *Non-smoker (%)*: 70
- *History of PONV/motion sickness (%)*: 26.1/9.3
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 83
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: diagnostic or therapeutic gynaecological laparoscopy

Droperidol (1.25 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 47
- *Age (mean ± SD, median (IQR), median (range))*: 35 (25 to 48)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 22 (19 to 33)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 55.6
- *History of PONV/motion sickness (%)*: 29.8/15.6
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: diagnostic or therapeutic gynaecological laparoscopy

Droperidol (2.5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 46
- *Age (mean ± SD, median (IQR), median (range))*: 35 (24 to 48)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23 (20 to 28)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 50
- *History of PONV/motion sickness (%)*: 21.7/2.2
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 85
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: diagnostic or therapeutic gynaecological laparoscopy

Included criteria: female, inpatients and outpatients, ASA I and II, undergoing gynaecological laparoscopy

Excluded criteria: contraindications to droperidol, history of psychiatric disease, therapy with centrally acting drugs, pregnancy, breastfeeding, history of antiemetic therapy, not well-speaking German patients

Pretreatment: baseline characteristics (age, ASA, BMI): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): yes

Interventions	**Intervention characteristics**

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Morin 1999 *(Continued)*

	Placebo • *Dose*: saline • *Time point of administration*: 10 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 17.7% (metoclopramide 0.3 mg/kg IV, at request 0.2 mg/kg every 2 hours) Droperidol (0.625 mg group) • *Dose*: 0.625 mg • *Time point of administration*: 10 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4.3% (metoclopramide 0.3 mg/kg IV, at request 0.2 mg/kg every 2 hours) Droperidol (1.25 mg group) • *Dose*: 1.25 mg • *Time point of administration*: 10 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 6.4% (metoclopramide 0.3 mg/kg IV, at request 0.2 mg/kg every 2 hours) Droperidol (2.5 mg group) • *Dose*: 2.5 mg • *Time point of administration*: 10 minutes before end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2.1% (metoclopramide 0.3 mg/kg IV, at request 0.2 mg/kg every 2 hours)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 1 hour)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient and outpatient, single-centre **Author's name:** Astrid Marie Morin **Institution:** Universitätsklinik für Anästhesiologie der Universität Ulm **Email:** NA **Address:** Universitätsklinik für Anästhesiologie, D-89070 Ulm **Duration of study:** NA

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Morin 1999 *(Continued)*

	Language: German **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomisierte" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "doppelblindstudie durchgeführt" Judgement comment: no detailed information on blinding provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "von den 200 in die Studie aufgenommenen Patientinnen konnten Daten von 184 Patientinnen ausgewertet werden (Plazebo: n=45; 0,625 mg Droperidol: n=46; 1,25 mg Droperidol: n=47; 2,5 mg Droperidol: n=46). Gründe für den Ausschluß der 16 Patientinnen waren: Änderung des Anästhesieverfahrens (n=9)" Judgement comment: missing outcome data described
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, ASA, BMI): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): yes

Morris 1998

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Morris 1998 *(Continued)*

- *Randomized (n)*: 465 (per protocol -> efficacy analysis), 468 (intention to treat -> safety analysis)
- *Received treatment (n)*: 465
- *Analysed (n)*: 465 (per protocol -> efficacy analysis), 468 (intention to treat -> safety analysis)
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 67.4 ± 12.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 35.2/NA
- *Type of general anaesthesia*: balanced anaesthesia (halothane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93
- *Use of perioperative opioids (if yes, which?)*: 458 patients received intraoperative opioids (fentanyl, morphine, alfentanil), 451 patients received postoperative opioids (morphine, papaveretum)
- *Type of surgery*: major intra-abdominal gynaecological surgery, vaginal hysterectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 462 (per-protocol)
- *Received treatment (n)*: 462
- *Analysed (n)*: 462
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 67.1 ± 12.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 34.0/NA
- *Type of general anaesthesia*: balanced anaesthesia (halothane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 91
- *Use of perioperative opioids (if yes, which?)*: 459 patients received intraoperative opioids (fentanyl, morphine, alfentanil), 448 patients received postoperative opioids (morphine, papaveretum)
- *Type of surgery*: major intra-abdominal gynaecological surgery, vaginal hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 117 (per-protocol)
- *Received treatment (n)*: 117
- *Analysed (n)*: 117
- *Age (mean ± SD, median (IQR), median (range))*: 48 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 68.3 ± 11.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 37.6/NA
- *Type of general anaesthesia*: balanced anaesthesia (halothane/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95
- *Use of perioperative opioids (if yes, which?)*: 115 patients received intraoperative opioids (fentanyl, morphine, alfentanil), 115 patients received postoperative opioids (morphine, papaveretum)

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Morris 1998 *(Continued)*

- *Type of surgery*: major intra-abdominal gynaecological surgery, vaginal hysterectomy

Included criteria: female, inpatient, at least 18 years of age, having major intra-abdominal gynaecological surgery or vaginal hysterectomy performed under standardized general anaesthesia, hospitalized for at least 24 hours post recovery

Excluded criteria: pregnant or breastfeeding, body weight > 100 kg, ASA IV or V, given drugs with known antiemetic properties, severe nausea or emesis in the 24-hour period before receiving study medication, planned intraoperative gastric suctioning, planned intragastric tube postoperatively, known hypersensitivity to ondansetron, contraindications to metoclopramide or ondansetron as indicated in the local prescribing information, participation in another clinical trial during this study or in the 30 days before the start of this study

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; if ineffective, any other antiemetic could be administered Metoclopramide • *Dose*: 10 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; if ineffective, any other antiemetic could be administered Placebo • *Dose*: saline • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; if ineffective, any other antiemetic could be administered
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Mortality (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome

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Morris 1998 *(Continued)*

	Adverse events (general notes in the publication, 24 hours' observation) • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Australia, Canada, Denmark, France, Germany, Iceland, Israel, the Netherlands, Norway, South Africa, Sweden, United Kingdom **Setting:** inpatient, multi-centre (58) **Author's name:** R.W. Morris **Institution:** Department of Anaesthetics, Princess of Wales Hospital, Coity Road, Bridgend, Mid Glamorgan, UK **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** no emesis (e.g. complete response) during the 24-hour post-recovery period **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: per-protocol analysis (efficacy analysis): no missing outcome data (1074 participants were recruited, 1047 received study medication, 1044 were correctly randomized and analyzed for efficacy)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of

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Morris 1998 *(Continued)*

	PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Mortensen 1982

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Droperidol (group A 5 mg) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 59 • *Received treatment (n)*: NA • *Analysed (n)*: 59 • *Age (mean ± SD, median (IQR), median (range))*: 38.3 ± 11.5 • *Weight (mean ± SD, median (IQR), median (range))*: 61.2 ± 10.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (thiopental or pethidine), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 17.0 • *Use of perioperative opioids (if yes, which?)*: intraoperative pethidine • *Type of surgery*: termination of pregnancy, curettage Droperidol (group A 2.5 mg) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 59 • *Received treatment (n)*: NA • *Analysed (n)*: 59 • *Age (mean ± SD, median (IQR), median (range))*: 36.7 ± 11.8 • *Weight (mean ± SD, median (IQR), median (range))*: 60.6 ± 10.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (thiopental or pethidine), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 18.0 • *Use of perioperative opioids (if yes, which?)*: intraoperative pethidine • *Type of surgery*: termination of pregnancy, curettage Placebo (group A) • *Assessed for eligibility (n)*: -

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Mortensen 1982 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 60
- *Received treatment (n)*: NA
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 38.9 ± 12.7
- *Weight (mean ± SD, median (IQR), median (range))*: 61.5 ± 11.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (thiopental or pethidine), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 17.5
- *Use of perioperative opioids (if yes, which?)*: intraoperative pethidine
- *Type of surgery*: termination of pregnancy, curettage

Droperidol (group B 5 mg)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 38
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 38.3 ± 11.5
- *Weight (mean ± SD, median (IQR), median (range))*: 61.2 ± 10.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (thiopental or pethidine), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 71.1
- *Use of perioperative opioids (if yes, which?)*: intraoperative pethidine
- *Type of surgery*: laparotomy, other

Droperidol (group B 2.5 mg)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 36.7 ± 11.8
- *Weight (mean ± SD, median (IQR), median (range))*: 60.6 ± 10.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (thiopental or pethidine), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 70.0
- *Use of perioperative opioids (if yes, which?)*: intraoperative pethidine
- *Type of surgery*: laparotomy, other

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Mortensen 1982 *(Continued)*

Placebo (group B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 36
- *Received treatment (n)*: NA
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 38.9 ± 12.7
- *Weight (mean ± SD, median (IQR), median (range))*: 61.5 ± 11.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (thiopental or pethidine), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79.2
- *Use of perioperative opioids (if yes, which?)*: intraoperative pethidine
- *Type of surgery*: laparotomy, other

Included criteria: gynaecological patients subjected to elective operation under general anaesthesia

Excluded criteria: over 70 years of age, bronchial asthma or severe chronic bronchitis, patient who was to undergo caesarean section

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Droperidol (group A 5 mg)

- *Dose*: 5 mg
- *Time point of administration*: before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (group A 2.5 mg)

- *Dose*: 2.5 mg
- *Time point of administration*: before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo (group A)

- *Dose*: saline
- *Time point of administration*: before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (group B 5 mg)

- *Dose*: 5 mg
- *Time point of administration*: before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

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Mortensen 1982 *(Continued)*

	Droperidol (group B 2.5 mg) • *Dose*: 2.5 mg • *Time point of administration*: before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo (group B) • *Dose*: saline • *Time point of administration*: before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** JABSSEBPHARMA kindly supplied droperidol. The Consultant service of the state medical foundation contributed statistical advice **Country:** Denmark **Setting:** inpatient and outpatient, single-centre **Author's name:** Peter Thomas Mortensen **Institution:** Medical Department, Horsens Hospital, Horsens, Denmark **Email:** NA **Address:** Medical Department, Horsens Hospital, 8700 Horsens, Denmark **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Six groups pooled into 3 groups (same interventions) for analysis Outcome data only for "longer procedures" except for adverse events
Risk of bias	

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Mortensen 1982 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind", "unmarked ampoules")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "patients were kept under observation in the recovery room and in the ward by the nursing stall 'for the first 24 hour postoperatively" Judgement comment: insufficient information on blinding ("double-blind", "unmarked ampoules")
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "...or placebo, shortly prior to anaesthesia. Eight patients were excluded from the investigation, four of them from the placebo group, due to the fact that compounds other than those mentioned below were required during the anaesthesia. The material included all gynaecological..." Judgement comment: per-protocol analysis. Reasons for missing data not reported for 4 participants
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: quote: "Table 1 shows that the patient groups were comparable with regard to age, weight and type of anaesthesia" Baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Moussa 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Granisetron (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 29.50 ± 5.29 • *Weight (mean ± SD, median (IQR), median (range))*: 109.45 ± 7.34

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Moussa 2007 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 0/NA/NA/0
- *Gender (female in %)*: 73.33
- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: 10/13.3
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 124
- *Use of perioperative opioids (if yes, which?)*: 4 patients received buprenorphine as rescue analgesic
- *Type of surgery*: laparoscopic bariatric surgery

Granisetron + droperidol (group II)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 29.42 ± 5.39
- *Weight (mean ± SD, median (IQR), median (range))*: 105.14 ± 14.25
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 0/NA/NA/0
- *Gender (female in %)*: 70
- *Non-smoker (%)*: 83.3
- *History of PONV/motion sickness (%)*: 10/13.3
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 125
- *Use of perioperative opioids (if yes, which?)*: 6 patients received buprenorphine as rescue analgesic
- *Type of surgery*: laparoscopic bariatric surgery

Granisetron + dexamethasone (group III)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 28.62 ± 5.66
- *Weight (mean ± SD, median (IQR), median (range))*: 107.32 ± 11.35
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 0/NA/NA/0
- *Gender (female in %)*: 73.33
- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: 6.7/13.3
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 126
- *Use of perioperative opioids (if yes, which?)*: 5 patients received buprenorphine as rescue analgesic
- *Type of surgery*: laparoscopic bariatric surgery

Placebo (group IV)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA

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Moussa 2007 *(Continued)*

- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 30.29 ± 5.09
- *Weight (mean ± SD, median (IQR), median (range))*: 106.15 ± 11.33
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 0/NA/NA/0
- *Gender (female in %)*: 66.67
- *Non-smoker (%)*: 90
- *History of PONV/motion sickness (%)*: 6.7/13.3
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 126
- *Use of perioperative opioids (if yes, which?)*: 6 patients received buprenorphine as rescue analgesic
- *Type of surgery*: laparoscopic bariatric surgery

Included criteria: ASA II or III, between 18 and 44 years of age, both sexes, general anaesthesia for laparoscopic bariatric surgery

Excluded criteria: known hypersensitivity or contraindication to study medications, chronic nausea, vomiting, motion sickness or retching experience in the 24 hours before anaesthesia, received an antiemetic drug or drug with antiemetic properties during the 24 hours before anaesthesia, breastfeeding, menstruating, conditions that required long-term opioid administration, gastrointestinal disease, diabetes mellitus, neuromuscular disease, smoker

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Granisetron (group I)

- *Dose*: 1 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg IV

Granisetron + droperidol (group II)

- *Dose*: granisetron 1 mg, droperidol 1.25 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg IV

Granisetron + dexamethasone (group III)

- *Dose*: granisetron 1 mg, dexamethasone 8 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg IV

Placebo (group IV)

- *Dose*: saline
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg IV

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

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Moussa 2007 *(Continued)*

Vomiting (0 to 4 hours)

- Outcome type: dichotomous outcome

Vomiting (4 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 24 hours)

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Saudi Arabia **Setting:** inpatient, single-centre **Author's name:** Ashraf Ali Moussa **Institution:** Department of Anesthesiology MBC-22, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia **Email:** ashrafmoussa91@hotmail.com **Address:** Department of Anesthesiology MBC-22, King Faisal Specialist Hospital and Research Center, P.O. Box: 3354, Riyadh 11211, Saudi Arabia **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a random number table, to receive one of four treatment regimens"

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Moussa 2007 *(Continued)*

		Quote: "generated by a random number function in a computer spread sheet"
Allocation concealment (selection bias)	Unclear risk	Quote: "randomized numbers generated by a random number function in a computer spread sheet, resulted in a list of 30 assigned to patients receiving one of each four groups. According to this list, personnel not involved in the study prepared identical 5 ml syringes containing each regimen" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "personnel not involved in the study prepared identical 5 ml syringes containing each regimen"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "questioning by trained BSc students unaware about the patient antiemetic regimen or by spontaneous complaint by the patient"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Muhammad 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA

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Muhammad 2000 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: mini-laparotomy cholecystectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 16
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: mini-laparotomy cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 18
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: mini-laparotomy cholecystectomy

Included criteria: few or no other risk factors for anaesthesia, ASA I and II, between 22 and 71 years of age with cholelithiasis but no obvious bile duct pathology, had mini-laparotomy cholecystectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Tropisetron • *Dose*: 2 mg • *Time point of administration*: immediately after induction

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Muhammad 2000 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: immediately after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Placebo

- *Dose*: saline
- *Time point of administration*: immediately after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg

Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Pakistan **Setting:** inpatient, single-centre **Author's name:** Syed Razi Muhammad **Institution:** Department of Surgery, Baqai Medical University, Karachi **Email:** NA **Address:** 51, Deh Tor, Gadap Road, Near Toll Plaza, Super Highway P.O Box No 2407, Karachi - 74600, Pakistan **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "all patients were randomised to receive immediately after induction one of the following three: Injection Tropisteron 2mg" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement comment: no statement

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Muhammad 2000 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Mujoo 2017

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 38.44 ± 9.91 • *Weight (mean ± SD, median (IQR), median (range))*: 63.0 ± 5.11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 40 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 60.8 • *Use of perioperative opioids (if yes, which?)*: 0.1 mg/kg morphine before induction • *Type of surgery*: urological procedures Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 38.50 ± 9.725 • *Weight (mean ± SD, median (IQR), median (range))*: 63.74 ± 5.48

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Mujoo 2017 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 48
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 62.40
- *Use of perioperative opioids (if yes, which?)*: 0.1 mg/kg morphine before induction
- *Type of surgery*: urological procedures

Included criteria: ASA I and II, 20 to 60 years of age, undergoing elective urological procedure including pyelolithotomy, pyeloplasty, and upper ureter lithotomy under general anaesthesia

Excluded criteria: history of motion sickness, migraine, muscular dystrophy, or any other neurological problems; at particular risk for developing torsade de pointes including those with underlying heart conditions such as congenital long QT syndrome; predisposed to low levels of potassium and magnesium in the blood; taking other medications that lead to QT prolongation; received antiemetics within 48 hours before surgery; history of recurrent vomiting in the postoperative period; pregnant/lactating female

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: just before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Ondansetron • *Dose*: 6 mg • *Time point of administration*: just before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (18 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** nil **Country:** India **Setting:** inpatient, single-centre **Author's name:** Zulfiqar Ali **Institution:** Department of Anaesthesiology and Critical Care, Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu andKashmir, India **Email:** zulfiqaraliiii@yahoo.com

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Mujoo 2017 *(Continued)*

Address: Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated to one of the following two groups to receive either injection ramosetron 0.3 mg IV or injection ondansetron 6 mg IV just before extubation" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...received injection ondansetron (6 mg). To ensure blindness, either of the study drugs was diluted in 0.9% normal saline to a volume of 4 ml and coded by the technologist in charge of operation theater who did not reveal the nature of drug to anyone till the completion of the study. He also maintained a register..."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "after surgery, all the patients were observed for 24 hours. Throughout the study period, vital signs such as pulse rate, blood pressure, and respiratory rate were monitored and recorded every 6 hours, except during sleep" Judgement comment: no information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Muller 2003

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics**

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Muller 2003 *(Continued)*

Dolasetron (12.5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 18
- *Received treatment (n)*: NA
- *Analysed (n)*: 18
- *Age (mean ± SD, median (IQR), median (range))*: 59 (54 to 70)
- *Weight (mean ± SD, median (IQR), median (range))*: 75 (65 to 84)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 56
- *Non-smoker (%)*: 78
- *History of PONV/motion sickness (%)*: 33
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 76.2
- *Use of perioperative opioids (if yes, which?)*: remifentanil intraoperative, piritramide intraoperative
- *Type of surgery*: ocular surgery

Dolasetron (50 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 61 (48 to 69)
- *Weight (mean ± SD, median (IQR), median (range))*: 73 (66 to 85)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 40
- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: 50
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77.4
- *Use of perioperative opioids (if yes, which?)*: remifentanil intraoperative, piritramide intraoperative
- *Type of surgery*: ocular surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 18
- *Received treatment (n)*: NA
- *Analysed (n)*: 18
- *Age (mean ± SD, median (IQR), median (range))*: 61 (48 to 70)
- *Weight (mean ± SD, median (IQR), median (range))*: 78 (68 to 85)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 56
- *Non-smoker (%)*: 72
- *History of PONV/motion sickness (%)*: 28
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 85.2

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Muller 2003 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: remifentanil intraoperative, piritramide intraoperative
- *Type of surgery*: ocular surgery

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 23
- *Received treatment (n)*: NA
- *Analysed (n)*: 23
- *Age (mean ± SD, median (IQR), median (range))*: 63 (55 to 71)
- *Weight (mean ± SD, median (IQR), median (range))*: 73 (62 to 84)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 57
- *Non-smoker (%)*: 74
- *History of PONV/motion sickness (%)*: 26
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79.8
- *Use of perioperative opioids (if yes, which?)*: remifentanil intraoperative, piritramide intraoperative
- *Type of surgery*: ocular surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 23
- *Received treatment (n)*: NA
- *Analysed (n)*: 23
- *Age (mean ± SD, median (IQR), median (range))*: 62 (49 to 68)
- *Weight (mean ± SD, median (IQR), median (range))*: 74 (70 to 84)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 48
- *Non-smoker (%)*: 87
- *History of PONV/motion sickness (%)*: 35
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 75
- *Use of perioperative opioids (if yes, which?)*: remifentanil intraoperative, piritramide intraoperative
- *Type of surgery*: ocular surgery

Included criteria: ASA I or III, receiving implantation of an episcleral radioactive applicator for treatment of ocular malignant melanoma

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dolasetron (12.5 mg group) • *Dose*: 12.5 mg • *Time point of administration*: 15 minutes before induction

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Muller 2003 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dolasetron 12.5 mg (4)

Dolasetron (50 mg group)

- *Dose*: 50 mg
- *Time point of administration*: 15 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dolasetron 12.5 mg (2)

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: 15 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dolasetron 12.5 mg (2)

Droperidol

- *Dose*: 20 µg/kg
- *Time point of administration*: 15 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dolasetron 12.5 mg (2)

Placebo

- *Dose*: NaCl 0,9%
- *Time point of administration*: 15 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: dolasetron 12.5 mg (7)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Jürgen Peters **Institution:** Klinik für Anästhesiologie und Intensivmedizin, Universitätsklinikum Essen **Email:** juergen.peters@uni-essen.de **Address:** Klinik für Anästhesiologie und Intensivmedizin, Universitätsklinikum Essen, Hufelandstraße 55, 45122 Essen **Duration of study:** NA **Language:** German (2 German reviewers) **Study's primary outcome:** NA **Trial registry number:** NA

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Muller 2003 *(Continued)*

Notes	Five out of 7 groups relevant (retrobulbar anaesthesia)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomisiert" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind fashion")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "von einer nicht über Anästhesie und Art des Vorgehens informierten Person zu ihrem Befinden befragt" Judgement comment: outcome assessment by an independent, blinded investigator
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "alle Patientengruppen waren homogen im Hinblick auf Risikofaktoren für Übelkeit und Erbrechen (Tab. 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Mullick 2002

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 37.36 ± 5.81

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Mullick 2002 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 52.96 ± 9.81
- *BMI (mean ± SD, median (IQR), median (range))*: 22.66 ± 3.68
- *ASA I/II/III/IV (n)*: 25/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 8/32
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 123.6
- *Use of perioperative opioids (if yes, which?)*: morphine 0.1 mg/kg for induction
- *Type of surgery*: total abdominal hysterectomy

Metoclopramide (group M)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 39.76 ± 7.80
- *Weight (mean ± SD, median (IQR), median (range))*: 51.61 ± 10.58
- *BMI (mean ± SD, median (IQR), median (range))*: 21.544 ± 4.53
- *ASA I/II/III/IV (n)*: 25/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 4/24
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: morphine 0.1 mg/kg for induction
- *Type of surgery*: total abdominal hysterectomy

Metoclopramide + ondansetron (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 39.84 ± 6.7
- *Weight (mean ± SD, median (IQR), median (range))*: 50.24 ± 9.69
- *BMI (mean ± SD, median (IQR), median (range))*: 21.82 ± 3.84
- *ASA I/II/III/IV (n)*: 25/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/32
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 118.8
- *Use of perioperative opioids (if yes, which?)*: morphine 0.1 mg/kg for induction
- *Type of surgery*: total abdominal hysterectomy

Included criteria: adult, ASA grade I, scheduled for total abdominal hysterectomy under general anaesthesia

Excluded criteria: any major systemic illness, taking medication with antiemetic effect

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Mullick 2002 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: ondansetron 4 mg, saline 2 mL • *Time point of administration*: at time of closure of visceral peritoneum • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8% (metoclopramide 10 mg) Metoclopramide (group M) • *Dose*: metoclopramide 10 mg, saline 2 mL • *Time point of administration*: at time of closure of visceral peritoneum • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (metoclopramide 10 mg) Metoclopramide + ondansetron (group C) • *Dose*: metoclopramide 10 mg, ondansetron 4 mg • *Time point of administration*: at time of closure of visceral peritoneum • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Parul Mullick **Institution:** Department of Anaesthesia and Intensiv Care, Safdarjang Hospital, New Delhi, India **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English

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Mullick 2002 *(Continued)*

	Study's primary outcome: NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "allocated randomly" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind study")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind study")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Murmu 2015

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 63 • *Received treatment (n)*: 63 • *Analysed (n)*: 63 • *Age (mean ± SD, median (IQR), median (range))*: 41.3 ± 8.90 • *Weight (mean ± SD, median (IQR), median (range))*: 56.4 ± 6.87

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Murmu 2015 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 50/13/0/0
- *Gender (female in %)*: 69.84
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 129.92
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, 84.6 mg tramadol with study drug
- *Type of surgery*: hemithyroidectomy

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 63
- *Received treatment (n)*: 63
- *Analysed (n)*: 63
- *Age (mean ± SD, median (IQR), median (range))*: 42.4 ± 9.78
- *Weight (mean ± SD, median (IQR), median (range))*: 58.3 ± 5.13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 52/11/0/0
- *Gender (female in %)*: 79.37
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 131.75
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, 87.4 mg tramadol with study drug
- *Type of surgery*: hemithyroidectomy

Included criteria: euthyroid, ASA I and II, between 30 and 65 years of age, undergoing hemithyroidectomy under general anaesthesia

Excluded criteria: severe cardiovascular, pulmonary, hepatic, renal, and neurological disease (ASA III and IV); anticipated difficult airway; hypothyroidism or hyperthyroidism; known hypersensitivity to study drugs; history of alcohol or drug abuse; morbidly obese; pregnant and lactating; receiving monoamine oxidase inhibitors, study drugs or any other antiemetic medication within 24 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: ondansetron 0.1 mg/kg, tramadol 1.5 mg/kg • *Time point of administration*: at the time of closure of the strap muscles • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo (group C) • *Dose*: saline, tramadol 1.5 mg/kg • *Time point of administration*: at the time of closure of the strap muscles • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Sedation/drowsiness (at 60 minutes)*

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Murmu 2015 *(Continued)*

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Sudeshna Bhar Kundu **Institution:** Department of Anaesthesiology, Institute of Post Graduate Medical Education Research, Kolkata, India **Email:** sudeshna04cmc@yahoo.co.in **Address:** 244 A.J.C Bose Road, Kolkata, West Bengal 700020, India **Duration of study:** NA **Language:** English **Study's primary outcome:** time duration between intraoperative injection of tramadol and the requirement for rescue analgesia in the postoperative period **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the study population was randomly divided into two groups, group O and group C, with the help of a computer-generated random-number list"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "three patients in group O and two patients in group C required additional fentanyl for intraoperative analgesia. Two patients in group C required metoclopramide as rescue antiemetic in the postoperative period. One patient in group O needed urgent re-exploration of the wound postoperatively due to a hematoma. All these patients were excluded from the study. Finally, 126 patients (63 patients in each group) were included for statistical analysis" Judgement comment: subject requiring rescue antiemetics was excluded from the analysis
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the groups were comparable in terms of demographic profile, duration of surgery and dose of tramadol administered intraoperatively (Table..."

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Murmu 2015 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Murphy 2011a

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 63.1 ± 12.4 • *Weight (mean ± SD, median (IQR), median (range))*: 85.5 ± 17.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 0/NA/NA/NA • *Gender (female in %)*: 26.5 • *Non-smoker (%)*: 87.8 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 338 • *Use of perioperative opioids (if yes, which?)*: 15 µg/kg fentanyl intraoperative, 9 mg morphine • *Type of surgery*: coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass or single valvular repair/replacement surgery Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 63.2 ± 13.1 • *Weight (mean ± SD, median (IQR), median (range))*: 83.0 ± 18.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 0/0/NA/NA • *Gender (female in %)*: 31.7 • *Non-smoker (%)*: 83.3 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 322 • *Use of perioperative opioids (if yes, which?)*: 15 µg/kg fentanyl intraoperative, 8 mg morphine • *Type of surgery*: coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass or single valvular repair/replacement surgery

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Murphy 2011a *(Continued)*

	Included criteria: undergoing elective coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass or single valvular repair/replacement surgery and anticipated early tracheal extubation **Excluded criteria:** combined (CABG/valve) procedures, ejection fraction 30%, preoperative use of inotropic agents or an intra-aortic balloon pump, preoperative use of steroids or antiemetic agents, acute or chronic renal failure, pulmonary disease necessitating oxygen therapy or patient assessed as potentially requiring prolonged postoperative mechanical lung ventilation, poorly controlled diabetes, poor English comprehension or psychiatric/central nervous system disturbances precluding completion of the QoR-40 questionnaire **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: first dose at time of anaesthetic induction, second time on initiation of cardiopulmonary bypass • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA dexamethasone • *Dose*: 2 × 8 mg • *Time point of administration*: first time at time of anaesthetic induction, second time on initiation of cardiopulmonary bypass • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (during hospitalization)* • Outcome type: dichotomous outcome *Arrhythmia (during hospitalization)* • Outcome type: dichotomous outcome *Postoperative wound infection (during hospitalization)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, observation during hospitalization)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, multi-centre (2) **Author's name:** Glenn S. Murphy

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Murphy 2011a *(Continued)*

Institution: Department of Anesthesiology, NorthShore University HealthSystem, University of Chicago Pritzker School of Medicine, Chicago, IL, USA

Email: dgmurphy2@yahoo.com

Address: Department of Anesthesiology, NorthShore University HealthSystem, 2650 Ridge Avenue, Evanston, IL 60201, USA

Duration of study: NA

Language: English

Study's primary outcome: postoperative QoR-40 score

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomized to receive either dexamethasone (dexamethasone group) or saline placebo (control group) using a computer-generated randomization code"
Allocation concealment (selection bias)	Low risk	Quote: "the randomization code for the 117 subjects was provided to the operating room pharmacy before the start of the study. Study medications were prepared by the operating room pharmacy in a 3-mL syringes labeled with the patient's name. Either dexamethasone (8-mg to 2 mL total volume) or saline placebo (2-mL total volume) was drawn into each syringe"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all clinicians and researchers were blinded to group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all clinicians and researchers were blinded to group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 117 subjects were enrolled in this investigation. The operating room pharmacy was unable to prepare the study drug at the time of anesthetic induction in 8 patients (7 in the dexamethasone group and 1 in the control group); these subjects were excluded from the study. Data analysis was performed on the 109 patients who received the study drug (60 in the dexamethasone group and 49 in the control group)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "1. There were no differences between groups in sex, age, weight, height, pre-existing medical conditions, preoperative medications, baseline ejection fraction, or type of surgical procedure" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear

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Murphy 2011b

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 61 • *Received treatment (n)*: NA • *Analysed (n)*: 59 • *Age (mean ± SD, median (IQR), median (range))*: 49.2 ± 16.5 • *Weight (mean ± SD, median (IQR), median (range))*: 82.5 ± 23.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0; 2 (1-3) • *Gender (female in %)*: 66.1 • *Non-smoker (%)*: 84.7 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 96.8 • *Use of perioperative opioids (if yes, which?)*: 180 µg fentanyl intraoperative, 1 hydrocodone tablet (5 mg), 1 mg hydromorphone • *Type of surgery*: laparoscopic cholecystectomy Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 59 • *Received treatment (n)*: NA • *Analysed (n)*: 56 • *Age (mean ± SD, median (IQR), median (range))*: 51.4 ± 15.7 • *Weight (mean ± SD, median (IQR), median (range))*: 79.0 ± 15.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0; 2 (1-3) • *Gender (female in %)*: 66.1 • *Non-smoker (%)*: 82.1 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 89.5 • *Use of perioperative opioids (if yes, which?)*: 176 µg fentanyl intraoperative, 1 hydrocodone tablet (5 mg), 1 mg hydromorphone • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** undergoing elective LC surgery from February 2007 to April 2009 with anticipated same-day discharge **Excluded criteria:** use of steroids or antiemetic agents within 1 month of surgery, chronic pain requiring opioid treatment, history of allergy to any study medications, severe renal (i.e. serum creatinine > 1.6 mg/dL) or liver (i.e. liver enzymes > 2 times normal values) disease, pregnancy, poor English comprehension, psychiatric/central nervous system disturbance that would preclude completion of the

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Murphy 2011b *(Continued)*

	QoR-40 questionnaire. Patients were excluded after enrolment if the surgical procedure was changed from a laparoscopic to an open approach **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: saline approximately 60 minutes before anticipated time of surgical incision, ondansetron 30 minutes before end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 18.6% (ondansetron 4 mg) Dexamethasone + ondansetron • *Dose*: dexamethasone 8 mg, ondansetron 4 mg • *Time point of administration*: dexamethasone approximately 60 minutes before anticipated time of surgical incision, ondansetron 30 minutes before end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 5.4% (ondansetron 4 mg)
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (in the ambulatory surgery unit, only not admitted patients)* • Outcome type: dichotomous outcome *Headache (at postoperative day 1 or 24 hours after discharge)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, at postoperative day 1 or 24 hours after discharge)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** support was provided solely from institutional and/or departmental sources **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Glenn S. Murphy **Institution:** Department of Anesthesiology, NorthShore, University HealthSystem, Chicago, Illinois, USA **Email:** dgmurphy2@yahoo.com **Address:** Department of Anesthesiology, NorthShore University HealthSystem, 2650 Ridge Avenue, Evanston, Illinois 60201, USA **Duration of study:** February 2007 to April 2009 **Language:** English **Study's primary outcome:** QoR-40 score (40-item quality-of-recovery scoring system) on patient-perceived quality of recovery on postoperative day (POD) 1

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Murphy 2011b *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated randomization code"
Allocation concealment (selection bias)	Low risk	Quote: "study medications were prepared by the operating room pharmacy in 3-ml syringes labeled with the patient's name" Quote: "the randomization code for the 120 subjects was provided to the operating room pharmacy before the start of the study"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all care providers, researchers, and patients were blinded to group assignments"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "study; all care providers, researchers, and patients were blinded to group assignments"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "surveys were completed on POD1 by 91 of the 115 study subjects (79.1%)" Judgement comment: rate of missing outcome data > 15%. Reasons described and appeared to be unrelated to the outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between groups in age, weight, height, sex, preexisting medical conditions (with the exception of a higher incidence of hypertension in the dexamethasone group), or American Society of Anesthesiologists physical status (table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear

Murphy 2014

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, monoprophylaxis and combination prophylaxis, dose-finding study
Participants	**Baseline characteristics** Ondansetron (early assessment group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Murphy 2014 *(Continued)*

- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 33
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 78 ± 20
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 223
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl intraoperative, 1 mg hydromorphone PACU, 2.6 mg hydromorphone in 24 hours
- *Type of surgery*: elective hysterectomy (either transabdominal or laparoscopic transvaginal approach)

Dexamethasone 4 mg + ondansetron (early assessment group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 25
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 243
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl intraoperative, 1 mg hydromorphone PACU, 2.5 mg hydromorphone in 24 hours
- *Type of surgery*: elective hysterectomy (either transabdominal or laparoscopic transvaginal approach)

Dexamethasone 8 mg + ondansetron (early assessment group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 31
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 22
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 213
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl intraoperative, 1 mg hydromorphone PACU, 3 mg hydromorphone in 24 hours

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Murphy 2014 *(Continued)*

- *Type of surgery*: elective hysterectomy (either transabdominal or laparoscopic transvaginal approach)

Ondansetron (late assessment group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 57 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 231
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl intraoperative, 1.5 mg hydromorphone PACU, 1.75 mg hydromorphone in 24 hours
- *Type of surgery*: elective hysterectomy (either transabdominal or laparoscopic transvaginal approach)

Dexamethasone 4 mg + ondansetron (late assessment group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 53 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 18
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 215
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl intraoperative, 1 mg hydromorphone PACU, 3.25 mg hydromorphone in 24 hours
- *Type of surgery*: elective hysterectomy (either transabdominal or laparoscopic transvaginal approach)

Dexamethasone 8 mg + ondansetron (late assessment group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 33
- *Age (mean ± SD, median (IQR), median (range))*: 56 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 20
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA

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Murphy 2014 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 236
- *Use of perioperative opioids (if yes, which?)*: 200 µg fentanyl intraoperative, 0.6 mg hydromorphone PACU, 2.5 mg hydromorphone in 24 hours
- *Type of surgery*: elective hysterectomy (either transabdominal or laparoscopic transvaginal approach)

Included criteria: women, inpatients, 18 to 80 years of age, presenting for elective hysterectomy (either transabdominal or laparoscopic transvaginal approach) under general anaesthesia

Excluded criteria: preoperative use of steroids or antiemetic drugs; history of allergy to any study medications; preoperative diagnosis of type 1 or 2 diabetes; severe renal (serum creatinine > 1.6 mg/dL) or liver (liver enzymes > 2× normal values) disease; ASA IV and V

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Ondansetron (early assessment group)

- *Dose*: 4 mg
- *Time point of administration*: saline at induction of anaesthesia, ondansetron at conclusion of surgical procedure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Dexamethasone 4 mg + ondansetron (early assessment group)

- *Dose*: dexamethasone 4 mg + ondansetron 4 mg
- *Time point of administration*: dexamethasone at induction of anaesthesia, ondansetron at conclusion of surgical procedure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Dexamethasone 8 mg + ondansetron (early assessment group)

- *Dose*: dexamethasone 8 mg + ondansetron 4 mg
- *Time point of administration*: dexamethasone at induction of anaesthesia, ondansetron at conclusion of surgical procedure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Ondansetron (late assessment group)

- *Dose*: 4 mg
- *Time point of administration*: saline at induction of anaesthesia, ondansetron at conclusion of surgical procedure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Dexamethasone 4 mg + ondansetron (late assessment group)

- *Dose*: dexamethasone 4 mg + ondansetron 4 mg
- *Time point of administration*: dexamethasone at induction of anaesthesia, ondansetron at conclusion of surgical procedure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Dexamethasone 8 mg + ondansetron (late assessment group)

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Murphy 2014 *(Continued)*

- *Dose*: dexamethasone 8 mg + ondansetron 4 mg
- *Time point of administration*: dexamethasone at induction of anaesthesia, ondansetron at conclusion of surgical procedure
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg

Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Postoperative wound infection (until time of discharge)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** support was provided solely from institutional and/or departmental sources **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Glenn S. Murphy **Institution:** Department of Anesthesiology, NorthShore University HealthSystem, Evanston and Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA **Email:** dgmurphy2@yahoo.com **Address:** Department of Anesthesia, NorthShore University HealthSystem, 2650 Ridge Ave., Evanston, IL 60201, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** perioperative glucose concentrations **Trial registry number:** NCT01545700
Notes	Six groups (3 for early outcome assessment, 3 for late outcome assessment) pooled into 3 groups for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "two hundred patients were allocated randomly (block randomization computer-generated randomization code) to 1 of 6 groups (3 early groups, 3 late groups) to determine the effect of dexamethasone on the incidence of early and late hyperglycemic events"
Allocation concealment (selection bias)	Low risk	Quote: "the randomization code for the 200 subjects was provided to the operating room pharmacy before the start of the study; all care providers, patients, and researchers were blinded to group assignment. Study medications were prepared by the operating room pharmacy in 3-mL syringes labeled with the patient's name. Either dexamethasone (4 mg with 1 mL saline or 8 mg-2 mL total volume) or saline (control-2 mL total volume) was drawn into each syringe..."

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Murphy 2014 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all care providers, patients, and researchers were blinded to group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all care providers, patients, and researchers were blinded to group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "two hundred patients were enrolled in this clinical trial. One patient was excluded for a protocol violation, and 4 patients refused postoperative blood sampling. Therefore, complete data were collected on 96 patients in the early groups and 99 patients in the late groups. Patient characteristics are presented"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01545700 (retrospective registration)
Other bias	Unclear risk	Quote: "patients in the late groups. Patient characteristics are presented in Tables 3 and 4. There were no significant differences between the control, 4 mg, or 8 mg groups in baseline demographic characteristics (including preexisting medical conditions or use of preoperative medications, data not presented). The number of patients undergoing either a transabdominal or laparoscopic transvaginal surgical approach did not differ between groups. Intraoperative management data and postoperative" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Naghibi 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide (group G3) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 26 • *Received treatment (n)*: NA • *Analysed (n)*: 26 • *Age (mean ± SD, median (IQR), median (range))*: 42.3 ± 6.7 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 20/6/0/0 • *Gender (female in %)*: 65.38 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)

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Naghibi 2015 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 106
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl, 0.15 mg/kg morphine at induction, 12 mg morphine six hours postoperatively, 18 mg morphine 24 hours postoperatively
- *Type of surgery*: lower abdominal surgery

Placebo (group G4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 26
- *Received treatment (n)*: NA
- *Analysed (n)*: 26
- *Age (mean ± SD, median (IQR), median (range))*: 47.4 ± 5.3
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 6.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/4/0/0
- *Gender (female in %)*: 61.54
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 98
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl, 0.15 mg/kg morphine at induction, 9.6 mg morphine 6 hours postoperatively, 14.5 mg morphine 24 hours postoperatively
- *Type of surgery*: lower abdominal surgery

Included criteria: ASA I and II, 18 to 65 years of age, were scheduled for elective lower abdominal surgery under general anaesthesia

Excluded criteria: risk factor of PONV or prior history of motion sickness or PONV and administration of an antiemetic before surgery; history of drug or alcohol abuse; body mass index (BMI) > 30 kg/m^2; any unpredictable condition in surgery or any complication such as severe hypotension (whenever systolic blood pressure (SBP) was < 70% of baseline); bleeding more than 10% of total blood volume

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Metoclopramide (group G3) • *Dose*: 10 mg • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.15 mg/kg IV Placebo (group G4) • *Dose*: saline • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.15 mg/kg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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Naghibi 2015 *(Continued)*

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** study authors have no funding or support to report **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Azarnoush Hamed **Institution:** Department of Anesthesiology, Alzahra University Hospital, Isfahan University of Medical Sciences, Isfahan, Iran **Email:** hamedmds@yahoo.com **Address:** NA **Duration of study:** in 2009 **Language:** English **Study's primary outcome:** nausea, VAS scoring **Trial registry number:** NA
Notes	Two out of 4 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated into one of four groups (Propofol 20 mg (G1), Propofol 30 mg (G2), Metoclopramide 10 mg (G3), or isotonic saline as a placebo (G4)) using sealed envelopes, with 26 patients in each group" Judgement comment: no further information on sequence generation provided (shuffling envelopes?)
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the injected drugs were prepared in identical syringes by a researcher not otherwise involved in this study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...recorded. These variables were assessed by the investigators unaware of the group identities and subdivided into three time periods, 0-6 h, 6-12 h, and 12-24 h, postoperatively"
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Naghibi 2015 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the four groups of patients were comparable with respect to sex, mean age, weight, height, male to female ratio, ASA physical status, and duration of surgery and also recovery time [Table 1]" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Naguib 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 41.3 ± 13.1 • *Weight (mean ± SD, median (IQR), median (range))*: 72.2 ± 12.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 79.31 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 128.3 • *Use of perioperative opioids (if yes, which?)*: 189.7 µg fentanyl intraoperative, postoperative meperidine • *Type of surgery*: laparoscopic cholecystectomy Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 39.2 ± 8.4 • *Weight (mean ± SD, median (IQR), median (range))*: 76.8 ± 13.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 80

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Naguib 1996 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 113.4
- *Use of perioperative opioids (if yes, which?)*: 193 µg fentanyl intraoperative, postoperative meperidine
- *Type of surgery*: laparoscopic cholecystectomy

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 36.9 ± 8.9
- *Weight (mean ± SD, median (IQR), median (range))*: 72.4 ± 12.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 76
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 112.4
- *Use of perioperative opioids (if yes, which?)*: 162 µg fentanyl intraoperative, postoperative meperidine
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: 35.2 ± 10.6
- *Weight (mean ± SD, median (IQR), median (range))*: 71.3 ± 11.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 87.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 126.5
- *Use of perioperative opioids (if yes, which?)*: 219.8 µg fentanyl intraoperative, postoperative meperidine
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 29
- *Age (mean ± SD, median (IQR), median (range))*: 34.0 ± 8.6

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Naguib 1996 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 69.9 ± 13.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 86.21
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 129.5
- *Use of perioperative opioids (if yes, which?)*: 195.7 µg fentanyl intraoperative, postoperative meperidine
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, both sexes, 21 to 68 years of age, weighing 40 to 101 kg, undergoing elective laparoscopic cholecystectomy

Excluded criteria: receiving drugs known to have antiemetic effects (such as tricyclic antidepressants, scopolamine, phenothiazines, lorazepam, corticosteroids, and trimethobenzamide), had experienced nausea and vomiting or had taken antiemetic treatment in the 48 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: before induction and after establishment of venous access
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Tropisetron

- *Dose*: 5 mg
- *Time point of administration*: before induction and after establishment of venous access
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Granisetron

- *Dose*: 3 mg
- *Time point of administration*: before induction and after establishment of venous access
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: before induction and after establishment of venous access
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Placebo

- *Dose*: NaCl 0.9%
- *Time point of administration*: before induction and after establishment of venous access
- *Route of administration*: IV

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Naguib 1996 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Saudi Arabia **Setting:** inpatient, single-centre **Author's name:** Mohamed Naguib **Institution:** Department of Anaesthesia and ICU, King Khalid University Hospital, Riyadh, Saudi Arabia **Email:** F35A0O2@SAKSUO0 **Address:** Department of Anaesthesia and ICU, King Khalid University Hospital, PO Box 7805, Riyadh 11472, Saudi Arabia **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "all study drugs and placebo were diluted by a pharmacist to a fixed volume of 50 ml and marked only with a coded label to maintain the double-blind nature of the study and were administered intravenously over ten minutes''
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "all observations were by one anaesthetist who had been instructed in the study design and score system and who was unaware of the patients' group assignments"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Naguib 1996 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: quote: "there were no difference among the groups in age, weight, doses of intraoperative fentanyl, duration of anesthesia and recovery times, incidence and severity of pain, doses of meperidine administered for postoperative analgesia, times of postoperative ambulation or oral intake'' Baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Najeeb 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 53.33 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 84 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: major general surgery, plastic surgery, urological surgery Droperidol (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 4 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60

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Najeeb 2000 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 98
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major general surgery, plastic surgery, urological surgery

Granisetron (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 36 ± 3
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 73.33
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 87
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major general surgery, plastic surgery, urological surgery

Included criteria: ASA I and II; both sexes; 25 to 60 years of age; had to undergo general anaesthesia for major general surgery, plastic surgery, and urological surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear; (gender): yes

Interventions

Intervention characteristics

Placebo (group A)

- *Dose*: distilled water
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (group B)

- *Dose*: 2.5 mg
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Granisetron (group C)

- *Dose*: 3 mg
- *Time point of administration*: just before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

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Najeeb 2000 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Rukhsana Najeeb **Institution:** Department of Anaesthesiology SKIMS, Srinagar, India **Email:** NA **Address:** Department of Anaesthesiology SKIMS, Srinagar (Najeeb, Naqash, Shah, Kant) India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind study" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind study")
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Najeeb 2000 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the groups were comparable with regard to demographic data, type and duration of surgical procedure" Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear; (gender): yes

Nakata 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 26 • *Age (mean ± SD, median (IQR), median (range))*: 57 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 4/22/0/0 • *Gender (female in %)*: 57.69 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA + epidural anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 183 • *Use of perioperative opioids (if yes, which?)*: induction fentanyl, postoperative epidural injection of 2 mg morphine, continuous epidural infusion of morphine 4 mg/d post op for 4 days • *Type of surgery*: thoracic or abdominal surgery Droperidol (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 56 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 7/20/0/0 • *Gender (female in %)*: 44.44

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Nakata 2002 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA + epidural anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 163
- *Use of perioperative opioids (if yes, which?)*: induction fentanyl, postoperative epidural injection of 2 mg morphine, continuous epidural infusion of morphine 4 mg/d post op for 4 days
- *Type of surgery*: thoracic or abdominal surgery

Included criteria: ASA I and II, 16 to 70 years of age, scheduled for elective thoracic or abdominal surgery with combination general-epidural anaesthesia

Excluded criteria: recent use of opioids, history of convulsion, parkinsonism, drug abuse, psychiatric problems

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Control (group A) • *Dose*: normal saline • *Time point of administration*: 30 minutes after the start of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM Droperidol (group B) • *Dose*: 2.5 mg • *Time point of administration*: 30 minutes after the start of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM
Outcomes	*Extrapyramidal symptoms (0 to 4 days)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 4 days' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Yoshihiko Kishi **Institution:** Department of Anesthesiology, Osaka Medi cal Center for Cancer and Cardiovascular Diseases, Higashinari, Osaka, Japan **Email:** ykishi@anes. med.osaka-u.ac.jp **Address:** Department of Anesthesiology, Osaka Medi cal Center for Cancer and Cardiovascular Diseases, 1-3-3, Nakamichi, Higashinari, Osaka 537-8511, Japan **Duration of study:** NA **Language:** English **Study's primary outcome:** NA

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Nakata 2002 *(Continued)*

	Trial registry number: NA
Notes	Two out of 4 groups relevant (continuous infusion of droperidol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "via a computer random numbers table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "droperidol or normal saline was given within 30 minutes after the start of operation by an anesthesiologist who was blinded to the details of the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "...were evaluated at least twice in the first 24 hours and at least once until the fourth postoperative day by an anesthesiologist who was blinded to the study treatments"
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: quote: "epidural morphine was discontinued in 10 patients due to severe PONV (five patients), severe pruritus (two patients), excitement, and headache and respiratory depression (one patient each). These patients were also excluded from this study" Reasons for missing outcome data are related to the outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Nale 2007

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide (group II) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 35.85 (16 to 60) • *Weight (mean ± SD, median (IQR), median (range))*: 55.75 (41 to 70)

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Nale 2007 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 90
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 15/10
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: pentazocine
- *Type of surgery*: MTP, tubal ligation, resuturing, orchidectomy, cervical cerclage, fibro breast, cone biopsy, brachytherapy

Prochlorperazine (group III)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 33 (16 to 50)
- *Weight (mean ± SD, median (IQR), median (range))*: 59.4 (42 to 85)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 90
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 15/15
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: pentazocine
- *Type of surgery*: MTP, tubal ligation, resuturing, orchidectomy, cervical cerclage, fibro breast, cone biopsy, brachytherapy

Promethazine (group IV)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 34.9 (16 to 70)
- *Weight (mean ± SD, median (IQR), median (range))*: 55.4 (41 to 85)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 85
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 15/20
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: pentazocine
- *Type of surgery*: MTP, tubal ligation, resuturing, orchidectomy, cervical cerclage, fibro breast, cone biopsy, brachytherapy

Ondansetron (group V)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -

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Nale 2007 *(Continued)*

- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 33.75 (16 to 70)
- *Weight (mean ± SD, median (IQR), median (range))*: 58.15 (42 to 85)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 85
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 15/15
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: pentazocine
- *Type of surgery*: MTP, tubal ligation, resuturing, orchidectomy, cervical cerclage, fibro breast, cone biopsy, brachytherapy

Placebo (group VI)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 34.65 (21 to 80)
- *Weight (mean ± SD, median (IQR), median (range))*: 54.55 (40 to 75)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 85
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 20/25
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: pentazocine
- *Type of surgery*: MTP, tubal ligation, resuturing, orchidectomy, cervical cerclage, fibro breast, cone biopsy, brachytherapy

Included criteria: ASA I and II, patient posted for non-emergency surgery who had a potential for PONV (h/o motion sickness PONV during previous surgery), undergoing a surgical procedure known to have increased incidence of PONV (e.g. MTP, brachytherapy, gynaecological procedure)

Excluded criteria: procedures necessitating intubation or expected to last longer than 45 minutes

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide (group II) • *Dose*: 10 mg • *Time point of administration*: 1 hour before the surgical procedure and at subsequent 8-hour intervals for a total of 24 hours • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Prochlorperazine (group III)

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Nale 2007 *(Continued)*

- *Dose*: 5 mg
- *Time point of administration*: 1 hour before the surgical procedure and at subsequent 8-hour intervals for a total of 24 hours
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Promethazine (group IV)

- *Dose*: 20 mg
- *Time point of administration*: 1 hour before the surgical procedure and at subsequent 8-hour intervals for a total of 24 hours
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Ondansetron (group V)

- *Dose*: 4 mg
- *Time point of administration*: 1 hour before the surgical procedure and at subsequent 8-hour intervals for a total of 24 hours
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Placebo (group VI)

- *Dose*: empty capsules
- *Time point of administration*: 1 hour before the surgical procedure and at subsequent 8-hour intervals for a total of 24 hours
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Outcomes

Vomiting (0 to 6 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: India

Setting: inpatient, single-centre

Comments: repeated doses of antiemetics at subsequent 8-hour intervals for a total of 24 hours

Author's name: Ravikiran Nale

Institution: Department of Anaesthesia, Rural Medical College, Loni, Maharashtra, India

Email: NA

Address: Department of Anaesthesia, Rural Medical College, Loni, Maharashtra - 413 736, INDIA

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

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Nale 2007 *(Continued)*

Notes	Five out of 6 groups relevant Repetitive drug administration, vomiting 0 to 6 hours before second administration of drug Missing outcome data in promethazine group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "120 selected patients were randomly allocated to one of the six groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "to ensure double blinding of the study all the drugs were powdered and filled in similar looking capsules by the reporter were administered one hour prior the surgical procedure and subsequent at 8 hour intervals for a total of 24 hours" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the demographic features of all patients were comparable in our study" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

NCT00888329

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Aprepitant • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA

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NCT00888329 *(Continued)*

- *Randomized (n)*: 125
- *Received treatment (n)*: NA
- *Analysed (n)*: 35/34 (efficacy/safety)
- *Age (mean ± SD, median (IQR), median (range))*: 60 (12)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: standardized anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: hysterectomy

Placebo

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 131
- *Received treatment (n)*: NA
- *Analysed (n)*: 59/37 (efficacy/safety)
- *Age (mean ± SD, median (IQR), median (range))*: 53 (12)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: standardized anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: hysterectomy

Included criteria: scheduled for elective hysterectomy at Mayo Clinic in Arizona; ASA I, II, or III

Excluded criteria: pregnancy; concomitant bowel surgery other than appendectomy; hypersensitivity to study drug or rescue medication; preoperative score for nausea > 4 out of 10 points; severe hepatic insufficiency (Child-Pugh score > 9); any condition that impairs the patient's ability to complete study assessments; intraoperative haemodynamic instability; ICU admission; prolonged postoperative intubation; rifampin, carbamazepine, phenytoin, or other drugs that strongly induce CYP3A4 activity; other antiemetic within 12 hours before surgery; participation in a clinical trial using an investigational product

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker, perioperative opioids, duration of surgery): unclear

Interventions	**Intervention characteristics** Aprepitant • *Dose*: 40 mg • *Time point of administration*: before anaesthesia induction • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: NA

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NCT00888329 *(Continued)*

	Placebo • *Dose*: NA • *Time point of administration*: NA • *Route of administration*: NA • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** Mayo Clinic **Country:** USA **Setting:** inpatient/outpatient, single-centre **Author's name:** Javier Magrina **Institution:** Mayo Clinic, Phoenix, Arizona, United States, 85054, USA **Email:** magrina.javier@mayo.edu **Address:** Mayo Clinic, Phoenix, Arizona, United States, 85054, USA **Duration of study:** July 2007 to October 2011 **Language:** English **Study's primary outcome:** number of patients with emesis within 24 hours **Trial registry number:** NCT00888329
Notes	Results posted only on ClinicalTials.gov (study terminated due to slow accrual)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "results might have been influenced by selection bias“ (comment in limitations and caveats)
Allocation concealment (selection bias)	High risk	Quote "results might have been influenced by selection bias“ (comment in limitations and caveats)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote “masking: quadruple (participant, care provider, investigator, outcome assessor)” Judgement comment: no other statements
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote “masking: quadruple (participant, care provider, investigator, outcome assessor)” Judgement comment: no other statements
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote “primary outcome measure was not recorded for 84 participants in the Aprepitant group and 63 participants in the Placebo group” Judgement comment: substantial amount of missing data; no reason given

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NCT00888329 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00888329 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender): no; (history of ponv/motion sickness, non-smoker, perioperative opioids, duration of surgery): unclear

Nesek Adam 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 45.6 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: 73.0 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 25/10/0/0 • *Gender (female in %)*: 68.57 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 62.4 • *Use of perioperative opioids (if yes, which?)*: 204.3 µg fentanyl intraoperative, postoperative tramadol • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 41.8 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 70.5 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 27/8/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 61.4 • *Use of perioperative opioids (if yes, which?)*: 197.1 µg fentanyl intraoperative, postoperative tramadol

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Nesek Adam 2004 *(Continued)*

- *Type of surgery*: laparoscopic cholecystectomy

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 42.5 ± 15
- *Weight (mean ± SD, median (IQR), median (range))*: 73.7 ± 15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/11/0/0
- *Gender (female in %)*: 62.86
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 67.2
- *Use of perioperative opioids (if yes, which?)*: 211.4 µg fentanyl intraoperative, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 44.5 ± 15
- *Weight (mean ± SD, median (IQR), median (range))*: 71.5 ± 15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 25/10/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 68.0
- *Use of perioperative opioids (if yes, which?)*: 191.4 µg fentanyl intraoperative, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, undergoing general anaesthesia for elective laparoscopic cholecystectomy

Excluded criteria: previous allergic reactions to any of the protocol medications, had vomited or had received any antiemetic within 24 hours before surgery, pregnancy, history of smoking, conversion to open cholecystectomy

Pretreatment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 0.9% saline • *Time point of administration*: after induction of anaesthesia and at 12 hours • *Route of administration*: NA

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Nesek Adam 2004 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: after induction of anaesthesia and placebo at 12 hours
- *Route of administration*: NA
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol

- *Dose*: 2 × 1.25 mg
- *Time point of administration*: after induction of anaesthesia and at 12 hours
- *Route of administration*: NA
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide + droperidol

- *Dose*: metoclopramide 10 mg, droperidol 2 × 1.25 mg
- *Time point of administration*: metoclopramide after induction of anaesthesia, droperidol after induction of anaesthesia and at 12 hours
- *Route of administration*: NA
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours,)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Arrhythmia (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 4 hours, 4 to 12 hours, 12 to 24 hours, 0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Croatia

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Nesek Adam 2004 *(Continued)*

Setting: inpatient, single-centre

Author's name: Visnja Nesek-Adam

Institution: Department of Anesthesiology, Resuscitation, and Intensive Care, and University Department of Surgery, Sveti Duh General Hospital, Zagreb, Croatia

Email: tihomir.adam@zg.htnet.hr

Address: Department of Anesthesiology, Resuscitation, and Intensive Care, Sveti Duh General Hospital, Zagreb, Croatia

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	In 2 out of 4 groups repetitive doses of antiemetics were given after 12 hours; therefore only groups 1 and 2 are eligible (no repetitive doses)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized to one of the four medication groups" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "anesthetist technicians prepared the syringes" Judgement comment: no statement on blinding of anaesthetists and participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the nursing staff were blinded to the medication the patients had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): unclear

Nesek Adam 2007

Study characteristics

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Nesek Adam 2007 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 54.9 ± 15.5 • *Weight (mean ± SD, median (IQR), median (range))*: 71.8 ± 11.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/16/0/0 • *Gender (female in %)*: 67.5 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 68 • *Use of perioperative opioids (if yes, which?)*: 199 µg fentanyl, 2 patients received tramadol • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 49.4 ± 13.9 • *Weight (mean ± SD, median (IQR), median (range))*: 74.2 ± 14.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 26/14/0/0 • *Gender (female in %)*: 80 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 67 • *Use of perioperative opioids (if yes, which?)*: 188 µg fentanyl, 1 patient received tramadol • *Type of surgery*: laparoscopic cholecystectomy Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 49.6 ± 11.7 • *Weight (mean ± SD, median (IQR), median (range))*: 70.0 ± 12.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 25/15/0/0

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Nesek Adam 2007 *(Continued)*

- *Gender (female in %)*: 75
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 65
- *Use of perioperative opioids (if yes, which?)*: 199 µg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Dexamthasone + metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 50.9 ± 14.5
- *Weight (mean ± SD, median (IQR), median (range))*: 68.6 ± 10.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/18/0/0
- *Gender (female in %)*: 65
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66
- *Use of perioperative opioids (if yes, which?)*: 187 µg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, scheduled for elective laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: younger than 18 years of age; previous allergic reaction to any of the protocol medications; had vomited or had received any antiemetic within 24 hours before surgery; gastrointestinal, renal, or liver disease; pregnancy; smoking; history of motion sickness; conversion to open cholecystectomy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Placebo • *Dose*: 2 × saline 0.9% • *Time point of administration*: after induction of anaesthesia and at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 15% (thiethylperazine 10 mg) Metoclopramide • *Dose*: saline 0.9%, metoclopramide 10 mg • *Time point of administration*: metoclopramide at end of surgery; placebo after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (thiethylperazine 10 mg) Dexamethasone • *Dose*: dexamethasone 8 mg, saline 0.9%

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Nesek Adam 2007 *(Continued)*

- *Time point of administration*: dexamethasone after induction of anaesthesia; placebo at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 3 % (thiethylperazine 10 mg)

Dexamethasone + metoclopramide

- *Dose*: dexamethasone 8 mg, metoclopramide 10 mg
- *Time point of administration*: dexamethasone after induction of anaesthesia; metoclopramide at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 0% (thiethylperazine 10 mg)

Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Croatia **Setting:** inpatient, single-centre **Author's name:** V. Nesek-Adam **Institution:** Department of Anesthesiology, Resuscitation and Intensive Care, Sveti Duh General Hospital, Zagreb, Croatia **Email:** NA **Address:** Department of Anesthesiology, Resuscitation and Intensive Care, Sveti Duh General Hospital, Sveti Duh 64, Zagreb, 10000 Croatia **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None
Risk of bias	

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Nesek Adam 2007 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were allocated randomly to one of the four medication groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications were prepared by a technician anesthetist in identical 5-ml syringes and administered in a double-blind fashion. Each patient received two syringes, one just after the induction of anesthesia and the other at the end of surgery"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...by nursing staff without knowledge of which antiemetic the patients had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all 160 patients enrolled in the study had their surgical procedures completed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Ng 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: NA • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 49.2 ± 8.6 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 68.29 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Ng 2008 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 57.9
- *Use of perioperative opioids (if yes, which?)*: postoperative pethidine
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 48.6 ± 10.9
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 62.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 54.3
- *Use of perioperative opioids (if yes, which?)*: postoperative pethidine
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: symptomatic gallstones or benign gallbladder polyp scheduled for elective laparoscopic cholecystectomy, clinically and radiologically symptomatic gallstone disease, gallbladder polyps smaller than 1 cm, ASA I and II, between 18 and 70 years of age, postoperative home assistance available

Excluded criteria: body mass index > 28 kg/m^2, history of upper abdominal surgery, impaired liver function test, suspected biliary tree obstruction, concomitant pathology requiring additional surgical intervention, allergic to ondansetron, unsuccessful 2-port NC that included added ports or conversion to open surgery

Pretreatment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Control

- *Dose*: no treatment
- *Time point of administration*: at end of operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

ondansetron

- *Dose*: 8 mg
- *Time point of administration*: at end of operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Outcomes

Vomiting (0 to 4 hours)

- Outcome type: dichotomous outcome

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Ng 2008 *(Continued)*

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** China **Setting:** outpatient, multi-centre (2) **Author's name:** W.W.C. Ng **Institution:** Departments of Surgery and Anaesthesia, North District Hospital, Sheung Shui, Hong Kong SAR, China and Department of Surgery, Tuen Mun Hospital, Tuen Mun, Hong Kong SAR, China **Email:** lamyn@ha.org.hk **Address:** NA **Duration of study:** August 2003 to May 2004 **Language:** English **Study's primary outcome:** the degree of postoperative nausea and vomiting 4 hours after the operation **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients enrolled in the study. Randomisation was carried out at the end of the operation at the time of gallbladder retrieval by computer generated random number inside a numbered, sealed, opaque envelope. Patients were randomly allocated..."
Allocation concealment (selection bias)	Low risk	Quote: "patients enrolled in the study. Randomisation was carried out at the end of the operation at the time of gallbladder retrieval by computer generated random number inside a numbered, sealed, opaque envelope. Patients were randomly allocated..."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "...a numbered, sealed, opaque envelope. Patients were randomly allocated to receive either a single dose of ondansetron 8mg given intravenously or nothing immediately after randomisation. All patients received a standardised..." Judgement comment: no sham treatment. The anaesthesiologists knew the assignment. Randomization, however, was done at the end of the operation. Therefore, patients were blinded. It remains unclear whether unblinded anaesthesiologists could influence postoperative outcomes after randomization
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...conclusion of surgery. Post-operatively, a team of surgeon and nursing staff who were blinded to the study was responsible for managing these patients in the day surgery centres. Oral dologesic, ibuprofen or intramuscular..."
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Ng 2008 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...to the control group (C). Demographically, there was no statistically significant difference between the 2 groups (Table 1). The incidence of PONV..." Judgement comment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Nielsen 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: NA • *Analysed (n)*: 77 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 80 ± 17 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 45.45 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 51 • *Use of perioperative opioids (if yes, which?)*: 3.1 mg remifentanil at induction, 0.2 µg/kg sufentanil at end of operation, 36 mg morphine postoperative via PCA • *Type of surgery*: primary lumbar diskectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: NA • *Analysed (n)*: 76 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 79 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 34.21

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Nielsen 2015 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 60
- *Use of perioperative opioids (if yes, which?)*: 3.4 mg remifentanil at induction, 0.2 µg/kg sufentanil at end of operation, 36 mg morphine postoperative via PCA
- *Type of surgery*: primary lumbar diskectomy

Included criteria: undergoing one-level or two-level primary lumbar diskectomy during general anaesthesia, 18 to 85 years of age, ASA I to III, body mass index between 18 and 40 kg/m^2

Excluded criteria: inability to cooperate, inability to speak or understand Danish, previous spine surgery, pregnancy, allergy to drugs applied in the trial, daily use of systemic steroids or strong opioids (morphine, oxycodone, methadone, fentanyl, or ketobemidone), alcohol or drug abuse

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, Apfel's risk score): no

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 16 mg
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, droperidol if ondansetron was ineffective

Placebo

- *Dose*: saline
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV, droperidol if ondansetron was ineffective

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: the study was supported by the Department of Anaesthesiology, Glostrup University Hospital, Denmark

Country: Denmark

Setting: inpatient, single-centre

Author's name: Rikke V. Nielsen

Institution: Department of Anaesthesiology, Rigshospitalet, Glostrup University Hospital, Glostrup, Denmark

Email: rikkevibeke@gmail.com

Address: Department of Anaesthesiology, Rigshospitalet,Glostrup University Hospital, Nordre Ringvej 57, 2600 Glostrup, Denmark

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Duration of study: 7 December 2012 to 7 December 2014

Language: English

Study's primary outcome: primary outcome was pain during mobilization (visual analogue scale) 2 to 24 hours postoperatively

Trial registry number: NCT01953978

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed by the pharmacy according to a computer-generated block randomization list (each block containing 10 numbers), in a 1:1 ratio"
Allocation concealment (selection bias)	Low risk	Quote: "study medication was prepacked by the pharmacy in consecutively numbered boxes according to the computer-generated randomization list, containing identical 1 mL ampoules of either dexamethasone 4 mg/mL (Dexamethasone; GALEN-Pharma GmbH, Kiel, Germany) or isotonic sodium chloride 9 mg/ mL. After inclusion, patients were given the treatment corresponding to their randomization number and the corresponding box. Information about treatment was concealed in consecutively numbered, sealed, opaque envelopes to enable unblinding in case of acute complications"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the intervention was blinded to patients, investigators, surgeons, and clinical personnel"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: the intervention was blinded to patients, investigators, surgeons, and clinical personnel
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "three hundred ninety-nine consecutive patients were considered for inclusion and eventually, 160 patients were included and randomly assigned to the treatment or the placebo group. Seven patients were excluded, and consequently, 153 patients were included in the final analysis, 77 and 76 patients in the dexamethasone and placebo groups, respectively (Fig. 1)" Judgement comment: reasons for missing outcome data unrelated to the outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01953978 (retrospective registration)
Other bias	Unclear risk	Quote: "there were no significant differences in patient characteristics, or preoperative and perioperative characteristics between the 2 groups (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, Apfel's risk score): no

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NKO101287

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, different dose and route of administration, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron (group A) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 157 • *Received treatment (n)*: NA • *Analysed (n)*: 157/153 (efficacy/safety) • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 100 • *Type of general anaesthesia*: balanced anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 60 to 180 (overall) • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic/laparotomy, gynaecological surgery, laparoscopic cholecystectomy Ondansetron + vestipitant (group B) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 154 • *Received treatment (n)*: NA • *Analysed (n)*: 154/145 (efficacy/safety) • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 100 • *Type of general anaesthesia*: balanced anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 60 to 180 (overall) • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic/laparotomy, gynaecological surgery, laparoscopic cholecystectomy Ondansetron + vestipitant (group C) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 156 • *Received treatment (n)*: NA • *Analysed (n)*: 156/145 (efficacy/safety) • *Age (mean ± SD, median (IQR), median (range))*: NA

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- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 100
- *Type of general anaesthesia*: balanced anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 60 to 180 (overall)
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic/laparotomy, gynaecological surgery, laparoscopic cholecystectomy

Ondansetron + vestipitant (group D)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 154
- *Received treatment (n)*: NA
- *Analysed (n)*: 154/146 (efficacy/safety)
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 100
- *Type of general anaesthesia*: balanced anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 60 to 180 (overall)
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic/laparotomy, gynaecological surgery, laparoscopic cholecystectomy

Included criteria: female, known risk factors for PONV, undergoing gynaecological or gallbladder surgery, ASA I or II

1. Female with the following 3 risk factors:
- premenopausal or perimenopausal between the ages of 18 and 55 years, not of childbearing potential (i.e. physically incapable of becoming pregnant), demonstrating a negative serum or a negative urine pregnancy test within 24 hours before the first administration of study medication and agrees to:
- abstain from sexual intercourse for 2 weeks before administration of the first dose of study medication until 30 days after the final dose of study medication, or
- use hormonal methods of birth control (e.g. oral, injectable, implantable) or other highly effective method of contraception (e.g. an intrauterine device (IUD)) in conjunction with a barrier method of contraception (condom, spermicidal foam, sponge, gel, diaphragm) if engaging in sexual intercourse for at least 7 days before the first dose of study medication and continuing until 30 days after the final dose of study medication
- have never smoked or used (e.g. chewing) tobacco (including nicotine patches) for the previous 12 months
- have a history of postoperative nausea and vomiting and/or motion sickness
2. Undergoing a laparoscopic/laparotomy gynaecological surgical procedure or laparoscopic cholecystectomy that is scheduled for no less than 1 hour and no longer than 3 hours in duration. For the purposes of this study, “scheduled” is considered the duration of time that the surgical suite is blocked for the procedure (i.e. the operating room block time) or the duration of time in which it is anticipated that the subject will be in the operative preparation/operating room
3. Scheduled to receive general anaesthesia with an anaesthetic regimen as described in the Anesthetic Regimen (see Section 4.2., “Anesthetic and Analgesic Regimens”)
4. Meeting ASA Physical Status Classification of I or II preoperatively on the day of surgery

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5. Having haematology and blood chemistry values within acceptable limits (i.e. within 10% outside (either above or below) normal reference values, unless otherwise specified) for surgery, including, but not limited to:
- haemoglobin, hematocrit, total white blood cell count, platelet counts
- alkaline phosphatase, blood urea nitrogen or serum urea, electrolytes (sodium, potassium, chloride, bicarbonate)
- liver function tests (alanine aminotransferase (ALT) and aspartate aminotransferase (AST) < 1.5 times the upper limit of normal), serum creatinine (< 1.5 times the upper limit of normal), total bilirubin (< 1.5 times the upper limit of normal)
6. Able and willing to complete daily components of the subject diary preoperatively on the day of surgery and until the end of the 120-hour assessment period, and available to respond to follow-up by study personnel at the 120-hour study period post emergence from anaesthesia
7. Understanding the nature and purpose of this study and the study procedures and signed an informed consent form for this study to indicate this understanding

Excluded criteria:

1. Meeting ASA Physical Status Classification of III, IV, or V preoperatively on the day of surgery
2. Pregnant or lactating
3. Post-menopausal. If the last menstrual period was within the previous 18 months, a follicle-stimulating hormone (FSH) evaluation in the postmenopausal range will satisfy that the subject is post-menopausal
4. Scheduled to undergo only a laparoscopic biopsy
5. Scheduled to receive neuraxial anaesthesia (e.g. epidural, spinal, caudal anaesthesia) or total IV anaesthesia
6. Scheduled to receive propofol for maintenance of anaesthesia
7. Scheduled to have gastric contents suctioned continuously during the surgical procedure via a nasogastric tube, or a nasogastric or oral gastric tube during the postoperative period. A single pass at the beginning or at the end of the surgical procedure and intraoperative gastric suctioning of air are permitted
8. Taking more than 10 mg to 15 mg of oxycodone, or an equivalent opioid dose, on a regular, daily basis, for more than 3 consecutive days in the week before surgery
9. Received an investigational drug in the previous 30 days or scheduled to receive any investigational drug in addition to GW597599 during the study period
10. Persistent or recurrent nausea and/or vomiting due to other aetiologies, including, but not limited to, gastric outlet obstruction, hypercalcaemia, active peptic ulcer, increased intracranial pressure, or brain metastases
11. Experienced retching or vomiting or uncontrolled nausea within 48 hours before administration of the GW597599 study medications
12. Experienced significant nausea in the 24-hour period before receiving the GW597599 study medications
13. Received radiation therapy to the abdomen or the pelvis in the seven days before receiving study medications and/or will receive radiation therapy to the abdomen or the pelvis in the evaluation period
14. History of wound dehiscence
15. History of any other illness, which, in the opinion of the Investigator, may pose an unacceptable risk when study medication is administered
16. Any current or past medical condition (e.g. vagotomy) and/or requiring medication to treat a condition that could confound evaluation of the data collected in this clinical trial
17. Known hypersensitivity or contraindication to ondansetron hydrochloride or ondansetron, another 5-HT3 receptor antagonist, any scheduled anaesthetic or analgesic agents, or any component of GW597599
18. Known hypersensitivity to fentanyl and/or ketorolac tromethamine
19. Known allergy to eggs or egg products (component of propofol)
20. Scheduled to receive antiemetics not outlined in the study dosing scheme
21. Received medication with known or potential antiemetic activity within the 24-hour period before receiving study medications. This includes, but is not limited to:
- 5-HT3 receptor antagonists (e.g. ondansetron, granisetron, dolasetron, tropisetron, ramosetron). Palonosetron is not permitted for 7 days before the study
- benzamide/benzamide derivatives (e.g. metoclopramide, alizapride)
- benzodiazepines (except if the subject is receiving such medication for sleep and has been on a stable dose for at least 7 days before the first dose of study medication; however, lorazepam is prohibited)

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NKO101287 *(Continued)*

	- phenothiazines (e.g. prochlorperazine, promethazine, fluphenazine) **Pretreatment:** baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness): no, (perioperative opioids, duration of anaesthesia,): unclear
Interventions	**Intervention characteristics** Ondansetron (group A) • *Dose*: 4 mg, placebo • *Time point of administration*: before induction • *Route of administration*: ondansetron IV, placebo IV and PO • *Rescue antiemetics (if yes, which?)*: yes (NA) Ondansetron + vestipitant (group B) • *Dose*: ondansetron 4 mg, vestipitant 25 mg, placebo • *Time point of administration*: before induction • *Route of administration*: ondansetron IV, vestipitant PO, placebo IV • *Rescue antiemetics (if yes, which?)*: yes (NA) Ondansetron + vestipitant (group C) • *Dose*: ondansetron 4 mg, vestipitant 3 mg, placebo • *Time point of administration*: before induction • *Route of administration*: ondansetron IV, vestipitant IV, placebo PO • *Rescue antiemetics (if yes, which?)*: yes (NA) Ondansetron + vestipitant (group D) • *Dose*: ondansetron 4 mg, vestipitant 18 mg, placebo • *Time point of administration*: before induction • *Route of administration*: ondansetron IV, vestipitant IV, placebo PO • *Rescue antiemetics (if yes, which?)*: yes (NA)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (time point unknown)* • Outcome type: dichotomous outcome *Subjects with any AE (time point unknown)* • Outcome type: dichotomous outcome *Mortality (time point unknown)* • Outcome type: dichotomous outcome *Headache (time point unknown)* • Outcome type: dichotomous outcome *Constipation (time point unknown)* • Outcome type: dichotomous outcome

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NKO101287 *(Continued)*

	Adverse events (general notes in the publication, observation period unknown) • Outcome type: general notes on side effects
Identification	**Sponsorship source:** GlaxoSmithKline **Country:** international **Setting:** NA, multi-centre (49) **Author's name:** NA **Institution:** NA **Email:** NA **Address:** NA **Duration of study:** December 2004 to July 2006 **Language:** English **Study's primary outcome:** complete response in 24 hours **Trial registry number:** EUCTR2004-001021-22-FI
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “randomized” Judgement comment: no further statement
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: “double-blind” Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: “double-blind” Judgement comment: insufficient information on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: in total, 92% of participants completed the study (all assessments). No missing efficacy data. Missing data for safety outcomes < 15%. One participant was withdrawn due to AEs (ondansetron-vestipitant 3 mg group)
Selective reporting (reporting bias)	Low risk	Judgement comment: NCT00600990 (retrospective registration), EUCTR2004-001021-22-FI (prospective registration). The prospectively registered primary outcome (complete response in 24 hours) was reported in the pre-specified way in the final study report
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness):no; (perioperative opioids, duration of anaesthesia): unclear

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NKT102245

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, dose-finding study, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 146 • *Received treatment (n)*: NA • *Analysed (n)*: 146/141 (ITT/safety) • *Age (mean ± SD, median (IQR), median (range))*: 41.3 ± 7.2 • *Weight (mean ± SD, median (IQR), median (range))*: 64.69 ± 17.05 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 107/38/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 95 • *History of PONV/motion sickness (%)*: 41/84 • *Type of general anaesthesia*: balanced general anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 92 • *Use of perioperative opioids (if yes, which?)*: intraoperative morphine (43 patients), intraoperative fentanyl (70 patients), postoperative morphine (15 patients) • *Type of surgery*: laparoscopic gynaecological procedures, laparoscopic cholecystectomy Ondansetron + casopitant (50 mg group) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 144 • *Received treatment (n)*: NA • *Analysed (n)*: 144/140 (ITT/safety) • *Age (mean ± SD, median (IQR), median (range))*: 39.9 ± 7.31 • *Weight (mean ± SD, median (IQR), median (range))*: 65.13 ± 16.41 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 109/35/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 92 • *History of PONV/motion sickness (%)*: 42/78 • *Type of general anaesthesia*: balanced general anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 89 • *Use of perioperative opioids (if yes, which?)*: intraoperative morphine (48 patients), intraoperative fentanyl (63 patients), postoperative morphine (12 patients) • *Type of surgery*: laparoscopic gynaecological procedures, laparoscopic cholecystectomy Ondansetron + casopitant (150 mg group) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 145

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- *Received treatment (n)*: NA
- *Analysed (n)*: 145/144 (ITT/safety)
- *Age (mean ± SD, median (IQR), median (range))*: 39.1 ± 7.88
- *Weight (mean ± SD, median (IQR), median (range))*: 64.04 ± 16.89
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 109/36/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 92
- *History of PONV/motion sickness (%)*: 32/88
- *Type of general anaesthesia*: balanced general anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 87
- *Use of perioperative opioids (if yes, which?)*: intraoperative morphine (55 patients), intraoperative fentanyl (76 patients), postoperative morphine (15 patients)
- *Type of surgery*: laparoscopic gynaecological procedures, laparoscopic cholecystectomy

Included criteria: female, 18 to 55 years of age, ASA I or II, non-smoker, history of PONV/MS, standardized balanced general anaesthesia, laparoscopic gynaecological procedures or laparoscopic cholecystectomy

Excluded criteria: pregnant or breastfeeding, post-menopausal, neuraxial anaesthesia, with certain pre-existing medical conditions or taking certain medications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of surgery, perioperative opioids, history of PONV/motion sickness, non-smoker): no

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg, placebo • *Time point of administration*: ondansetron immediately before induction, placebo 60 minutes before induction of anaesthesia • *Route of administration*: ondansetron IV, placebo PO • *Rescue antiemetics (if yes, which?)*: many different antiemetics (36 patients) Ondansetron + casopitant (50 mg group) • *Dose*: ondansetron 4 mg, casopitant 50 mg • *Time point of administration*: ondansetron immediately before induction, casopitant 60 minutes before induction of anaesthesia • *Route of administration*: ondansetron IV, casopitant PO • *Rescue antiemetics (if yes, which?)*: many different antiemetics (30 patients) Ondansetron + casopitant (150 mg group) • *Dose*: ondansetron 4 mg, casopitant 150 mg • *Time point of administration*: ondansetron immediately before induction, casopitant 60 minutes before induction of anaesthesia • *Route of administration*: ondansetron IV, casopitant PO • *Rescue antiemetics (if yes, which?)*: many different antiemetics (38 patients)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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	Complete response (no PONV) in 24 hours • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** GlaxoSmithKline **Country:** international, 40 sites in 10 countries (United Kingdom, United States, Denmark, Slovenia, Norway, Hungary, Spain, Thailand, Hong Kong, and Phillippines) **Setting:** inpatient, multi-centre (39) **Author's name:** GSK Clinical Trials (NKT102245) **Institution:** GlaxoSmithKline **Email:** NA **Address:** NA **Duration of study:** 15 February 2005 to 23 August 2005 **Language:** English **Study's primary outcome:** complete response within 0 to 72 hours **Trial registry number:** NCT00274690, EUCTR2004-000369-37
Notes	Repeated doses of casopitant at days 2 and 3 postoperatively (only data from 0 to 24 hours are eligible); study report available on GSK study register

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: interactive voice response telephone-based system (RAMOS) was used for registration and randomization
Allocation concealment (selection bias)	Low risk	Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: tablet supplies were blinded. So neither the research pharmacist, the investigator, nor the subject would know whether the dose contained active or placebo investigational product
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: tablet supplies were blinded. So neither the research pharmacist, the investigator, nor the subject would know whether the dose contained active or placebo investigational product
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: in total, 93% of participants completed the study; reasons for withdrawal described and equally distributed among groups. AE was the reason for withdrawal for 2 subjects (ondansetron) and for 1 subject each in the casopitant-ondansetron groups
Selective reporting (reporting bias)	Low risk	Judgement comment: NCT00274690 (retrospective registration), EUCTR2004-000369-37 (prospective registration). The prospectively registered primary outcome (complete response in 72 hours) was reported in the pre-specified way in the final study report

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Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of surgery, perioperative opioids, history of PONV/motion sickness, non-smoker): no

NKT102260

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, dose-finding study, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 140 • *Received treatment (n)*: NA • *Analysed (n)*: 140/130 (ITT/safety) • *Age (mean ± SD, median (IQR), median (range))*: 39.3 ± 8.15 • *Weight (mean ± SD, median (IQR), median (range))*: 75.1 ± 18.27 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 66/66/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 79 • *History of PONV/motion sickness (%)*: 52/76 • *Type of general anaesthesia*: standardized balanced general anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 77,2 • *Use of perioperative opioids (if yes, which?)*: morphine (66 patients), hydromorphone (15 patients), fentanyl (18 patients), pethidine (13 patients) • *Type of surgery*: laparoscopic gynaecological procedures, laparoscopic cholecystectomy Casopitant + ondansetron (50 mg group) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 140 • *Received treatment (n)*: NA • *Analysed (n)*: 140/135 (ITT/safety) • *Age (mean ± SD, median (IQR), median (range))*: 38.1 ± 8.24 • *Weight (mean ± SD, median (IQR), median (range))*: 75.1 ± 17.32 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 69/67/1/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 86 • *History of PONV/motion sickness (%)*: 54/71 • *Type of general anaesthesia*: standardized balanced general anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 77 • *Use of perioperative opioids (if yes, which?)*: morphine (63 patients), hydromorphone (25 patients), fentanyl (17 patients), pethidine (10 patients) • *Type of surgery*: laparoscopic gynaecological procedures, laparoscopic cholecystectomy

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Casopitant + ondansetron (100 mg group)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 140
- *Received treatment (n)*: NA
- *Analysed (n)*: 140/134 (ITT/safety)
- *Age (mean ± SD, median (IQR), median (range))*: 39.5 ± 8.58
- *Weight (mean ± SD, median (IQR), median (range))*: 73.8 ± 19.66
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 77/61/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: 58/72
- *Type of general anaesthesia*: standardized balanced general anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80,5
- *Use of perioperative opioids (if yes, which?)*: morphine (66 patients), hydromorphone (31 patients), fentanyl (28 patients), pethidine (18 patients)
- *Type of surgery*: laparoscopic gynaecological procedures, laparoscopic cholecystectomy

Casopitant + ondansetron (150 mg group)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 140
- *Received treatment (n)*: NA
- *Analysed (n)*: 140/131 (ITT/safety)
- *Age (mean ± SD, median (IQR), median (range))*: 39.3 ± 7.84
- *Weight (mean ± SD, median (IQR), median (range))*: 74.6 ± 17.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 73/59/1/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 76
- *History of PONV/motion sickness (%)*: 54/69
- *Type of general anaesthesia*: standardized balanced general anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77,8
- *Use of perioperative opioids (if yes, which?)*: morphine (62 patients), hydromorphone (25 patients), fentanyl (14 patients), pethidine (14 patients)
- *Type of surgery*: laparoscopic gynaecological procedures, laparoscopic cholecystectomy

Casopitant

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 142
- *Received treatment (n)*: NA
- *Analysed (n)*: 142/132 (ITT/safety)
- *Age (mean ± SD, median (IQR), median (range))*: 38.5 ± 8.33
- *Weight (mean ± SD, median (IQR), median (range))*: 74.5 ± 17.84
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 65/66/2/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 78
- *History of PONV/motion sickness (%)*: 58/67

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- *Type of general anaesthesia*: standardized balanced general anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79,1
- *Use of perioperative opioids (if yes, which?)*: morphine (62 patients), hydromorphone (25 patients), fentanyl (16 patients), pethidine (16 patients)
- *Type of surgery*: laparoscopic gynaecological procedures, laparoscopic cholecystectomy

Included criteria: 18 to 55 years of age, ASA I or II, female, non-smoker, history of PONV/MS, standardized balanced general anaesthesia, laparoscopic gynaecological procedures or laparoscopic cholecystectomy

Excluded criteria: pregnant or breastfeeding, post-menopausal, neuraxial anaesthesia, certain pre-existing medical conditions or taking certain medications, TIVA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of surgery, perioperative opioids, history of PONV/motion sickness, non-smoker): no

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: ondansetron immediately before induction, placebo 60 minutes before induction • *Route of administration*: ondansetron IV, placebo PO • *Rescue antiemetics (if yes, which?)*: yes, if required (NA) Casopitant + ondansetron (50 mg group) • *Dose*: ondansetron 4 mg, casopitant 50 mg • *Time point of administration*: ondansetron immediately before induction, casopitant 60 minutes before induction • *Route of administration*: ondansetron IV, casopitant PO • *Rescue antiemetics (if yes, which?)*: yes, if required (NA) Casopitant + ondansetron (100 mg group) • *Dose*: ondansetron 4 mg, casopitant 100 mg • *Time point of administration*: ondansetron immediately before induction, casopitant 60 minutes before induction • *Route of administration*: ondansetron IV, casopitant PO • *Rescue antiemetics (if yes, which?)*: yes, if required (NA) Casopitant + ondansetron (150 mg group) • *Dose*: ondansetron 4 mg, casopitant 150 mg • *Time point of administration*: ondansetron immediately before induction, casopitant 60 minutes before induction • *Route of administration*: ondansetron IV, casopitant PO • *Rescue antiemetics (if yes, which?)*: yes, if required (NA) Casopitant • *Dose*: 150 mg • *Time point of administration*: placebo immediately before induction, casopitant 60 minutes before induction • *Route of administration*: casopitant PO, placebo IV • *Rescue antiemetics (if yes, which?)*: yes, if required (NA)
Outcomes	*Vomiting (0 to 24 hours)*

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- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Subjects with any SAE (0 to 5 days)

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 5 days)

- Outcome type: dichotomous outcome

Mortality (0 to 5 days)

- Outcome type: dichotomous outcome

Headache (0 to 5 days)

- Outcome type: dichotomous outcome

Constipation (0 to 5 days)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 5 days' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** GlaxoSmithKline **Country:** North America and Europe **Setting:** inpatient, multi-centre (53) **Author's name:** GSK Clinical Trials (NKT102260) **Institution:** GlaxoSmithKline **Email:** NA **Address:** NA **Duration of study:** 22 October 2004 to 9 August 2005 **Language:** English **Study's primary outcome:** complete response within 24 hours **Trial registry number:** EUCTR2004-000370-31-HU
Notes	Study report available on GSK study register

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: IVRS was used for randomization

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Allocation concealment (selection bias)	Low risk	Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: tablet supplies were blinded. So neither the research pharmacist, the investigator, nor the subject would know whether the dose contained active or placebo investigational product
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: tablet supplies were blinded. So neither the research pharmacist, the investigator, nor the subject would know whether the dose contained active or placebo investigational product
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: in total, 90% of participants completed the study; reasons for withdrawal are described and are equally distributed among groups. AE was the reason for withdrawal for 3 subjects (1 in ondansetron-casopitant 100 mg, 2 in casopitant 150 mg)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: EUCTR2004-000370-31, NCT00108095 (retrospective registration)
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of surgery, perioperative opioids, history of PONV/motion sickness, non-smoker): no

NKT102552

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 258 • *Received treatment (n)*: NA • *Analysed (n)*: 249 • *Age (mean ± SD, median (IQR), median (range))*: 46.4 ± 12.19 • *Weight (mean ± SD, median (IQR), median (range))*: 71.6 ± 17.99 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 83/171/1 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 100 • *Type of general anaesthesia*: standardized balanced general anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 95.6 • *Use of perioperative opioids (if yes, which?)*: morphine (75 patients), hydromorphone (29 patients), pethidine (30 patients), oxycodone (19 patients), piritramide (25 patients) • *Type of surgery*: certain abdominal, breast, thyroid, or shoulder surgery Casopitant + ondansetron

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- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 256
- *Received treatment (n)*: NA
- *Analysed (n)*: 244
- *Age (mean ± SD, median (IQR), median (range))*: 45.2 ± 12.6
- *Weight (mean ± SD, median (IQR), median (range))*: 70.7 ± 17.97
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 95/157/1
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 100
- *Type of general anaesthesia*: standardized balanced general anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 92,4
- *Use of perioperative opioids (if yes, which?)*: morphine (75 patients), hydromorphone (28 patients), pethidine (23 patients), oxycodone (28 patients), piritramide (18 patients)
- *Type of surgery*: certain abdominal, breast, thyroid, or shoulder surgery

Included criteria: over 18 years of age; ASA I or II; all 4 Apfel risk factors (female, non-smoker, history of PONV/MS, postoperative opioids); standardized balanced general anaesthesia; certain abdominal, breast, thyroid, or shoulder surgery

Excluded criteria: pregnant or breastfeeding, certain pre-existing medical conditions or taking certain medications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of surgery, perioperative opioids, history of PONV/motion sickness, non-smoker): no

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: placebo 15 minutes before induction, ondansetron immediately before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: many different antiemetics (72 patients) Casopitant + ondansetron • *Dose*: casopitant 30 mg, ondansetron 4 mg • *Time point of administration*: casopitant 15 minutes before induction, ondansetron immediately before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: many different antiemetics (61 patients)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (from first dose of drug to the final visit, time point unknown)*

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- Outcome type: dichotomous outcome

Subjects with any AE (from first dose of drug to the final visit, time point unknown)

- Outcome type: dichotomous outcome

Mortality (from first dose of drug to the final visit, time point unknown)

- Outcome type: dichotomous outcome

Headache (from first dose of drug to the final visit, time point unknown)

- Outcome type: dichotomous outcome

Constipation (from first dose of drug to the final visit, time point unknown)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, observation period unknown)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** GlaxoSmithKline **Country:** North America, Europe, and Asia (11 countries) **Setting:** inpatient, multi-centre (55) **Author's name:** GSK Clinical Trials (NKT102552) **Institution:** GlaxoSmithKline **Email:** NA **Address:** NA **Duration of study:** 22 March 2006 to 1 August 2006 **Language:** English **Study's primary outcome:** complete response within 24 hours **Trial registry number:** NCT00334152, EUCTR2005-005855-16-BE
Notes	Study report available on GSK study register

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: interactive voice response telephone-based system (RAMOS) was used for registration and randomization
Allocation concealment (selection bias)	Low risk	Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: casopitant supplies were blinded so that the research pharmacist, the investigator, nor the subject did not know whether the numbered box contained active or placebo investigational products

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NKT102552 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: casopitant supplies were blinded so that the research pharmacist, the investigator, nor the subject did not know whether the numbered box contained active or placebo investigational products
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: in total, 94% of participants completed the study; reasons for withdrawal were described and were equally distributed among groups. Only 1 subject was withdrawn due to an AE (casopitant-ondansetron group)
Selective reporting (reporting bias)	Low risk	Judgement comment: EUCTR2005-005855-16, NCT00334152 (prospective registration). The prospectively registered primary outcome (complete response in 72 hours) was reported in the pre-specified way in the final study report
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of surgery, perioperative opioids, history of PONV/motion sickness, non-smoker): no

Oksuz 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 75 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 37.48 ± 7.58 • *Weight (mean ± SD, median (IQR), median (range))*: 69.96 ± 11.36 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 1.36 ± 0.49 • *Gender (female in %)*: 72 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 8% (PONV) • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 82.2 • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: laparoscopic cholecystectomy Granisetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 39.37 ± 6.84

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Oksuz 2007 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 70.23 ± 10.68
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 1.33 ± 0.47
- *Gender (female in %)*: 64
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 12% (PONV)
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79.7
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 41.68 ± 7.01
- *Weight (mean ± SD, median (IQR), median (range))*: 68.52 ± 11.50
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 1.24 ± 0.44
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 8% (PONV)
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 81.6
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II; 21 to 72 years of age; 52 to 102 kg; free of cardiovascular, pulmonary, renal, hepatic, or neurological disease; undergoing elective laparoscopic cholecystectomy

Excluded criteria: receiving drugs known to have antiemetic effects such as tricyclic antidepressants, scopolamine, phenothiazines, lorazepam, corticosteroids, and trimethobenzamides; experienced nausea or vomiting; had received antiemetic treatment in the 48 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide • *Dose*: 10 mg • *Time point of administration*: 30 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide Granisetron • *Dose*: 40 µg/kg • *Time point of administration*: 30 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron Ondansetron

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Oksuz 2007 *(Continued)*

- *Dose*: 15 µg/kg
- *Time point of administration*: 30 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron

Outcomes	*Vomiting and retching (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting and retching (4 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** single-centre, inpatient **Author's name:** Hafize Oksuz **Institution:** Department of Anesthesiology and Reanimation, The Kahramanmaras Sutcu Imam University, University Medici Hospital, Kahramanmaras,Turkey. **Email:** drhoksuz@hotmail.com **Address:** Department of Anesthesiology and Reanimation, The Kahramanmaras Sutcu Imam University, University Medical School Hospital, 46050 Kahramanmaras, Turkey **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: no statement on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement on allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no information on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "all observations were done by one of the anesthetists who had been instructed in the study design and score system and who was unaware of the patients' group assignments"

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Oksuz 2007 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Olajumoke 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Pacebo (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 48 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: all patients had balanced general anaesthesia with halothane • *Duration of anaesthesia or surgery (in min; as mean or median)*: 163.2 • *Use of perioperative opioids (if yes, which?)*: postoperative tramadol • *Type of surgery*: total abdominal hysterectomy, myomectomy Dexamethasone (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 48 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Olajumoke 2013 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: all patients had balanced general anaesthesia with halothane
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 156
- *Use of perioperative opioids (if yes, which?)*: postoperative tramadol
- *Type of surgery*: total abdominal hysterectomy, myomectomy

Included criteria: 18 to 65 years of age, ASA I and II, scheduled for elective gynaecological procedure under general anaesthesia

Excluded criteria: requiring insertion of nasogastric tube intraoperatively or postoperatively

Pretreatment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Pacebo (group A) • *Dose*: 0.9% saline • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone (group B) • *Dose*: 4 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Headache (0 to 3 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 3 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 3 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 3 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Nigeria **Setting:** inpatient, single-centre **Author's name:** T.O. Olajumoke **Institution:** Department of Anaesthesia, Ladoke Akintola University of Technology, Teaching Hospital Osogbo, Osun State **Email:** busamide@yahoo.com

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Olajumoke 2013 *(Continued)*

Address: NA

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the patients were randomly assigned into two groups for the treatment of PONV by using table of random numbers"
Allocation concealment (selection bias)	High risk	Quote: "an anaesthesia resident and a pharmacist in the hospital prepared the medications in 2 ml syringes, A containing 2 ml normal saline and B containing 2 ml of 4mg of dexamethasone while the researcher was blinded. At induction of anaesthesia the contents of the labelled syringes were administered to patients by the researcher according to the alphabets A and B assigned to the patients" Judgement comment: high possibility to foresee the assignments by using an open random allocation schedule (list of random numbers, coding A and B)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "an anaesthesia resident and a pharmacist in the hospital prepared the medications in 2 ml syringes, A containing 2 ml normal saline and B containing 2 ml of 4 mg of dexamethasone while the researcher was blinded. At induction of anaesthesia the contents of the labelled syringes were administered to patients by the researcher according to the alphabets A and B assigned to the patients"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were subsequently assessed by the blinded investigator"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred patients participated in this study but four were disqualified for the following reasons: two had severe postoperative haemorrhage which required re-exploration, one had failed intubation and surgery was cancelled while the fourth had severe hypertension postoperatively necessitating the use of hydralazine intravenously in the postoperative period. Therefore only data from ninety six patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Olanders 2014

Study characteristics

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Olanders 2014 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Betamethasone • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 53 (35 to 65) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 26.0 (18 to 40) • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 77 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, 60% N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 95 • *Use of perioperative opioids (if yes, which?)*: 3.0 mg ketobemidone postoperative, 75 µg fentanyl intra-operative • *Type of surgery*: partial mastectomy Control • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 55 (31 to 66) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.3 (16 to 38) • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 76 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, 60% N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 97 • *Use of perioperative opioids (if yes, which?)*: 2,9 mg ketobemidone postoperative, 77 µg fentanyl intra-operative • *Type of surgery*: partial mastectomy **Included criteria:** ASA I and II, women 18 to 65 years of age, scheduled for elective partial mastectomy with or without axillary gland removal **Excluded criteria:** previous PONV events or severe travel sickness, medication with corticosteroids or neuroleptics, known allergy to any of the study drugs, neurological disease, pregnancy **Pretreatment:** baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, intraoperative opioids): no
Interventions	**Intervention characteristics**

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Olanders 2014 *(Continued)*

	Betamethasone • *Dose*: 8 mg • *Time point of administration*: before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Sweden **Setting:** inpatient, single-centre **Author's name:** Knut Olanders **Institution:** Department of Intensive-and Perioperative Care, Lund University Hospital **Email:** knut.olanders@skane.se **Address:** Department of Intensive and Perioperative Care, Lund University Hospital, S-221 85 Lund, Sweden **Duration of study:** NA **Language:** English **Study's primary outcome:** NRS scoring of nausea and pain **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated by sealed envelope assignment"
Allocation concealment (selection bias)	Unclear risk	Quote: "patients were randomly allocated by sealed envelope assignment to two groups" Judgement comment: insufficient information on whether allocation could be foreseen (SNOSE)

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Olanders 2014 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Group B received 8 mg of IV betamethasone before the start of surgery, whereas Group C received no PONV prophylaxis before surgery" Judgement comment: no blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the nursing staff in the recovery room, blinded to group allocation details"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 80 patients were included in the study, of whom 5 were excluded due to violation of the study protocol. Thirty-seven patients were allocated to the betamethasone group (Group B) and 38 patients to the control group (Group C)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, intraoperative opioids): no

Olatosi 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Promethazine • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 36.60 ± 6.07 • *Weight (mean ± SD, median (IQR), median (range))*: 67.80 ± 10.07 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 141.00 • *Use of perioperative opioids (if yes, which?)*: pentazocine • *Type of surgery*: myectomy 5, total abdominal hysterectomy 7, exploratory laparotomy 2, tuboplasty 1 Ondansetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA

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Olatosi 2008 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 35.56 ± 7.33
- *Weight (mean ± SD, median (IQR), median (range))*: 65.28 ± 11.99
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 135.40
- *Use of perioperative opioids (if yes, which?)*: pentazocine
- *Type of surgery*: myectomy 15, total abdominal hysterectomy 6, exploratory laparotomy 4,tuboplasty 0

Placebo

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 36.16 ± 7.09
- *Weight (mean ± SD, median (IQR), median (range))*: 66.28 ± 11.85
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 139.40
- *Use of perioperative opioids (if yes, which?)*: pentazocine
- *Type of surgery*: myectomy 13, total abdominal hysterectomy 8, exploratory laparotomy 4, tuboplasty 0

Included criteria: ASA I to III, between 18 and 65 years of age, scheduled for major gynaecological surgery under general anaesthesia

Excluded criteria: evidence of uncontrolled clinically important neurological, renal, hepatic, cardiovascular, metabolic, or endocrine dysfunction; scheduled to have a nasogastric tube in situ postoperatively; weighed less than 45 kg or more than 90 kg; pregnant or breastfeeding

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics**

Promethazine

- *Dose*: 25 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron

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Olatosi 2008 *(Continued)*

	• *Dose*: 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: 20 ml saline • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Nigeria **Setting:** inpatient, single-centre **Author's name:** John Olatosi **Institution:** Department of Anaesthesia, Lagos University Teaching Hospital **Email:** tola_olatosi@yahoo.com **Address:** Department of Anaesthesia, Lagos University Teaching Hospital, Idi-Araba, Lagos **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Olatosi 2008 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "the patients were randomly assigned by computer-generated balloting to one of three groups (A, B, C). The study..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "...and investigator blinding was ensured. The study drugs were drawn and labelled A, B or C (A – promethazine 25 mg, B – ondansetron 8 mg, and C – placebo) in sterile 20 ml syringes and made to equal volumes of 20 ml with normal saline. All the drugs were colourless" Judgement comment: because study drugs are labelled A, B, or C, anaesthetists may be aware of group allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "achieved with atropine and neostigmine. Postoperatively, the patients were evaluated for nausea and vomiting by a senior registrar blinded to the designated agent. Nausea and vomiting were assessed"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Ozdamar 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 47.1 ± 12.0 • *Weight (mean ± SD, median (IQR), median (range))*: 71.6 ± 13.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 9/12/4/0 • *Gender (female in %)*: 56 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 8/NA • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 96.8

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Ozdamar 2006 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 2076 µg remifentanil intraoperative, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron (group 2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 46.5 ± 14.7
- *Weight (mean ± SD, median (IQR), median (range))*: 73.3 ± 9.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 10/13/2/0
- *Gender (female in %)*: 64
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 4/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104.8
- *Use of perioperative opioids (if yes, which?)*: 1919 µg remifentanil intraoperative, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Ondansetron + dexamethasone (group 3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 44.2 ± 10.4
- *Weight (mean ± SD, median (IQR), median (range))*: 71.1 ± 8.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 13/11/1/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 16/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 111.4
- *Use of perioperative opioids (if yes, which?)*: 2222 µg remifentanil intraoperative, postoperative tramadol
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I to III, 18 to 75 years of age, undergoing elective cholecystectomy

Excluded criteria: antiemetic medication (e.g. tricyclic antidepressants, phenothiazines, lorazepam, corticosteroids), BMI > 30% of normal, ingestion of antiemetics in the last 48 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Dexamethasone (group 1)

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Ozdamar 2006 *(Continued)*

- *Dose*: 8 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ondansetron (group 2)

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Ondansetron + dexamethasone (group 3)

- *Dose*: ondansetron 4 mg + dexamethasone 8 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Dilek Özdamar **Institution:** Kocaeli Universitesi Tip FakUhesi Anesteziyoloji ve Reanimasyon **Email:** asozdmar@yahoo.com **Address:** University Department of Anaesthesiology and Reanimation Anabilim Dalt, Izmit **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly allocated" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Low risk	Judgement comment: quote: "drugs were administered by blinded researchers" (translated)

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Ozdamar 2006 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "outcome assessors were blinded" (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Ozmen 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Granisetron (group G) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 43.2 ± 6.4 • *Weight (mean ± SD, median (IQR), median (range))*: 74.1 ± 11.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 73.33 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 62.3 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl • *Type of surgery*: laparoscopic cholecystectomy Granisetron + droperidol (group GD) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 46.4 ± 7.3 • *Weight (mean ± SD, median (IQR), median (range))*: 76.1 ± 12.6

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Ozmen 2002 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 66.67
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 64.1
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I and II, undergoing elective laparoscopic cholecystectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Granisetron (group G) • *Dose*: 3 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Granisetron + droperidol (group GD) • *Dose*: granisetron 3 mg, 1.25 mg droperidol • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** S. Ozmen **Institution:** Department of Anaesthesiology and Reanimation, Faculty of Medicine **Email:** drfatih2000@hotmail.com **Address:** Hizirbey Mahallesi, 1556 Sokak, Yunusevler Yapi Kooperatifi, No: 7/8, 32100 Isparta, Turkey

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Ozmen 2002 *(Continued)*

	Duration of study: NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly assigned" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Ozunlu 2005

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA

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Ozunlu 2005 *(Continued)*

- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 33.6 ± 5.5
- *Weight (mean ± SD, median (IQR), median (range))*: 60.7 ± 10.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 56.0
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil
- *Type of surgery*: gynaecological laparoscopic surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 31.1 ± 5.1
- *Weight (mean ± SD, median (IQR), median (range))*: 58.0 ± 7.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 53.5
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: female, ASA I or II, 18 to 50 years of age, scheduled for day-case laparoscopic procedure, no pregnancy, at least secondary school level

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (25%) 10 mg metoclopramide Ondansetron • *Dose*: 4 mg ondansetron • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (10%) 10 mg metoclopramide

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Ozunlu 2005 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** outpatient, single-centre **Author's name:** Özlem Özünlü **Institution:** Ege Üni. Tip Fak. Anesteziyoloji ve Reanimasyon Anabilim Dali, Izmir **Email:** ozlemozunlu@liolmail.com **Address:** NA **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (propofol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "randomized by computer-generated codes" (translated)
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the preparation of the syringe was made by an independent researcher" (translated)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "outcomes were assessed by a blinded observer" (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Ozunlu 2005 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Paech 1995

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 83 • *Age (mean ± SD, median (IQR), median (range))*: 49 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 17 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 30/NA • *Type of general anaesthesia*: balanced anaesthesia (volatile anaesthetic, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 120 • *Use of perioperative opioids (if yes, which?)*: fentanyl (intraoperative and postoperative) • *Type of surgery*: major open abdominal gynaecological or gynaecological oncology surgery Droperidol (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 89 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 21/NA • *Type of general anaesthesia*: balanced anaesthesia (volatile anaesthetic, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 120 • *Use of perioperative opioids (if yes, which?)*: fentanyl (intraoperative and postoperative) • *Type of surgery*: major open abdominal gynaecological or gynaecological oncology surgery Placebo (group P)

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Paech 1995 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 87
- *Age (mean ± SD, median (IQR), median (range))*: 49 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 34/NA
- *Type of general anaesthesia*: balanced anaesthesia (volatile anaesthetic, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105
- *Use of perioperative opioids (if yes, which?)*: fentanyl (intraoperative and postoperative)
- *Type of surgery*: major open abdominal gynaecological or gynaecological oncology surgery

Included criteria: women, scheduled for major open abdominal gynaecological or gynaecological oncology surgery, no preoperative radiotherapy or chemotherapy drugs

Excluded criteria: women scheduled for bowel resection, with preoperative nausea or vomiting, on medication with antiemetic activity, underwent unplanned bowel, vaginal, or laparoscopic surgery

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 8 mg • *Time point of administration*: immediately post induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Droperidol (group D) • *Dose*: 2.5 mg • *Time point of administration*: immediately post induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Placebo (group P) • *Dose*: 0.9% NaCl • *Time point of administration*: immediately post induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (in the recovery room)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)*

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Paech 1995 *(Continued)*

- Outcome type: dichotomous outcome

Headache (at 24 hours)

- Outcome type: dichotomous outcome

Visual disturbances (e.g. blurred vision) (at 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this study was supported by a research grant from the King Edward Memorial Hospital Foundation for Women's and Infants' Health **Country:** Australia **Setting:** inpatient, single-centre **Author's name:** M.J. Paech **Institution:** King Edward Memorial Hospital for Women, Perth, Western Australia **Email:** NA **Address:** Department of Anaesthesia, King Edward Memorial Hospital, 374 Bagot Road, Subiaco, W.A. 6008 **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of vomiting in the first 24 hours postoperatively **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "according to a computer-derived random number sequence"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: quote: "the study drug, only known to the attending anaesthetist who took no further part in the study, was administered IV"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "nursing staff recorded the time of vomiting or retching episodes" No further information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "two hundred and seventy women were enrolled and eleven excluded from analysis, due to vaginal or bowel surgery (6), protocol violation (2), inadequate data collection (2) and premature dislodgement

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Paech 1995 *(Continued)*

		of an extradural catheter (1). Included in the analysis of 259 sets (group O, n=83; group D, n=89; group P, n=87) were 15 women who requested withdrawal due to intractable PONV not responding to rescue antiemetic. One came from group O versus six and eight from groups D and P respectively"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Paech 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dolasetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 33 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 66 • *History of PONV/motion sickness (%)*: 30/34 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 30 • *Use of perioperative opioids (if yes, which?)*: 21 mg morphine, 32 patients received postoperative opioids • *Type of surgery*: gynaecological laparoscopy Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 47 • *Age (mean ± SD, median (IQR), median (range))*: 30 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 18 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA

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Paech 2002 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: 60
- *History of PONV/motion sickness (%)*: 16/38
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 30
- *Use of perioperative opioids (if yes, which?)*: 20 mg morphine, 22 patients received postoperative opioids
- *Type of surgery*: gynaecological laparoscopy

Included criteria: un-premedicated patients scheduled for day-case gynaecological laparoscopy

Excluded criteria: contraindications or allergies to any drugs used in the study, current symptoms of nausea or vomiting, treatment with drugs with antiemetic activity, patient preference for premedication, change in surgical procedure that inpatient admission was required on surgical grounds

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dolasetron • *Dose*: 12.5 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: first prochlorperazine 12.5 mg, second droperidol 1 mg, third ondansetron 4 mg Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: first prochlorperazine 12.5 mg, second droperidol 1 mg, third ondansetron 4 mg
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (discharge to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Australia **Setting:** outpatient, single-centre **Author's name:** M. J. Paech **Institution:** Department of Anaesthesia, King Edward Memorial Hospital for Women, and Women and Infants Research Foundation, Perth, Western Australia **Email:** NA **Address:** Department of Anaesthesia,King Edward Memorial Hospital for Women, 374 Bagot Rd, Subiaco. W.A. 6008 **Duration of study:** NA

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Paech 2002 *(Continued)*

	Language: English **Study's primary outcome:** incidence of complete response, defined as the absence of vomiting and treatment for either nausea or vomiting **Trial registry number:** NA
Notes	Two out of 3 groups relevant (different anaesthesia regimens)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "randomized according to a computer-generated random number sequence"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "using a sealed envelope technique" Not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: quote: "patients were unaware of their group allocation... but anaesthetic chart detailing anaesthetic drugs administered was not concealed" Due to different interventions, anaesthesiologists cannot be unaware of group allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "postoperative nursing staff and research nurses collection data were blind to the use of antiemetic"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "data was not available for five patients, four due to hospital admission following more complex surgery and one in whom it was not collected after a major protocol violation"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Paech 2003

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 42 • *Received treatment (n)*: NA

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Paech 2003 *(Continued)*

- *Analysed (n)*: 42
- *Age (mean ± SD, median (IQR), median (range))*: 49.4 ± 14.1
- *Weight (mean ± SD, median (IQR), median (range))*: 79.3 ± 22.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 42.9/14.3
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: epidural postoperative infusion with 4 µg/mL fentanyl (140 mL)
- *Type of surgery*: major open abdominal gynaecological or gynaecological oncological procedure

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 38
- *Received treatment (n)*: NA
- *Analysed (n)*: 36
- *Age (mean ± SD, median (IQR), median (range))*: 48.3 ± 12.3
- *Weight (mean ± SD, median (IQR), median (range))*: 74.6 ± 15.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 30.6/22.2
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95
- *Use of perioperative opioids (if yes, which?)*: epidural postoperative infusion with 4 µg/mL fentanyl (143 mL)
- *Type of surgery*: major open abdominal gynaecological or gynaecological oncological procedure

Dolasetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 48.7 ± 14.4
- *Weight (mean ± SD, median (IQR), median (range))*: 74.4 ± 16.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 27.5/20.0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 92
- *Use of perioperative opioids (if yes, which?)*: epidural postoperative infusion with 4 µg/mL fentanyl (144 mL)
- *Type of surgery*: major open abdominal gynaecological or gynaecological oncological procedure

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Paech 2003 *(Continued)*

	Included criteria: scheduled for major open abdominal gynaecological or gynaecological oncological procedure **Excluded criteria:** experiencing preoperative nausea, receiving medication with antiemetic activity or with contraindications to non-steroidal anti-inflammatory medication or epidural anaesthesia, women in whom an open procedure was not performed or who underwent unplanned bowel surgery **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Tropisetron • *Dose*: 2 mg • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM, droperidol 1 mg IV Ondansetron • *Dose*: 4 mg • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM, droperidol 1 mg IV Dolasetron • *Dose*: 12.5 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM, droperidol 1 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (recovery room)* • Outcome type: dichotomous outcome *Vomiting (18 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** a small proportion of each study drug was supplied free by the respective pharmaceutical companies (Novartis for tropisetron, GlaxoWellcome for ondansetron, Hoechst Marion Roussel for dolasetron) **Country:** Australia

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Paech 2003 *(Continued)*

Setting: inpatient, single-centre

Author's name: M. J. Peach

Institution: Department of Anaesthesia and Pain Medicine, King Edward Memorial Hospitalfor Women and Women and Infants Research Foundation, Perth, Western Australia

Email: NA

Address: King Edward Memorial Hospital for Women, 374 Bagot Road, Subiaco, W.A. 6008

Duration of study: NA

Language: English

Study's primary outcome: incidence of vomiting

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "using a computer-derived randomisation sequence"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "in blinded envelopes" Not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: quote: "the study drugs, known only to the attending anaesthetist who took no part in the collection of subsequent data"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the study drug, known only to the attending anaesthetist who took no part in the collection of subsequent data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "a total of 120 patients were recruited into the study. Excluded from analysis were two patients from group O, one of whom did not have the procedure and one who was transferred to an intensive care unit postoperatively, precluding data collection"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

PALO-04-07

Study characteristics

Methods	**Study design:** randomized controlled trial

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PALO-04-07 *(Continued)*

Study grouping: 4 groups, dose-finding study, monoprophylaxis

Participants

Baseline characteristics

Placebo

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 136
- *Received treatment (n)*: NA
- *Analysed (n)*: 168/90 (safety/efficacy)
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: elective gynaecological or breast surgery

Palonosetron (0.025 mg group)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 136
- *Received treatment (n)*: NA
- *Analysed (n)*: 168/88 (safety/efficacy)
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: elective gynaecological or breast surgery

Palonosetron (0.05 mg group)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 136
- *Received treatment (n)*: NA
- *Analysed (n)*: 169/96 (safety/efficacy)
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100

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PALO-04-07 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: elective gynaecological or breast surgery

Palonosetron (0.075 mg group)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 136
- *Received treatment (n)*: NA
- *Analysed (n)*: 168/95 (safety/efficacy)
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: elective gynaecological or breast surgery

Included criteria: female, at least 18 years of age, ASA I to III, undergoing elective gynaecological or breast surgery under general anaesthesia that was expected to last a minimum of 1 hour and requires hospitalization of at least 72 hours. Patients must provide written informed consent and have at least 1 of the 2 following PONV risk factors: (1) history of PONV and/or currently prone to motion sickness; (2) non-smoking status. Scheduled to receive nitrous oxide as part of the maintenance phase of the anaesthesia

Excluded criteria: any drug with potential antiemetic efficacy within 24 hours before anaesthetic procedures; any vomiting, retching, or nausea in the 24 hours preceding anaesthesia; scheduled to receive nasogastric suctioning postoperatively; body mass index (BMI) > 40; known hypersensitivity/contraindication to 5-HT3 antagonists or study drug excipients

Pretreatment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender): no, (perioperative opioids, duration of anaesthesia, non-smoker, history of PONV/motion sickness): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: before start of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Palonosetron (0.025 mg group) • *Dose*: 0.025 mg • *Time point of administration*: before start of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA

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PALO-04-07 *(Continued)*

	Palonosetron (0.05 mg group) • *Dose*: 0.025 mg • *Time point of administration*: before start of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Palonosetron (0.075 mg group) • *Dose*: 0.025 mg • *Time point of administration*: before start of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 3 days)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 3 days)* • Outcome type: dichotomous outcome *Mortality (during the study)* • Outcome type: dichotomous outcome *Constipation (0 to 3 days)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, observation period unknown)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Helsinn Healthcare SA **Country:** Czech Republic, Germany **Setting:** inpatient, multi-centre (28) **Author's name:** NA **Institution:** NA **Email:** NA **Address:** DNA **Duration of study:** August 2005 to May 2006 **Language:** English **Study's primary outcome:** complete response **Trial registry number:** EUCTR2005-000298-23-CZ
Notes	Summary on EUCTR reported
Risk of bias	

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PALO-04-07 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "stratified, balanced" Judgement comment: no other comment
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: blinding was broken in part but steps were taken accordingly to ensure that there is no influence on results
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: blinding was broken in part but steps were taken accordingly to ensure that there is no influence on results
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: missing outcome data balanced across groups with reasons provided
Selective reporting (reporting bias)	Low risk	Judgement comment: EUCTR2005-000298-23 (prospective registration). The prospectively registered primary outcome (complete response) was reported in the pre-specified way in the final study report
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender): no; (perioperative opioids, duration of anaesthesia, non-smoker, history of PONV/motion sickness): unclear

Pan 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 32 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 34 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 81 ± 24 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 100 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)

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Pan 2008 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 64
- *Use of perioperative opioids (if yes, which?)*: 208 µg fentanyl intraoperative, 106 µg fentanyl PACU
- *Type of surgery*: laparoscopic gynaecological

Dexamethasone + ondansetron

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 32
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 35 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 79 ± 25
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 100
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 65
- *Use of perioperative opioids (if yes, which?)*: 215 µg fentanyl intraoperative, 109 µg fentanyl PACU
- *Type of surgery*: laparoscopic gynaecological

Included criteria: ASA I or II, women undergoing outpatient laparoscopic gynaecological surgery with GA, over 18 years of age, non-smoker, history of PONV or motion sickness, willing to complete the daily diary and be interviewed

Excluded criteria: history of allergy to study medications, pregnancy, nausea or vomiting or receiving any antiemetic drugs within 24 hours before anaesthetic induction, long-term opioid use, BMI > 45

Pretreatment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids, duration of anaesthesia): no

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 2 ml saline, ondansetron 4 mg • *Time point of administration*: immediately after successful intubation, 15 minutes before tracheal extubation at end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: promethazine 25 mg to 50 mg Dexamethasone 8 mg + ondansetron 4 mg • *Dose*: dexamethasone 8 mg, ondansetron 4 mg • *Time point of administration*: immediately after successful intubation, 15 minutes before tracheal extubation at end of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: promethazine 25 mg to 50 mg
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this is an investigator-initiated research study. It is, in part, supported by a research grant from GlaxoSmithKline

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Pan 2008 *(Continued)*

Country: USA

Setting: outpatient, single-centre

Author's name: Peter H. Pan

Institution: Department of Anesthesiology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC, USA

Email: ppan@wfubmc.edu

Address: Department of Anesthesiology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA

Duration of study: NA

Language: English

Study's primary outcome: incidence of post-discharge nausea and vomiting

Trial registry number: NA

Notes	Only data during PACU are relevant because patients received ondansetron routinely after discharge from PACU

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a computer-generated random-number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "the randomization was concealed before consent and remained double-blind and concealed until after completion of the study" Judgement comment: no statement on how randomization was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the patients, the investigators administering the medications, collecting data, or interviewing the patients, and all the health care providers involved in the direct care of the patients were blinded to the patient group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients, the investigators administering the medications, collecting data, or interviewing the patients, and all the health care providers involved in the direct care of the patients were blinded to the patient group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "percentages as appropriate. Sixty-four patients were enrolled in the study. However, four patients (2 in the control group and 2 in the investigation treatment group) were excluded from final data analysis for the following reasons: 1 patient had a protocol violation due to difficult intubation, one had emetic symptoms within 24 hours before surgery, and 2 had a change of surgical plan. Of the remaining 60 evaluable patients, each group had 30 patients. Data analysis was conducted and results reported were obtained from the full data set of all 60 evaluable patients without missing or excluded data. All patients in both groups..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Pan 2008 *(Continued)*

Other bias	Low risk	Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids, duration of anaesthesia): no

Pandit 1989

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 7 groups, monoprophylaxis and combination prophylaxis, dose-finding study
Participants	**Baseline characteristics** Metoclopramide (5 mg group) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 30.3 ± 6.59 • *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 68.0 • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: laparoscopy Metoclopramide (10 mg group) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 31.1 ± 7.11 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 67.0 • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: laparoscopy Droperidol (5 µg/kg group)

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Pandit 1989 *(Continued)*

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 30.0 ± 7.24
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 16
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 69.8
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopy

Droperidol (10 µg/kg group)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 30.3 ± 5.65
- *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: Inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 71.5
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopy

Droperidol (20 µg/kg group)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 29.0 ± 5.68
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 65.1
- *Use of perioperative opioids (if yes, which?)*: fentanyl

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Pandit 1989 *(Continued)*

- *Type of surgery*: laparoscopy

Placebo

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 31.5 ± 4.49
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 16
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 64.8
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopy

Metoclopramide + droperidol

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 29.0 ± 6.51
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 65.0
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: laparoscopy

Included criteria: female, ASA I or II, scheduled for an outpatient laparoscopy, participated in this study

Excluded criteria: NA

Pretreatment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide (5 mg group) • *Dose*: 5 mg • *Time point of administration*: 30 minutes before induction of anaesthesia, placebo 2 minutes before induction • *Route of administration*: orally, placebo IV

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Pandit 1989 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: prochlorperazine 5 mg, droperidol 0.6 mg

Metoclopramide (10 mg group)

- *Dose*: 10 mg
- *Time point of administration*: 30 minutes before induction of anaesthesia, placebo 2 minutes before induction
- *Route of administration*: orally, placebo IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 5 mg, droperidol 0.6 mg

Droperidol (5 µg/kg group)

- *Dose*: 5 µg/kg
- *Time point of administration*: 2 minutes before induction of anaesthesia, placebo 30 minutes before induction of anaesthesia
- *Route of administration*: IV, placebo orally
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 5 mg, droperidol 0.6 mg

Droperidol (10 µg/kg group)

- *Dose*: 10 µg/kg
- *Time point of administration*: 2 minutes before induction of anaesthesia, placebo 30 minutes before induction of anaesthesia
- *Route of administration*: IV, placebo orally
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 5 mg, droperidol 0.6 mg

Droperidol (20 µg/kg group)

- *Dose*: 20 µg/kg
- *Time point of administration*: 2 minutes before induction of anaesthesia, placebo 30 minutes before induction of anaesthesia
- *Route of administration*: IV, placebo orally
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 5 mg, droperidol 0.6 mg

Placebo

- *Dose*: NA
- *Time point of administration*: 30 minutes and 2 minutes before induction of anaesthesia
- *Route of administration*: orally/IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 5 mg, droperidol 0.6 mg

Metoclopramide + droperidol

- *Dose*: metoclopramide 10 mg, droperidol 10 µg/kg
- *Time point of administration*: metoclopramide 30 minutes before induction of anaesthesia; droperidol 2 minutes before induction of anaesthesia
- *Route of administration*: metoclopramide orally; droperidol IV
- *Rescue antiemetics (if yes, which?)*: prochlorperazine 5 mg, droperidol 0.6 mg

Outcomes	*Vomiting (in the PACU)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA

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Pandit 1989 *(Continued)*

Setting: outpatient, single-centre

Author's name: Sujit K. Pandit

Institution: Department of Anesthesiology, University of Michigan Medical Center, Ann Arbor, MI, USA

Email: NA

Address: Department of Anesthesiology, University of Michigan Medical Center, 1500 East Medical Center Drive, Box 0048, Ann Arbor, MI 48109, USA

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "following a computer- generated random list."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: insufficient information on allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "a nurse not involved in any of the subsequent evaluations, dispensed and administered the medications"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the same blinded observer (SPK) performed all the assessments in the recovery room and conducted telephone follow-up after 24 hours"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Papadima 2013

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis

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Papadima 2013 *(Continued)*

Participants

Baseline characteristics

Granisetron + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: NA
- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 49 ± 14.1
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 9.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 80
- *Non-smoker (%)*: 71
- *History of PONV/motion sickness (%)*: 8/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 113.8
- *Use of perioperative opioids (if yes, which?)*: remifentanil, meperidine
- *Type of surgery*: total thyroidectomy

Tropisetron + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 48 ± 13.2
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 8.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 77.5
- *Non-smoker (%)*: 79
- *History of PONV/motion sickness (%)*: 18/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 128.4
- *Use of perioperative opioids (if yes, which?)*: remifentanil, meperidine
- *Type of surgery*: total thyroidectomy

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 42
- *Received treatment (n)*: NA
- *Analysed (n)*: 42
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 14.8
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 9.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 78.5
- *Non-smoker (%)*: 67
- *History of PONV/motion sickness (%)*: 14/NA

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Papadima 2013 *(Continued)*

- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 127.1
- *Use of perioperative opioids (if yes, which?)*: remifentanil, meperidine
- *Type of surgery*: total thyroidectomy

Included criteria: male or female patients scheduled for total thyroidectomy under general anaesthesia, between 18 and 75 years of age, ASA I or II

Excluded criteria: known hypersensitivity to 5-HT3 drugs; body mass index (BMI) ≥ 35; significant systemic disease; history of atypical or known gastrointestinal problems and/or previous gastrointestinal operations (not including appendectomy); menstruation on admission; history of tinnitus; reception of steroids, H2 antagonists, anticholinergics, antihistamines, butyrophenones, phenothiazines, or metoclopramide 24 hours before admission; intrathoracic goiter or undergoing a difficult endotracheal intubation (more than 2 attempts at tracheal intubation)

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (perioperative opioids): unclear; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Granisetron + droperidol • *Dose*: granisetron 3 mg, droperidol 0.625 mg • *Time point of administration*: approximately 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Tropisetron + droperidol • *Dose*: tropisetron 5 mg, droperidol 0.625 mg • *Time point of administration*: approximately 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Droperidol • *Dose*: 0.625 mg, saline • *Time point of administration*: approximately 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** no grants or funds from pharmaceutical companies were acquired **Country:** Greece **Setting:** inpatient, single-centre **Author's name:** Stavros Gourgiotis

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Papadima 2013 *(Continued)*

Institution: Departments of Anesthesiology, Hippocrateion Hospital, Surgical, 401 General Army Hospital of Athens, Propedeutic Surgery, Hippocrateion Hospital, Athens Medical School, University of Athens, Athens, Greece

Email: drsgourgiotis@tiscali.co.uk

Address: 41 Zakinthinou Street, 15669, Papagou, Athens, Greece

Duration of study: January 2009 until January 2010

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "study patients were enrolled and randomized with Bernoulli tables (which allow “complete” or “unrestricted” randomization, minimizing both selection and accidental biases), to receive prophylactic either intravenous"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the anesthesiologist and staff nurses, as well as the operative team, were blinded to the administered agent"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients and investigators collecting the data were blinded to the patient’s group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "during the study period, 127 patients were enrolled and randomized into the granisetron (G group, n=45), tropisetron (T group, n=40), or the control group (C group, n=42)..." Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the three groups were homogenous in respect to age, gender, weight, height, and operative time as well as to all the usually recognized risk factors for PONV (female sex, history of motion sickness and/or previous PONV, nonsmoking status) [Table 1]. Anesthesia time was significantly lower in the granisetron group [Table 1]" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, non-smoker): no; (perioperative opioids): unclear; (duration of anaesthesia): yes

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Papadimitriou 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 57 • *Received treatment (n)*: 57 • *Analysed (n)*: 57 • *Age (mean ± SD, median (IQR), median (range))*: 36.5 ± 5.8 • *Weight (mean ± SD, median (IQR), median (range))*: 65.5 ± 5.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 67 • *History of PONV/motion sickness (%)*: 9/0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 74.0 • *Use of perioperative opioids (if yes, which?)*: fentanyl, codeine • *Type of surgery*: laparoscopic gynaecological surgery Tropisetron + metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 63 • *Received treatment (n)*: 63 • *Analysed (n)*: 63 • *Age (mean ± SD, median (IQR), median (range))*: 36 ± 5.6 • *Weight (mean ± SD, median (IQR), median (range))*: 65.9 ± 6.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 65 • *History of PONV/motion sickness (%)*: 11/0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 75.2 • *Use of perioperative opioids (if yes, which?)*: fentanyl, codeine • *Type of surgery*: laparoscopic gynaecological surgery **Included criteria:** female patients scheduled for minor gynaecological laparoscopy (i.e. ovarian cystectomy, tubal sterilization, or surgery for hydrosalpinx), ASA I or II, not pregnant **Excluded criteria:** gastrointestinal or liver disease, history of motion sickness, Parkinson's disease, had received antiemetic medication the day before surgery, menstruating or had a history of premenstrual syndrome (PMS) or were under hormonal therapy **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

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Papadimitriou 2001 *(Continued)*

Interventions	**Intervention characteristics** Metoclopramide • *Dose*: 10 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16% (metoclopramide 10 mg) Tropisetron + metoclopramide • *Dose*: metoclopramide 5 mg, tropisetron 5 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 3% (metoclopramide 10 mg)
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to discharge)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Greece **Setting:** inpatient, single-centre **Author's name:** L. Papadimitriou **Institution:** The Anaesthesiology Unit, Aretaieion Hospital, 115 28 Athens, Greece **Email:** NA **Address:** 8 Iassiou Street, 115 21, Athens, Greece **Duration of study:** September 1997 to March 2000 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Papadimitriou 2001 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated by means of a prearranged list to receive pretreatment" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "drugs were prepared in identical syringes by staff who were not involved in the study. The anaesthetist and investigator were unaware of the drug administered"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "data were collected by experienced trained personnel who were unaware of which treatment the patient had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients' demographic and baseline characteristics including age, body weight, history of previous PONV, duration of anaesthesia, operation and recovery time were similar in the two groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Park 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group 1 thiopental induction) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: NA • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 10.2 • *Weight (mean ± SD, median (IQR), median (range))*: 63.2 ± 8.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60.9 • *Non-smoker (%)*: NA

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Park 2006 *(Continued)*

- *History of PONV/motion sickness (%)*: 2.4/21.9
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 70.2
- *Use of perioperative opioids (if yes, which?)*: intraoperative alfentanil
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide (group 2 thiopental induction)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 41
- *Received treatment (n)*: NA
- *Analysed (n)*: 41
- *Age (mean ± SD, median (IQR), median (range))*: 42.1 ± 11.4
- *Weight (mean ± SD, median (IQR), median (range))*: 64.3 ± 19.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 46.3
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 4.8/14.6
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 65.9
- *Use of perioperative opioids (if yes, which?)*: intraoperative alfentanil
- *Type of surgery*: laparoscopic cholecystectomy

Control (group 3 propofol induction)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 41.7 ± 11.2
- *Weight (mean ± SD, median (IQR), median (range))*: 62.7 ± 11.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 2.5/22.5
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 72.1
- *Use of perioperative opioids (if yes, which?)*: intraoperative alfentanil
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide (group 4 propofol induction)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 43
- *Received treatment (n)*: NA
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 43.7 ± 12.0
- *Weight (mean ± SD, median (IQR), median (range))*: 63.9 ± 9.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA

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Park 2006 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 48.8
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 2.3/25.5
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 64.9
- *Use of perioperative opioids (if yes, which?)*: intraoperative alfentanil
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: healthy adult, ASA I or II, underwent laparoscopic cholecystectomy

Excluded criteria: history of cardiovascular disease; respiratory, endocrine, or neurological disorders; > 20% of normal weight, antinociceptive drugs within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control (group 1 thiopental induction) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: (17.1%) NA Metoclopramide (group 2 thiopental induction) • *Dose*: 10 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (2.4%) NA Control (group 3 propofol induction) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: (10.0%) NA Metoclopramide (group 4 propofol induction) • *Dose*: 10 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (4.7%) NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA

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Park 2006 *(Continued)*

Country: South Korea

Setting: inpatient, single-centre

Author's name: Kwan Sik Park

Institution: Department of Anesthesiology and Pain Medicine, Ajou University Hospital, Korea

Email: anesylee@ajou.ac.kr

Address: Department of Anesthesiology and Pain Medicine, Ajou University Hospital, Postal Code: 442-721, Korea

Duration of study: NA

Language: Korean (Google Translator)

Study's primary outcome: NA

Trial registry number: NA

Notes	Four groups pooled into 2 groups for analysis (different anaesthesia regimens)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly divided" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: there was no placebo intervention in the control group. Blinding of anaesthesiologists not possible
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "nurses not involved in the study observed PONV..." (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Park 2011

Study characteristics

Methods	**Study design:** randomized controlled trial

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Park 2011 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants

Baseline characteristics

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: 45
- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 7.3
- *Weight (mean ± SD, median (IQR), median (range))*: 55.3 ± 7.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 37/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 95.6
- *History of PONV/motion sickness (%)*: 42.2
- *Type of general anaesthesia*: inhalational (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 137.1
- *Use of perioperative opioids (if yes, which?)*: PCA fentanyl 4 µg bolus with 16 µg/h background infusion for postoperative pain
- *Type of surgery*: laparoscopic ovarian cystectomy 18, laparoscopic hysterectomy 27

Palonosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: 45
- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 42.4 ± 10.0
- *Weight (mean ± SD, median (IQR), median (range))*: 56.9 ± 7.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 40/5/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 86.7
- *History of PONV/motion sickness (%)*: 44.4
- *Type of general anaesthesia*: inhalational (N_2O, sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 130.4
- *Use of perioperative opioids (if yes, which?)*: PCA fentanyl 4 µg bolus with 16 µg/h background infusion for postoperative pain
- *Type of surgery*: laparoscopic ovarian cystectomy 17, laparoscopic hysterectomy 28

Included criteria: at least 21 years old, ASA I or II, scheduled to undergo elective laparoscopic gynaecological surgery of at least 1 hour duration at Incheon St Mary's Hospital, Incheon, female, used opioids to control postoperative pain, had at least 2 risk factors for PONV

Excluded criteria: received antiemetics, steroids or psychoactive medications within 24 hours of study initiation, vomiting or retching in 24 hours before surgery, had received cancer chemotherapy within 4 weeks or emetogenic radiotherapy within 8 weeks before study entry, ongoing vomiting from gastrointestinal disease

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

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Park 2011 *(Continued)*

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg iv, 2nd line ondansetron 4 mg iv; 15.6% Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg iv, 2nd line ondansetron 4 mg iv; 17.8%
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Eun Jung Cho **Institution:** Incheon St Mary's Hospital, Catholic University of Korea **Email:** gkjw2000@catholic.ac.kr **Address:** Department of Anaeshtesiology and Pain Medicine, Incheon St Mary's Hospital, College of Medicine, The Catholic University of Korea, 665-8 Bupyeong 6 dong, Pupyeonggu, Incheon 403-720, Republic of Korea **Duration of study:** June to September 2010 **Language:** English

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Park 2011 *(Continued)*

	Study's primary outcome: incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "assigned by computer- generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Quote: "placed them in numbered, sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "trained nurses who did not participate in the study prepared the drugs according to manufacturers' instructions" Judgement comment: no statement whether drugs were unlabelled and were undistinguishable from one another
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "in total, 90 patients were recruited, all of whom completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Park 2012

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Palonosetron (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: 41 • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 39.9 ± 10.8

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Park 2012 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 59.1 ± 10.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 39/2/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 82.93
- *History of PONV/motion sickness (%)*: 24.39
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 117.1
- *Use of perioperative opioids (if yes, which?)*: 9 postoperative opioid usages
- *Type of surgery*: laparoscopic gynaecological surgery, mastoidectomy with tympanoplasty or thyroidectomy

Palonosetron + dexamethasone (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 43
- *Received treatment (n)*: 43
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 38.4 ± 11.4
- *Weight (mean ± SD, median (IQR), median (range))*: 56.6 ± 8.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 40/3/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 93.02
- *History of PONV/motion sickness (%)*: 32.56
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 123.1
- *Use of perioperative opioids (if yes, which?)*: 8 postoperative opioid usages
- *Type of surgery*: laparoscopic gynaecological surgery, mastoidectomy with tympanoplasty or thyroidectomy

Included criteria: female; ASA I and II; 18 to 60 years of age; scheduled to undergo laparoscopic gynaecological surgery, mastoidectomy with tympanoplasty, or thyroidectomy; 2 or more risk factors, among which were female gender, non-smoking status, and history of PONV and/or motion sickness, according to the suggestion by Apfel et al

Excluded criteria: asked for patient-controlled analgesia using opioids; difficulties in receiving intubation; pregnant; psychiatric disorder; clinically ill with intestinal disease; took antiemetic drugs 24 hours preoperatively, unexpected blood loss occurred, laparoscopy was converted to a laparotomy or open surgery; patients transferred to an intensive care unit after surgery; patients who underwent day surgery; patients who were not able to communicate

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Palonosetron (group P) • *Dose*: 0.075 mg • *Time point of administration*: 5 minutes before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Palonosetron + dexamethasone (group C)

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Park 2012 *(Continued)*

- *Dose*: palonosetron 0.075 mg, dexamethasone 4 mg
- *Time point of administration*: 5 minutes before anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours,)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this work was supported by the 2011 Inje University research grant **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Jun Heum Yon **Institution:** Department of Anesthesiology and Pain Medicine, Sanggye Paik Hospital, Inje University College of Medicine, Korea **Email:** yonjh@paik.ac.kr **Address:** Sanggye Paik Hospital, Inje University College of Medicine, 761-1, Sanggye 7-dong, Nowon-gu, Seoul 139-707, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response for PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "they were randomly allotted" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Park 2012 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an anesthesiologist who was not related to this survey and did not know the subjects recorded the Rhodes index, 0-100 mm VAS score, and complete response on the questionnaires at the ward during the allotted time in order to assess PONV"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "there was no significant difference in age, postoperative nausea and vomiting, or motion sickness, medical history, smoking history, types of surgeries, and duration of anesthesia between the two groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Park 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 9.2 • *Weight (mean ± SD, median (IQR), median (range))*: 59.4 ± 7.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 36/14/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 92 • *History of PONV/motion sickness (%)*: 36 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 137.2 • *Use of perioperative opioids (if yes, which?)*: fentanyl (PCA) • *Type of surgery*: gynaecological laparoscopic surgery Palonosetron

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Park 2013 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 43.7 ± 8.0
- *Weight (mean ± SD, median (IQR), median (range]))*: 61.0 ± 8.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 33/17/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 94
- *History of PONV/motion sickness (%)*: 30
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 143.4
- *Use of perioperative opioids (if yes, which?)*: fentanyl (PCA)
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: at least 20 years of age, ASA I or II

Excluded criteria: received antiemetics, steroids, or psychoactive medications within 24 hours of study enrolment; vomiting or retching in the 24 hours preceding surgery; ongoing vomiting from gastrointestinal disease; had received emetogenic cancer chemotherapy within 4 weeks or radiotherapy within 8 weeks before study entry

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions

Intervention characteristics

Ramosetron

- *Dose*: 0.3 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 20.0% (metoclopramide 10 mg)

Palonosetron

- *Dose*: 0.075 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 14.0% (metoclopramide 10 mg)

Outcomes

Vomiting (0 to 6 hours)

- Outcome type: dichotomous outcome

Vomiting (6 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 48 hours)

- Outcome type: dichotomous outcome

Constipation (0 to 48 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

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Park 2013 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Eun Jung Cho **Institution:** Department of Anesthesiology and Pain Medicine, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea **Email:** gkjw2000@yahoo.co.kr **Address:** The Catholic University of Korea, 665, Bupyeong-dong, Bupyeong-gu, Incheon 403-720, Korea **Duration of study:** May to August 2011 **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NCT01476280
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "by a computer generated number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "trained nurses, who were blinded to the study, opened the envelopes containing the allocation group before induction of anesthesia, and then prepared study medications diluted to 2 ml"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all subjects were observed and interviewed by doctors unaware of the study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred patients were recruited, all of whom completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01476280 (retrospective registration)
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

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Pascucci 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 56.1 (24 to 84) • *Weight (mean ± SD, median (IQR), median (range))*: 58.8 (45 to 91) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (propofol, N_2O, Isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 0.0015 mg/kg (premedication) • *Type of surgery*: laparoscopic cholecystectomy Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 49.2 (22 to 80) • *Weight (mean ± SD, median (IQR), median (range))*: 62.9 (48 to 97) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (propofol, N_2O, Isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 0.0015 mg/kg (premedication) • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** undergoing laparoscopic cholecystectomy **Excluded criteria:** presence of nasogastric intubation for over 1 hour after the end of the intervention; pre-, intra-, and postoperative use of emetic drugs (except for fentanyl); simultaneous use of other antiemetic drugs; pathologies and other factors such as uremia, severe liver failure, acute infection, decompensated diabetes, intestinal obstruction, etc.

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Pascucci 1996 *(Continued)*

	Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Tropisetron • *Dose*: 5 mg • *Time point of administration*: 15 minutes before closing the surgical wound • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** G. Pascucci **Institution:** Servizio di Anestesia e Rianimazione dell'U.S.L. n. 5 della Regione Campania P.O.M. "G. Rummo", Benevento **Email:** NA **Address:** NA **Duration of study:** February to November 1994 **Language:** Italian (translated by Insa Backhaus) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "comparative, prospective, randomized and controlled" (translated)

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Pascucci 1996 *(Continued)*

		No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Patterson 1991

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 42.1 ± 2.7 • *Weight (mean ± SD, median (IQR), median (range))*: 61.8 ± 2.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: postoperative analgesia with 0.4 mg/kg papaveretum IM • *Type of surgery*: gynaecological surgery, breast biopsy Prochlorperazine

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Patterson 1991 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 40.5 ± 2.3
- *Weight (mean ± SD, median (IQR), median (range))*: 64.3 ± 1.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: postoperative analgesia with 0.4 mg/kg papaveretum IM
- *Type of surgery*: gynaecological surgery, breast biopsy

Included criteria: patients admitted for day-care gynaecological surgery or breast biopsy were included in the study. All patients were classified ASA I and II.

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: prochlorperazine (10%) Prochlorperazine • *Dose*: 3 mg • *Time point of administration*: one hour preoperatively • *Route of administration*: buccal • *Rescue antiemetics (if yes, which?)*: prochlorperazine (13.3%)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** outpatient, single-centre

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Patterson 1991 *(Continued)*

Author's name: Kenneth W. Patterson

Institution: Department of Anaesthesia and Intensive Care, University College Hospital, Galway

Email: NA

Address: Newcastle Road, Galway

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated to two groups..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the technique for correct placement of the buccal tablet was explained to each patient by one of three anaesthetists involved in the study..." Judgement comment: blinding impossible because control participants received no placebo treatment
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the assessment was by a blinded observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Patterson 1993

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis

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Patterson 1993 *(Continued)*

Participants	**Baseline characteristics** Control (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 26 • *Age (mean ± SD, median (IQR), median (range))*: 40.5 ± 2.2 • *Weight (mean ± SD, median (IQR), median (range))*: 62.4 ± 2.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg for induction, papaveretum for postoperative analgesia • *Type of surgery*: gynaecological surgery, breast biopsy Prochlorperazine (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 26 • *Age (mean ± SD, median (IQR), median (range))*: 35.8 ± 1.4 • *Weight (mean ± SD, median (IQR), median (range))*: 62.1 ± 2.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg for induction, papaveretum for postoperative analgesia • *Type of surgery*: gynaecological surgery, breast biopsy **Included criteria:** ASA I or II, admitted for day-case gynaecological surgery or breast biopsy **Excluded criteria:** known allergy to phenothiazines, currently taking phenothiazines, pregnant or nursing, any condition associated with nausea and vomiting **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Control (group 1) • *Dose*: no treatment

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Patterson 1993 *(Continued)*

- *Time point of administration*: -
- *Route of administration*: -
- *Rescue antiemetics (if yes, which?)*: 19.23% (prochlorperazine 12.5 mg IM)

Prochlorperazine (group 2)

- *Dose*: 6 mg
- *Time point of administration*: 1 hour before transfer to the operating theatre
- *Route of administration*: buccal
- *Rescue antiemetics (if yes, which?)*: 3.85% (prochlorperazine 12.5 mg IM)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Ireland **Setting:** outpatient, single-centre **Author's name:** Patterson K.W. **Institution:** Department of Anaesthesia and Intensive Care, University College Hospital, Galway **Email:** NA **Address:** Deptartment of Anaesthesia and Intensive Care, E-91, University of Texas Medical Branch, Galveston, Texas, 77550, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated to one of two groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	High risk	Judgement comment: no placebo intervention in the control group. Blinding of participants and personnel impossible

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Patterson 1993 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the assessment was by a blinded observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "52 female patients scheduled for day case gynaecological surgery or breast biopsy were studied" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no difference between the groups..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Patton 1974

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 21 • *Age (mean ± SD, median (IQR), median (range))*: 37 (29 to 52) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 21/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (diethyl ether, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 97.6 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: hysterectomy (12 vaginal, 9 abdominal) Placebo • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA

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Patton 1974 *(Continued)*

- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 35 (22 to 50)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 20/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (diethyl ether, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 106.0
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: hysterectomy (11 vaginal, 9 abdominal)

Included criteria: ASA I, female patients with vaginal or abdominal hysterectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Droperidol • *Dose*: 5 mg • *Time point of administration*: shortly after beginning of surgery • *Route of administration*: 1.25 mg IV and 3.75 mg IM • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: 2 mL saline • *Time point of administration*: shortly after beginning of surgery • *Route of administration*: 0.5 mL IV and 1.5 mL IM • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Comments:** NA **Author's name:** Clifton M. Patton **Institution:** USAF Regional Hospital Eglin AFB, Florida **Email:** NA **Address:** Anesthesiology Service, Wilford Hall USAF Medical Center (AFSC), Lackland Air Force Base, San Antonio, Texas 78236, USA

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Patton 1974 *(Continued)*

	Duration of study: NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "forty-four A.S.A. class I patients were randomly assigned to either a control or a droperidol group" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Low risk	Quote: "group assignments were made by a pharmacy officer, and at no time did any physician or nurse have access to this information until the completion of the study"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the pharmacy provided for each patient an unlabeled 2-ml ampoule of either saline solution or 2.5 mg/ml of droperidol. Shortly after the surgical procedure had begun, 0.5 ml of this unknown was administered I.V. and 1.5 ml was given I.M"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "group assignments were made by a pharmacy officer, and at no time did any physician or nurse have access to this information until the completion of the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "three patients were excluded from the analysis because they had received unnecessary antiemetic agents in the recovery room. Three control patients and one droperidol patient received antiemetic drugs during the study for severe vomiting, but are included in the analysis"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Pawar 2008

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + dexamethasone (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Pawar 2008 *(Continued)*

- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 35.65
- *Weight (mean ± SD, median (IQR), median (range))*: 58.75
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: less than 30 minutes
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological laparoscopic intervention

Ondansetron (group 2)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 32.62
- *Weight (mean ± SD, median (IQR), median (range))*: 56.65
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: less than 30 minutes
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological laparoscopic intervention

Dexamethasone (group 3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 33.82
- *Weight (mean ± SD, median (IQR), median (range))*: 57.65
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: less than 30 minutes
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological laparoscopic intervention

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Pawar 2008 *(Continued)*

	Included criteria: 18 to 65 years of age, ASA I or II, undergoing gynaecological laparoscopic intervention under general anaesthesia **Excluded criteria:** ASA III or above, previous history of drug reaction to any of the drugs used in this study, history of PONV, history of motion sickness, received antiemetics in the previous 24 hours, evidence of respiratory infection **Pretreatment:** baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Ondansetron + dexamethasone (group 1) • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 1 mg Ondansetron (group 2) • *Dose*: 4 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 1 mg Dexamethasone (group 3) • *Dose*: 8 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 1 mg
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** NA, single-centre **Author's name:** Aarti Nandkumar Pawar **Institution:** Department of Anaesthesia, KEM Hospital **Email:** NA **Address:** Acharya Donde Marg, Parel, Mumbai, Maharashtra 400012, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None
Risk of bias	

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Pawar 2008 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "prospective, randomized study was conducted..." Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...of nausea episodes of vomiting. These observations were recorded by independent recovery room personnel who did not know which anti-emetic each patient had received. Every complaint of nausea..."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no Information on number of patients who were randomized and analysed
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...be 58.75, 56.65, 57.65 respectively. Therefore the age and the weight distribution was comparable in the 3 groups. Average number of patients with..." Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Pearman 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo (study 1/2) • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 282; 139 (study 1), 143 (study 2) • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Pearman 1994 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O, fentanyl or alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, alfentanil
- *Type of surgery*: gynaecological, orthopaedic, peripheral, ENT/oral

Ondansetron (1 mg group - study 1/2)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 264; 133 (study 1), 131 (study 2)
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O, fentanyl or alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, alfentanil
- *Type of surgery*: gynaecological, orthopaedic, peripheral, ENT/oral

Ondansetron (4 mg group - study 1/2)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 272; 136 (study 1), 136 (study 2)
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O, fentanyl or alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, alfentanil
- *Type of surgery*: gynaecological, orthopaedic, peripheral, ENT/oral

Ondansetron (8 mg group - study 1/2)

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 265; 136 (study 1), 129 (study 2)
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA

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Pearman 1994 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O, fentanyl or alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, alfentanil
- *Type of surgery*: gynaecological, orthopaedic, peripheral, ENT/oral

Included criteria: in study 1, ASA grade I or II, female, 18 to 70 years of age, scheduled to undergo gynaecological laparoscopy on a day-case basis; in study 2, female, 18 to 70 years of age, scheduled to undergo day-case surgery

Excluded criteria: had vomited or received antiemetics within 24 hours of surgery, pregnant or breastfeeding (studies 1 and 2), scheduled to undergo liver biopsy, required continuous gastric suction intraoperatively, > 100% over ideal body weight

Pretreatment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker, perioperative opioids, duration of anaesthesia): unclear

Interventions

Intervention characteristics

Placebo (study 1/2)

- *Dose*: 20 mL normal saline
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: "rescue antiemetics were allowed upon request or after physician determination"

Ondansetron (1 mg group - study 1/2)

- *Dose*: 1 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: "rescue antiemetics were allowed upon request or after physician determination"

Ondansetron (4 mg group - study 1/2)

- *Dose*: 4 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: "rescue antiemetics were allowed upon request or after physician determination"

Ondansetron (8 mg group - study 1/2)

- *Dose*: 8 mg
- *Time point of administration*: immediately before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: "rescue antiemetics were allowed upon request or after physician determination"

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

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Pearman 1994 *(Continued)*

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, NA **Author's name:** M.H. Pearman **Institution:** Department of Anesthesia, Baptist Medical Center **Email:** NA **Address:** Department of Anesthesia, Baptist Medical Center, 1330 Taylor Street, Columbia, South Carolina 29220, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** number of emetic episodes **Trial registry number:** NA
Notes	Three studies with 4 groups each. Only 2 out of 3 studies relevant "Study 1" and "study 2" combined. "Study 3" excluded (patients ≥ 12 years of age)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no information on allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no information on blinding of participants and study personnel provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "vital signs, emetic episodes, nausea scores and adverse events were assessed by a blinded observer during this time" Judgement comment: no information on blinding provided

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Pearman 1994 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: in study 1 and study 2, about 9% of enrolled participants were not analysed. No information provided on missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "in all three studies, there were no significant differences between treatment groups with regard to age, weight, height, number of days since last menstrual cycle..." Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker, perioperative opioids, duration of anaesthesia): unclear

Peixoto 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 68.9 ± 10.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) and epidural anaesthesia • *Duration of anaesthesia or surgery (in min; as mean or median)*: 109 • *Use of perioperative opioids (if yes, which?)*: 50 µg fentanyl before epidural block, ketoprofen for postoperative analgesia • *Type of surgery*: major gynaecological surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 69.5 ± 10.7

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Peixoto 2000 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) and epidural anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102
- *Use of perioperative opioids (if yes, which?)*: 50 µg fentanyl before epidural block, ketoprofen for post-operative analgesia
- *Type of surgery*: major gynaecological surgery

Droperidol + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 67.3 ± 8.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) and epidural anaesthesia
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 103
- *Use of perioperative opioids (if yes, which?)*: 50 µg fentanyl before epidural block, ketoprofen for post-operative analgesia
- *Type of surgery*: major gynaecological surgery

Included criteria: women 18 to 70 years, ASA I or II, weighing 45 to 90 kg, undergoing major gynaecological surgery

Excluded criteria: preoperative nausea/vomiting, receiving opioid analgesic in the 24 hours preceding the procedure

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Droperidol • *Dose*: 1.25 mg • *Time point of administration*: upon arrival at the operating room • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide IV Ondansetron • *Dose*: 4 mg • *Time point of administration*: upon arrival at the operating room • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide IV Droperidol + ondansetron

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Peixoto 2000 *(Continued)*

- *Dose*: droperidol 1.25 mg, ondansetron 4 mg
- *Time point of administration*: upon arrival at the operating room
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide IV

Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Brazil **Setting:** inpatient, single-centre **Author's name:** A. J. Peixoto **Institution:** Hospital de Caridade, Brazil **Email:** NA **Address:** Departamento de Anestesiologia, Hospital de Caridade, Rua Sao Paulo 256/101, 99700-000, Erechim, RS, Brazil **Duration of study:** NA **Language:** English **Study's primary outcome:** occurrence of PONV in the first 24 hours after the procedure **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "a study nurse aware of the randomization status prepared the study solution and handed it to one of the anaesthesiologists who administered the drug"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors provided

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Peixoto 2000 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Perez Ascencio 1992

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 28 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: balanced general anaesthesia (enflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 207 • *Use of perioperative opioids (if yes, which?)*: 359 µg fentanyl intraoperative • *Type of surgery*: head and neck surgery Diphenidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 27 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA

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Perez Ascencio 1992 *(Continued)*

- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced general anaesthesia (enflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 192
- *Use of perioperative opioids (if yes, which?)*: 303 µg fentanyl intraoperative
- *Type of surgery*: head and neck surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 29 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced general anaesthesia (enflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 249
- *Use of perioperative opioids (if yes, which?)*: 456 µg fentanyl intraoperative
- *Type of surgery*: head and neck surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 30 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: balanced general anaesthesia (enflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 155
- *Use of perioperative opioids (if yes, which?)*: 340 µg fentanyl intraoperative
- *Type of surgery*: head and neck surgery

Included criteria: both sexes, 18 to 60 years of age, scheduled for elective surgery of the head and neck (maxillofacial surgery, plastic surgery, reconstructive surgery), ASA I or II

Excluded criteria: old history of nausea and postoperative vomiting, obese, women, pregnant or in the menstrual period, pathology leading to vomiting

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (history of PONV): no; (gender, non-smoker, history of motion sickness): unclear; (perioperative opioids, duration of anaesthesia): yes

Interventions	**Intervention characteristics**

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Perez Ascencio 1992 *(Continued)*

	Droperidol • *Dose*: 15 µg/kg to 20 µg/kg • *Time point of administration*: 30 minutes before end of anaesthetic procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Diphenidol • *Dose*: 150 µg/kg • *Time point of administration*: 30 minutes before end of anaesthetic procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 150 µg/kg • *Time point of administration*: 30 minutes before end of anaesthetic procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: 3 ml saline • *Time point of administration*: 30 minutes before end of anaesthetic procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Mexico **Setting:** inpatient, single-centre **Author's name:** Rebeca E. Pérez-Ascencio **Institution:** Departemento de Anestesiología del Hospital de Escpecialidades del Centro Médico La Raza **Email:** NA **Address:** Departemento de Anestesiología del Hospital de Escpecialidades del Centro Médico La Raza, Instituto Mexicano del Seguro social (IMSS), México D.F. **Duration of study:** NA **Language:** Spanish (translated by Insa Backhaus) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Perez Ascencio 1992 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "a random population of 60 patients ..." (translated) No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessor
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (history of PONV): no; (gender, non-smoker, history of motion sickness): unclear; (perioperative opioids, duration of anaesthesia): yes

Perez Garcia 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, halothane, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA

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Perez Garcia 2000 *(Continued)*

- *Type of surgery*: elective surgery (general surgery, gynaecological, ophthalmological, maxillofacial, other)

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, halothane, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: elective surgery (general surgery, gynaecological, ophthalmological, maxillofacial, other)

Included criteria: adult; ASA I, II, or III; scheduled for elective surgery under general anaesthesia with endotracheal intubation and administration of narcotic analgesic fentanyl

Excluded criteria: received an antiemetic within 24 hours before surgery; with antecedents of nausea and/or vomiting due to kidney disease, liver disease, peptic acid, and stomach surgery; those who in the postoperative period received a prophylactic antiemetic treatment equal to or different from the drugs studied

Pretreatment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (12 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

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Perez Garcia 2000 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Mexiko **Setting:** inpatient, single-centre **Author's name:** Austreberto Pérez Garcia **Institution:** Departemento de Anestesiologia, Hospital General de Zona 1 del IMSS, Tapachula Chiapas **Email:** austreberto@acnet.net **Address:** Andador Cafetales Manzaneros 1 Casa 3 Fracc. Santa Clara, Tapachula Chiapas CP 30788 **Duration of study:** NA **Language:** Spanish (translated by Insa Backhaus) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "..prospective, randomized, triple-blind..." No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "..prospective, randomized, triple-blind..." Insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the evaluator did not know which medication had been administered"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no reasons for exclusion described for 3 participants
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

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Pertusa 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Dehydrobenzperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 54.2 ± 12.7 • *Weight (mean ± SD, median (IQR), median (range))*: 72.4 ± 11.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 70.8 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 12.5/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 81.0 • *Use of perioperative opioids (if yes, which?)*: 7.9 µg/kg fentanyl • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 22 • *Age (mean ± SD, median (IQR), median (range))*: 47.6 ± 10.9 • *Weight (mean ± SD, median (IQR), median (range))*: 69.6 ± 13.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 68.18 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 13.6/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 90.8 • *Use of perioperative opioids (if yes, which?)*: 6.9 µg/kg fentanyl • *Type of surgery*: laparoscopic cholecystectomy Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 23 • *Age (mean ± SD, median (IQR), median (range))*: 52.4 ± 12.0 • *Weight (mean ± SD, median (IQR), median (range))*: 73.7 ± 13.5

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Pertusa 1996 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 65.2
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 17.4/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 89.5
- *Use of perioperative opioids (if yes, which?)*: 6.0 µg/kg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 22
- *Age (mean ± SD, median (IQR), median (range))*: 53.4 ± 16.7
- *Weight (mean ± SD, median (IQR), median (range))*: 70.1 ± 12.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 72.73
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 18.2/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 82.1
- *Use of perioperative opioids (if yes, which?)*: 5.9 µg/kg fentanyl
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: 20 to 70 years of age; ASA I, II, and III; undergoing simple laparoscopic cholecystectomy

Excluded criteria: obstructive jaundice or choledocholithiasis diagnosed by ultrasound; cholecystitis at the time of the intervention or in the 30 days before it; history of allergies or intolerances to any of the drugs submitted to the study or used in anaesthetic technology or for postoperative analgesia; treatment based on coracoid; insufficient renal, hepatic, or cardiac; ASA IV or V

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions

Intervention characteristics

Dehydrobenzperidol

- *Dose*: 1.25 mg
- *Time point of administration*: before anaesthetic induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: before anaesthetic induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

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Pertusa 1996 *(Continued)*

	Ondansetron • *Dose*: 4 mg • *Time point of administration*: before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: 2 ml saline • *Time point of administration*: before anaesthetic induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (time point unclear)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Spain **Setting:** inpatient, single-centre **Author's name:** V. Pertusa **Institution:** Serviciosde Anestesiologfa, Reanimaci6ny Terapeutica del Dolor **Email:** NA **Address:** Torrente, 18, esc. 5, puerta 10. 46014 Valencia **Duration of study:** NA **Language:** Spanish (translated by Insa Backhaus) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "in a double-blind random study" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Pertusa 1996 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: quote: "neither the patient nor the researcher knew the product administered" (translated) No information on anaesthesiologists provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "neither the patient nor the researcher knew the product administered" (translated)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: 9 of the 100 participants were excluded from the study. No information on reasons for exclusion provided
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker): unclear; (perioperative opioids): yes

Philip 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 208 • *Received treatment (n)*: NA • *Analysed (n)*: 208 • *Age (mean ± SD, median (IQR), median (range))*: 37.6 ± 12.4 • *Weight (mean ± SD, median (IQR), median (range))*: 77.1 ± 17.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 110/91/0/0 • *Gender (female in %)*: 70 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 15/22 • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl/alfentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 66 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: ear/nose/throat, ophthalmological, orthopaedic, urologic, breast, other Dolasetron (12.5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 206

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Philip 2000 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 206
- *Age (mean ± SD, median (IQR), median (range))*: 37.0 ± 13.4
- *Weight (mean ± SD, median (IQR), median (range))*: 73.4 ± 17.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 113/87/0/0
- *Gender (female in %)*: 71
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 22/20
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl/alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: ear/nose/throat, ophthalmological, orthopaedic, urologic, breast, other

Dolasetron (50 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 205
- *Received treatment (n)*: NA
- *Analysed (n)*: 205
- *Age (mean ± SD, median (IQR), median (range))*: 35.9 ± 11.8
- *Weight (mean ± SD, median (IQR), median (range))*: 74.7 ± 16.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 102/98/0/0
- *Gender (female in %)*: 71
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 28/26
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl/alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: ear/nose/throat, ophthalmological, orthopaedic, urologic, breast, other

Dolasetron (25 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 203
- *Received treatment (n)*: NA
- *Analysed (n)*: 203
- *Age (mean ± SD, median (IQR), median (range))*: 35.6 ± 10.6
- *Weight (mean ± SD, median (IQR), median (range))*: 74.2 ± 16.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 102/98/0/0
- *Gender (female in %)*: 69
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 25/23
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl/alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 66
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: ear/nose/throat, ophthalmological, orthopaedic, urologic, breast, other

Dolasetron (100 mg group)

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Philip 2000 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 208
- *Received treatment (n)*: NA
- *Analysed (n)*: 208
- *Age (mean ± SD, median (IQR), median (range))*: 36.9 ± 11.9
- *Weight (mean ± SD, median (IQR), median (range))*: 72.1 ± 17.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 112/91/0/0
- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 23/19
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl/alfentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 72
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: ear/nose/throat, ophthalmological, orthopaedic, urologic, breast, other

Included criteria: male and female, 18 years of age or older, ASA I to III, undergoing outpatient surgery with general anaesthesia

Excluded criteria: had received any drug with potential antiemetic activity within 24 hours of surgery, had received previous treatment with dolasetron, had any clinically significant cardiovascular abnormality (complete bundle-branch block, cardiomyopathy, congestive heart failure, arrhythmia, second- or third-degree heart block), exceeded ideal body weight by over 100%, had any clinically significant laboratory abnormalities or major organ system dysfunction, undergoing liver or gastrointestinal surgery, experienced nausea and/or vomiting within 24 hours of the present surgery, had taken an investigational drug within 30 days

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (non-smoker, perioperative opioids): unclear; (history of PONV): yes

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Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: approximately 15 minutes before cessation of nitrous oxide
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol and metoclopramide most frequently given

Dolasetron (12.5 mg group)

- *Dose*: 12.5 mg
- *Time point of administration*: approximately 15 minutes before cessation of nitrous oxide
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol and metoclopramide most frequently given

Dolasetron (50 mg group)

- *Dose*: 50 mg
- *Time point of administration*: approximately 15 minutes before cessation of nitrous oxide
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol and metoclopramide most frequently given

Dolasetron (25 mg group)

- *Dose*: 25 mg

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Philip 2000 *(Continued)*

- *Time point of administration*: approximately 15 minutes before cessation of nitrous oxide
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol and metoclopramide most frequently given

Dolasetron (100 mg group)

- *Dose*: 100 mg
- *Time point of administration*: approximately 15 minutes before cessation of nitrous oxide
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol and metoclopramide most frequently given

Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Arrhythmia (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, multi-centre (17) **Author's name:** B.K. Philip **Institution:** Brigham and Women's Hospital, Department of Anesthesiology **Email:** NA **Address:** Brigham and Women's Hospital, Department of Anesthesiology, Perioperative and Pain Medicine, 75 Francis St., Boston, MA 02115, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response, defined as no emetic episodes and no rescue antiemetic medication during the 24-hour study period **Trial registry number:** NA
Notes	Study included in a pooled analysis (secondary publication)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "all were randomized, double-blind, placebo-controlled, multicenter trials with 24-hour monitoring periods"

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Philip 2000 *(Continued)*

		Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (non-smoker, perioperative opioids): unclear; (history of PONV): yes

Phillips 1993

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 70 • *History of PONV/motion sickness (%)*: 32/32 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 25 • *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 2 µg/kg fentanyl, 18 patients received pethidine • *Type of surgery*: laparoscopic surgery

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Phillips 1993 *(Continued)*

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 63
- *History of PONV/motion sickness (%)*: 25/32
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 25
- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 2 µg/kg fentanyl, 17 patients received pethidine
- *Type of surgery*: laparoscopic surgery

Included criteria: women, ASA I to III, over 16 years of age, scheduled for elective laparoscopic surgery as day patients

Excluded criteria: pregnant; had ingested alcohol, opioids, or antiemetics in the 24 hours before surgery

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Metoclopramide

- *Dose*: 10 mg
- *Time point of administration*: 1 hour before induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: 32.5% (prochlorperazine)

Control

- *Dose*: 1 g lactose
- *Time point of administration*: 1 hour before induction of anaesthesia
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: 37.5% (prochlorperazine)

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

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Phillips 1993 *(Continued)*

Country: UK

Setting: outpatient, single-centre

Author's name: S. Phillips

Institution: The Hospitals for Sick Children, Great Ormond Street, London WClN 3BR

Email: NA

Address: NA

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	Two out of 3 groups relevant (ginger)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "by random allocation" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "all capsules were prepared by Martindale Pharmaceuticals Pty Ltd specifically for this trial and their contents were known only to the hospital pharmacist until completion of the study. The capsules were identical in size, colour, taste and smell" Judgement comment: no information on who enrolled participants
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all capsules were prepared by Martindale Pharmaceuticals Pty Ltd specifically for this trial and their contents were known only to the hospital pharmacist until completion of the study. The capsules were identical in size, colour, taste and smell"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all hospital observations were made by the nursing staff, who had no knowledge of which treatment each patient had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the demographic data were similar in the three groups (Table 1). The groups were also comparable with regard to the duration of pre-operative fasting and duration of surgical procedure. There was no difference between groups in respect of previous postoperative nausea and vomiting, motion sickness or smoking"

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Phillips 1993 *(Continued)*

	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Piper 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dolasetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 75 • *Received treatment (n)*: NA • *Analysed (n)*: 75 • *Age (mean ± SD, median (IQR), median (range))*: 52 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 29/37/9/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 65.33 • *History of PONV/motion sickness (%)*: 24/20 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 111 • *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperative, 3.75 mg piritramide postoperative • *Type of surgery*: hysterectomy, breast surgery Dolasetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 75 • *Received treatment (n)*: NA • *Analysed (n)*: 75 • *Age (mean ± SD, median (IQR), median (range))*: 54 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 22/46/7/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 69.33 • *History of PONV/motion sickness (%)*: 21.33/16 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 117 • *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperative, 3.75 mg piritramide postoperative • *Type of surgery*: hysterectomy, breast surgery **Included criteria:** women, ASA I to III, undergoing elective hysterectomy or breast surgery

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Piper 2003 *(Continued)*

	Excluded criteria: known intolerance or allergy to any of the drugs used in the study, positive gastritis or ulcer history, pregnancy or breastfeeding, gastrointestinal infection within the last 2 weeks, intake of corticosteroids or antiemetics within the last week before surgery, known cardiac arrhythmia or therapy with antiarrhythmics grade II or III, fever (> 37.5°C), renal (creatinine > 1.4 mg%) and/or hepatic disease (glutamate-oxaloacetate-transaminases > 40 U/L and or glutamate-pyruvate-transaminases > 40 U/L); disease of the nervous system, addiction **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear
Interventions	**Intervention characteristics** Dolasetron • *Dose*: 50 mg • *Time point of administration*: with premedication • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 20% (droperidol 1.25 mg IV) Dolasetron + dexamethasone • *Dose*: dolasetron 50 mg, dexamethasone 8 mg • *Time point of administration*: dolasetron with premedication, dexamethasone after induction of anaesthesia • *Route of administration*: dolasetron: PO, dexamethasone: IV • *Rescue antiemetics (if yes, which?)*: 9.3% (droperidol 1.25 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** drugs were provided by Aventis Deutschland GmbH, Bad Soden, Deutschland. There was no other sponsorship **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** S.N. Piper **Institution:** Klinik für Anästhesiologie und Operative Intensivmedizin, Klinikum Ludwigshafen **Email:** swen.n.piper@t-online.de **Address:** Klinik für Anästhesiologie und Operative Intensivmedizin, Klinikum Ludwigshafen, Bremserstraße 79, 67063 Ludwigshafen **Duration of study:** NA **Language:** German (2 German reviewers) **Study's primary outcome:** incidence of PONV

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Piper 2003 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "mit einer Randomisierungsliste wurden die Patientinnen einer der folgenden Gruppen zugeteilt" Judgement comment: sequence generation by random number tables
Allocation concealment (selection bias)	Low risk	Quote: "der Einschluss in die Studie erfolgte in Unkenntnis der Gruppenzuteilung" Judgement comment: inclusion of participants into the study without knowledge of group allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "in Unkenntnis der Gruppenzuteilung. Weder dem Anästhesisten, der die Narkose durchführte und die i.v.- Studienmedikation verabreichte, noch dem Aufwachraumpersonal, noch dem Personal auf Normalstation war bekannt, welche Medikation die Patientin erhalten hatte. Alle Patientinnen hatten eine Nah..." Judgement comment: anaesthetists were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "in Unkenntnis der Gruppenzuteilung. Weder dem Anästhesisten, der die Narkose durchführte und die i.v.- Studienmedikation verabreichte, noch dem Aufwachraumpersonal, noch dem Personal auf Normalstation war bekannt, welche Medikation die Patientin erhalten hatte. Alle Patientinnen hatten eine Nah..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "zwischen den beiden Patientengruppen bestanden bezüglich demographischer und perioperativer Daten keine signifikanten Unterschiede (Tabelle 1)..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Ploner 1997

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different routes of administration
Participants	**Baseline characteristics**

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Ploner 1997 *(Continued)*

Ondansetron (group A)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 18
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 67.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138
- *Use of perioperative opioids (if yes, which?)*: 600 µg fentanyl
- *Type of surgery*: laparoscopic and open gynaecological surgery

Ondansetron (group B)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 19
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 62.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 126
- *Use of perioperative opioids (if yes, which?)*: 575 µg fentanyl
- *Type of surgery*: laparoscopic and open gynaecological surgery

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 19
- *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 57.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 156

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Ploner 1997 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 625 µg fentanyl
- *Type of surgery*: laparoscopic and open gynaecological surgery

Included criteria: gynaecological abdominal patients with an expected operation duration of at least 60 minutes, ASA I or II

Excluded criteria: younger than 18 or over 75 years of age, ASA III or IV, obese with BMI > 28, history of PONV after general anaesthesia, liver or renal disease, cardiovascular disease, pregnant or given birth in the last 3 months, intake of antiemetic medication in the last 24 hours before operation, feeling of nausea

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV): no; (history of motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron (group A) • *Dose*: 4 mg • *Time point of administration*: ondansetron 10 minutes before initiation of anaesthesia, saline 10 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 5% metoclopramide Ondansetron (group B) • *Dose*: 4 mg • *Time point of administration*: saline 10 minutes before initiation of anaesthesia, ondansetron 10 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 17.5% metoclopramide Placebo (group C) • *Dose*: 2 x 0.9% NaCl • *Time point of administration*: 10 minutes before initiation of anaesthesia and 10 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 42.5% metoclopramide
Outcomes	*Adverse events (general notes in the publication, 12 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** Dr. F. Ploner **Institution:** Abteilung für Anästhesie und allgemeine Intensivmedizin, Landeskrankenhaus Brixen **Email:** NA **Address:** Abteilung für Anästhesie und allgemeine Intensivmedizin, Landeskrankenhaus Brixen, Dantestraße 81, I-39042 Brixen **Duration of study:** NA

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Ploner 1997 *(Continued)*

	Language: German (2 German reviewers) **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "die Patienten wurden randomisiert in drei Gruppen gleicher Anzahl und gleicher Art" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Doppelblindstudie" Judgement comment: insufficient information on blinding ("double-blinded study")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded study")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV): no; (history of motion sickness, non-smoker): unclear

Prescott 1976

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 52 • *Received treatment (n)*: NA

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Prescott 1976 *(Continued)*

- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 41.7 ± 9.6
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 59.61
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (mean overall: 79)
- *Use of perioperative opioids (if yes, which?)*: pentazocine, phenazocine
- *Type of surgery*: operation for varicose veins or hernia

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 56
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: 46.8 ± 11.5
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 55.36
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (mean overall: 79)
- *Use of perioperative opioids (if yes, which?)*: pentazocine, phenazocine
- *Type of surgery*: operation for varicose veins or hernia

Included criteria: undergoing operation for varicose veins or hernia

Excluded criteria: participants whose operations were expected to take less than 45 minutes

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, perioperative opioids): unclear

Interventions

Intervention characteristics

Control

- *Dose*: atropine 0.6 mg
- *Time point of administration*: as premedication before surgery
- *Route of administration*: NA
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol

- *Dose*: atropine 0.6 mg, droperidol 5 mg
- *Time point of administration*: as premedication
- *Route of administration*: NA
- *Rescue antiemetics (if yes, which?)*: NA

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Prescott 1976 *(Continued)*

Outcomes	*Vomiting (leaving day bed area - morning after operation)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours, morning after operation)* • Outcome type: dichotomous outcome *Headache (on morning after operation)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** Roche and Janssen Pharmaceuticals kindly provided test agents. Roche also gave financial support **Country:** UK **Setting:** inpatient and outpatient, single-centre **Author's name:** R.J. Prescott **Institution:** University Department of Medical Statistics and Computing, and Department of Anesthetics and Clinical Surgery, Western General Hospital, Edinburgh **Email:** NA **Address:** Crewe Rd S, Edinburgh EH4 2XU, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (diazepam)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "a randomization list was prepared ... using a system of restricted randomization designed to prevent the possibility of unbalanced allocation"
Allocation concealment (selection bias)	Low risk	Judgement comment: quote: "the premedications were prepared in identical serially numbered vials"; "A randomization list was prepared ... using a system of restricted randomization designed to prevent the possibility of unbalanced allocation"; "On admission to the trial each patient was assigned the next available serial number in the appropriate group, and received as their premedication the contents of the corresponding vial"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the details of the randomisation were kept by one of us not directly involved with the individual patients"; "The premedications were prepared in identical serially numbered vials"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the details of the randomisation were kept by one of us not directly involved with the individual patients"; "The premedications were prepared in identical serially numbered vials"

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Prescott 1976 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: different number of analysed patients. No information on reasons for missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, perioperative opioids): unclear

Principi 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Ondansetron (4 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 50 • *Type of general anaesthesia*: balanced (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (mean overall 110.8 (40 to 320)) • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: major gynaecological Ondansetron (8 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA

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Principi 1996 *(Continued)*

- *History of PONV/motion sickness (%)*: 50
- *Type of general anaesthesia*: balanced (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (mean overall 110.8 (40 to 320))
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: major gynaecological

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 50
- *Type of general anaesthesia*: balanced (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (mean overall 110.8 (40 to 320))
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: major gynaecological

Included criteria: ASA I or II; non-pregnant; female; 18 to 75 years of age; 45 to 95 kg; normal hepatic, haematological, renal laboratory tests

Excluded criteria: significant laboratory or clinical evidence of renal, haematological, hepatic, or cardiovascular abnormalities; endocrine dysfunction; pregnancy or breastfeeding; receipt of antiemetic in the 24 hours before administration of study medication; required a nasogastric tube in situ postoperatively

Pretreatment: no information on distribution of baseline characteristics and potential effect modifiers presented for the different groups. Baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics**

Ondansetron (4 mg group)

- *Dose*: 4mg
- *Time point of administration*: 10 minutes before starting general anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Ondansetron (8 mg group)

- *Dose*: 8mg
- *Time point of administration*: 10 minutes before starting general anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo

- *Dose*: 20 mL saline
- *Time point of administration*: 10 minutes before starting general anaesthesia

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Principi 1996 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** F. Principi **Institution:** Department of Anesthesiology, Regina Elena Centre Institute, Rome **Email:** NA **Address:** Department of Anesthesiology, Regina Elena Cancer Institute, Rome, Italy **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Before randomization, stratification to history of PONV/no history of PONV (45 patients each), then randomization to 2 × 3 subgroups of 15 patients each and subsequent analysis of the resulting 3 subgroups of 30 patients each

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "this stratified, randomized..." No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")

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Principi 1996 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: no information on distribution of baseline characteristics and potential effect modifiers presented for the different groups. Baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Pueyo 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 47 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 28/24 • *Type of general anaesthesia*: balanced (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 167 • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine • *Type of surgery*: intra-abdominal surgery (gynaecological, gastrointestinal, and urological) Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Pueyo 1996 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 32/36
- *Type of general anaesthesia*: balanced (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 162
- *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine
- *Type of surgery*: intra-abdominal surgery (gynaecological, gastrointestinal, and urological)

Included criteria: female, ASA I or II, 18 to 65 years of age, weighing < 90 kg, scheduled for intra-abdominal surgery

Excluded criteria: analgesic or antiemetic medicine during previous month; > 30% above ideal body weight; hypersensitivity to opioids, NSAIDs, or 5-HT3 antagonists

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline 0.9% • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Spain

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Pueyo 1996 *(Continued)*

Setting: inpatient, single-centre

Author's name: F.J. Pueyo

Institution: University of Navarra, Pamplona

Email: NA

Address: Departamento de Anestesiologia, Clinica Universitaria, Apartado 192, 37080 Pamplona, Spain

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	Two out of 4 groups relevant (repeated doses of droperidol: 12 hours after surgery)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "had a stratified randomization (age and type of surgery)" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind" Judgement comment: syringes were prepared centrally (by pharmacy); unlikely participant and personnel know the allocated group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double-blind, placebo-controlled" Judgement comment: syringes were prepared centrally (by pharmacy); unlikely participant, personnel, and outcome assessors know the allocated group
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Purhonen 1997

Study characteristics

Methods	**Study design:** randomized controlled trial

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Purhonen 1997 *(Continued)*

Study grouping: 3 groups, monoprophylaxis

Participants

Baseline characteristics

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 48
- *Age (mean ± SD, median (IQR), median (range))*: 51 ± 1
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 43.8/29.6
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 149
- *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg just before incision and every 30 minutes thereafter for anaesthesia, 73 mg oxycodone
- *Type of surgery*: gynaecological incontinence operation

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 1
- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 57.1/41.3
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 144
- *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg just before incision and every 30 minutes thereafter for anaesthesia, 66 mg oxycodone
- *Type of surgery*: gynaecological incontinence operation

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 1
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0

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Purhonen 1997 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 65.3/42.2
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 145
- *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg just before incision and every 30 minutes thereafter for anaesthesia, 73 mg oxycodone
- *Type of surgery*: gynaecological incontinence operation

Included criteria: female inpatients, ASA I to III, scheduled to undergo elective gynaecological incontinence operation under general anaesthesia

Excluded criteria: had experienced nausea or vomiting 24 hours before the study, taking antiemetic medication

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of motion sickness): no; (non-smoker): unclear; (history of PONV): yes

Interventions	**Intervention characteristics** Tropisetron • *Dose*: 5 mg • *Time point of administration*: within 15 minutes of the end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 43.75% (metoclopramide 10 mg IV, tropisetron 5 mg IV) Droperidol • *Dose*: 1.25 mg • *Time point of administration*: within 15 minutes of the end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 51.02% (metoclopramide 10 mg IV, droperidol 1.25 mg IV) Placebo • *Dose*: 0.9% saline • *Time point of administration*: within 15 minutes of the end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 69.39% (metoclopramide 10 mg IV)
Outcomes	*Extrapyramidal symptoms (tremor, 0 to 48 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Finland

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Purhonen 1997 *(Continued)*

Setting: inpatient, single-centre

Author's name: Sinikka Purhonen

Institution: Departments of Anesthesiology and Gynecology, University Hospital of Kuopio, Kuopio, Finland

Email: NA

Address: Department of Anesthesiology, Kuopio University Hospital, PL 1777, FIN-70211 Kuopio, Finland

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were prospectively randomized to receive..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...at this small dose (10). The test infusions were prepared by a nurse who did not take part in the study and were thus, blinded for the personnel performing the study. We used oxycodone (0.12 mg/kg..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "these nurses, blinded to the study group, performed continuous observation of the patients in the recovery room. On the ward, they observed the patients at various intervals according to their normal ward routine"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "...receiving tropisetron were excluded because of missing data. One patient in the droperidol group and one in the placebo group discontinued the study because of profuse vomiting on the ward, and they were excluded due to their refusal to continue the study. The treatment groups were similar" Judgement comment: exclusion due to profuse vomiting. Missing data related to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "...refusal to continue the study. The treatment groups were similar, except for the patients' height (Table 1). More than a half of the patients had a history of previous PONV with equal frequency among the groups. They experienced more nausea and vomiting" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, periopera-

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Purhonen 1997 *(Continued)*

	tive opioids, history of motion sickness): no; (non-smoker): unclear; (history of PONV): yes

Purhonen 2006a

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 52 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 3 • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 96.42 • *History of PONV/motion sickness (%)*: 21.43/32.14 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 125 • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg given before the skin incision and every 45 minutes during the operation, 16 mg oxycodone • *Type of surgery*: breast surgery (partial or radical mastectomy, breast reconstruction, or both) Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 55 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 3 • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 78.57 • *History of PONV/motion sickness (%)*: 32.14/42.86 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 129 • *Use of perioperative opioids (if yes, which?)*: fentanyl 1 µg/kg given before the skin incision and every 45 minutes during the operation, 14 mg oxycodone • *Type of surgery*: breast surgery (partial or radical mastectomy, breast reconstruction, or both)

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Purhonen 2006a *(Continued)*

	Included criteria: females between 18 and 75 years of age, ASA I to III, scheduled to undergo breast surgery (partial or radical mastectomy, breast reconstruction, or both) **Excluded criteria:** contraindication to the anaesthetics used, nausea or vomiting within 24 hours before the scheduled anaesthesia, antiemetic drugs within the preceding 24 hours, pregnancy or breastfeeding, obesity (body mass index > 30 kg/m^2), abuse of alcohol or drugs, diabetes, any pulmonary disease **Pretreatment:** baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no
Interventions	**Intervention characteristics** Control • *Dose*: saline 2 mL • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg IV was administered as the first, dexamethasone 5 mg IV as the second, and ondansetron 4 mg IV as the third rescue treatment; 61% Ondansetron • *Dose*: 4 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg IV was administered as the first, dexamethasone 5 mg IV as the second, and ondansetron 4 mg IV as the third rescue treatment; 29%
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatient, single-centre **Author's name:** Sinikka Purhonen **Institution:** Department of Anesthesiology and Intensive Care, Kuopio University Hospital, Kuopio, Finland **Email:** sinikka.purhonen@kuh.fi **Address:** Department of Anesthesiology and Intensive Care, Kuopio University Hospital, P.O. Box 1777, FIN-70211 Kuopio, Finland

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Purhonen 2006a *(Continued)*

	Duration of study: September 2003 to June 2004 **Language:** English **Study's primary outcome:** the predefined primary outcome measure was total response (no vomiting or retching and a nausea score of zero) over the initial 24 postoperative hours **Trial registry number:** NA
Notes	Two out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random number schedule"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the anesthesiologists were aware of the administered oxygen concentration. Patients, surgeons and the nurses reporting PONV were blinded to group assignments. Shielding the oxygen blender post-operatively blinded the inspired oxygen concentration" Judgement comment: anaesthetists were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...ward, specifically trained nurses blinded to the group assignment and the actual inspired oxygen concentration monitored the patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "two patients randomized to group 30, and two patients to group O, discontinued the study because they felt that the oxygen mask was uncomfortable (Fig. 1). The data of one patient randomized to group 80 were excluded because she needed to undergo a re-operation for bleeding"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no differences in patient demographics between the study groups" Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Purhonen 2006b

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron

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Purhonen 2006b *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 51
- *Received treatment (n)*: NA
- *Analysed (n)*: 51
- *Age (mean ± SD, median (IQR), median (range))*: 35 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 82
- *History of PONV/motion sickness (%)*: 22/43
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 65
- *Use of perioperative opioids (if yes, which?)*: 66 µg fentanyl, 2 mg oxycodone
- *Type of surgery*: gynaecological laparoscopy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 49
- *Received treatment (n)*: NA
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 33 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 82
- *History of PONV/motion sickness (%)*: 29/39
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 73
- *Use of perioperative opioids (if yes, which?)*: 68 µg fentanyl, 4 mg oxycodone
- *Type of surgery*: gynaecological laparoscopy

Included criteria: female, ASA I or II, scheduled to undergo gynaecological laparoscopy

Excluded criteria: contraindications to the anaesthetics used, experienced nausea or vomiting 24 hours before the scheduled anaesthesia, had taken drugs with known antiemetic potency during the same period

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: approximately 1 hour before the operation
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: 22% (metoclopramide 10 mg IV)

Placebo

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Purhonen 2006b *(Continued)*

- *Dose*: placebo tablet
- *Time point of administration*: approximately 1 hour before the operation
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: 35% (metoclopramide 10 mg IV)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatient and outpatient, single-centre **Author's name:** Sinikka Purhonen **Institution:** Department of Anesthesiology and Intensive Care, University Hospital of Kuopio, Finland **Email:** sinikka.purhonen@kuh.fi **Address:** Department of Anesthesiology and Intensive Care, University Hospital of Kuopio, PO Box 1777, FIN-70211 Kuopio, Finland **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV (any nausea, vomiting, or both) within the first 24 hours postoperatively **Trial registry number:** NA
Notes	Two out of 3 groups relevant (propofol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the random allocation was performed using sealed opaque envelopes" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "the random allocation was performed using sealed opaque envelopes"

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Purhonen 2006b *(Continued)*

		Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...induction, isoflurane-N_2O maintenance. An 8-mg ondansetron tablet (Zofran; Glaxo, London, UK) or similar placebo tablet was given with the premedication approximately 1 hour before the operation by a nurse blinded to the patient's group allocation" Quote: "the study design was prospective, randomized, and double blind for ondansetron, and single blind for the anesthetic technique used"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the observer nurse was blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "we recruited 50 patients to each group, but 1 patient randomized to group I inadvertently received an 8-mg ondansetron tablet instead of placebo. Because the observer nurse was blinded to this mistake, we included this patient in group I + O. There were no differences between..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "...in group I + O. There were no differences between the groups in patient demographics or factors predisposing to PONV (Table 1). Twenty-seven percent..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Quan 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 120 • *Received treatment (n)*: NA • *Analysed (n)*: 120 • *Age (mean ± SD, median (IQR), median (range))*: 47.5 ± 14.1 • *Weight (mean ± SD, median (IQR), median (range))*: 63.6 ± 10.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 76.7 • *Non-smoker (%)*: 92.5 • *History of PONV/motion sickness (%)*: 4.2 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane)

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Quan 2007 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 106.4
- *Use of perioperative opioids (if yes, which?)*: 15% of patients received postoperative opioids
- *Type of surgery*: elective operation

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 120
- *Received treatment (n)*: NA
- *Analysed (n)*: 118
- *Age (mean ± SD, median (IQR), median (range))*: 44.3 ± 13.8
- *Weight (mean ± SD, median (IQR), median (range))*: 62.7 ± 10.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 78.0
- *Non-smoker (%)*: 95.8
- *History of PONV/motion sickness (%)*: 2.5
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 98.6
- *Use of perioperative opioids (if yes, which?)*: 12.7% of patients received postoperative opioids
- *Type of surgery*: elective operation

Granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 120
- *Received treatment (n)*: NA
- *Analysed (n)*: 118
- *Age (mean ± SD, median (IQR), median (range))*: 44.9 ± 14.9
- *Weight (mean ± SD, median (IQR), median (range))*: 62.7 ± 12.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 76.3
- *Non-smoker (%)*: 97.5
- *History of PONV/motion sickness (%)*: 4.2
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 112.7
- *Use of perioperative opioids (if yes, which?)*: 15.3% of patients received postoperative opioids
- *Type of surgery*: elective operation

Included criteria: ASA I or II, 18 to 75 years of age, received elective operation with endotracheal intubation and general anaesthesia

Excluded criteria: obesity; pregnancy; breastfeeding; preoperative use of antiemetics or drugs; severe cardiac, liver, renal, pulmonary, neurological, or psychiatric disease, postoperative care (?), use of gastric tube

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg

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Quan 2007 *(Continued)*

- *Time point of administration*: before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide

Tropisetron

- *Dose*: 5 mg
- *Time point of administration*: before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide

Granisetron

- *Dose*: 3 mg
- *Time point of administration*: before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Xiang Quan **Institution:** Department of Anesthesiology, PUMC Hospital, CAMS and PUMC, Beijing, China **Email:** quan79102@sina.com **Address:** Department of Anesthesiology, PUMC Hospital, CAMS and PUMC, Beijing 100730, China **Duration of study:** NA **Language:** Chinese (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Quan 2007 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "two patients with strong back pain after surgery were excluded and two patients were lost during the study" (translated)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Quan 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: NA • *Analysed (n)*: 98 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 103 • *Use of perioperative opioids (if yes, which?)*: fentanyl at induction, intraoperatively; morphine via PCIA • *Type of surgery*: NA (elective surgery)

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Quan 2011 *(Continued)*

Dexamethasone + granisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 100
- *Received treatment (n)*: NA
- *Analysed (n)*: 99
- *Age (mean ± SD, median (IQR), median (range))*: 44 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 109
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction, intraoperatively; morphine via PCIA
- *Type of surgery*: NA (elective surgery)

Included criteria: ASA I or II, 18 to 75 years of age, patients with 3 key risk factors for PONV (female, non-smoking, postoperative opioid use)

Excluded criteria: history of PONV/motion sickness, neurological or psychiatric disease, pregnant or breastfeeding, use of antiemetics in the 24 hours before surgery, need for gastric tube postoperatively

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions

Intervention characteristics

Dexamethasone + ondansetron

- *Dose*: dexamethasone 5 mg, ondansetron 4 mg
- *Time point of administration*: dexamethasone at induction of anaesthesia, ondansetron upon completion of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone + granisetron

- *Dose*: dexamethasone 5 mg, granisetron 3 mg
- *Time point of administration*: at induction of anaesthesia, upon completion of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

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Quan 2011 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Bo Zhu **Institution:** Department of Anesthesiology, PUMC Hospital, CAMA und PUMC, Beijing, China **Email:** sesha.dong@gmail.com **Address:** Department of Anesthesiology, PUMC Hospital, CAMA und PUMC, Beijing 100730, China **Duration of study:** NA **Language:** Chinese (translated by Jiechu Chen) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "totally 200 patients...were equally randomized into ondansetron group and granisetron group". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind"; translated)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind"; translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "out of 200 patients: 197 usable cases. In the ondansetron group: 1 patient in intensive care. From both groups, respectively, 1 patient was released earlier" (translated). Reasons for missing outcome data described
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

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Quan 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 72 • *Received treatment (n)*: 72 • *Analysed (n)*: 72 • *Age (mean ± SD, median (IQR), median (range))*: 26 ± 3 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 22 ± 3 • *ASA I/II/III/IV (n)*: 56/16/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 15 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 13 • *Use of perioperative opioids (if yes, which?)*: 40 µg remifentanil • *Type of surgery*: painless abortion Dexamethasone (group D1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 72 • *Received treatment (n)*: 72 • *Analysed (n)*: 71 • *Age (mean ± SD, median (IQR), median (range))*: 27 ± 3 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 22 ± 2 • *ASA I/II/III/IV (n)*: 58/13/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 18 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 12 • *Use of perioperative opioids (if yes, which?)*: 39 µg remifentanil • *Type of surgery*: painless abortion Dexamethasone (group D2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 72 • *Received treatment (n)*: 72 • *Analysed (n)*: 72 • *Age (mean ± SD, median (IQR), median (range))*: 28 ± 4 • *Weight (mean ± SD, median (IQR), median (range))*: NA

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Quan 2014 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 22 ± 3
- *ASA I/II/III/IV (n)*: 59/13/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 24
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 13
- *Use of perioperative opioids (if yes, which?)*: 39 µg remifentanil
- *Type of surgery*: painless abortion

Dexamethasone (group D3)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 71
- *Received treatment (n)*: 71
- *Analysed (n)*: 71
- *Age (mean ± SD, median (IQR), median (range))*: 27 ± 3
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 23 ± 2
- *ASA I/II/III/IV (n)*: 54/17/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 21
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 13
- *Use of perioperative opioids (if yes, which?)*: 38 µg remifentanil
- *Type of surgery*: painless abortion

Included criteria: underwent painless abortion; inclusion criteria were as follows: (1) age 18 to 36 years; (2) ASA I or II; (3) body mass index (BMI) 30 kg/m^2; (4) non-smoker

Excluded criteria: severe heart, lung, liver, or kidney function insufficiency; history of diabetes and gastrointestinal ulcer; history of chronic pain; contraindication or allergic to dexamethasone; administration of analgesic 24 hours before anaesthesia

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Control group • *Dose*: saline • *Time point of administration*: 30 minutes before operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone (group D1) • *Dose*: 0.1 mg/kg • *Time point of administration*: 30 minutes before operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone (group D2) • *Dose*: 0.15 mg/kg

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Quan 2014 *(Continued)*

- *Time point of administration*: 30 minutes before operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Dexamethasone (group D3)

- *Dose*: 0.2 mg/kg
- *Time point of administration*: 30 minutes before operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** outpatient, single-centre **Author's name:** Ping Chi **Institution:** Department of Anesthesiology, Beijing YouAn Hospital, Capital Medical University, Beijing, China **Email:** shimane126@126.com **Address:** Beijing YouAn Hospital, Capital Medical University, Beijing 100069, China **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "were randomly assigned to each group by using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...D1, D2 and D3, respectively. All drugs were prepared by a nurse blinded to the experimental conditions and were randomly assigned to each"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "hypotension and bradycardia were recorded. The visual analogue scale (VAS) scores were evaluated during coughing and at rest at 1, 2 and 24 h

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Quan 2014 *(Continued)*

		after operation by a nurse blinded to the experimental condition, using a 10 cm scale"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of 287 patients, one patient was excluded due to postoperative use of oxytocin"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "there were no significant differences in clinical characteristics among the four groups (P > 0.05, Table 1). There were no significant difference in the anesthesia time, operation time, and dosage of propofol and remifentanil among the four groups (P > 0.05)..." Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Quaynor 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range)) years*: 48 ± 16 • *Weight (mean ± SD, median (IQR), median (range)) kg*: 79 ± 16 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)* ´- 27/20/3/0 (one patient missing) • *Gender (female in %)*: 80 • *Non-smoker (%)*: NA • *History of PONV*: 23 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia (in min; as mean or median)*: 104 • *Use of perioperative opioids (if yes, which?)*: fentanyl, codeine • *Type of surgery*: laparoscopic cholecystectomy Ondansetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 56

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Quaynor 2002 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range)) years*: 48 ± 17
- *Weight (mean ± SD, median (IQR), median (range)) kg*: 75 ± 16
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n) ´*- 36/15/29/0 (too many patients in this result as compared to N)
- *Gender (female in %)*: 93
- *Non-smoker (%)*: NA
- *History of PONV*: 32
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia (in min; as mean or median)*: 105
- *Use of perioperative opioids (if yes, which?)*: fentanyl, codeine
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, undergoing elective laparoscopic cholecystectomy

Excluded criteria: younger than 18 years of age, using drugs with antiemetic properties

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Metoclopramide

- *Dose*: 20 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: first-line IV metoclopramide 10 mg, second-line IV droperidol 1.25 mg

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: first-line IV metoclopramide 10 mg, second-line IV droperidol 1.25 mg

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (0 to 6 hours)

- Outcome type: dichotomous outcome

Vomiting (12 to 24 hours)

- Outcome type: dichotomous outcome

PONV (0 to 24 hours)

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (muscle twitches, 0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

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Quaynor 2002 *(Continued)*

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this study was supported by an educational grant from GlaxoWellcome Ltd. of Norway, which markets ondansetron **Country:** Norway **Setting:** inpatient, single-centre **Author's name:** H. Quaynor **Institution:** Department of Anesthesia, Kongsberg Hospital **Email:** hen-qua@frisurf.no **Address:** Department of Anaesthesia, Kongsberg Hospital, P.O. Box 10, N-Kongsberg, Norway **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "instructions in numbered, sealed envelopes, randomized by random numbers generated by a computer. At the end of surgery..."
Allocation concealment (selection bias)	Unclear risk	Quote: "prepared the study drugs from instructions in numbered, sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque...envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "when the surgical procedure ended, the patients received the study drug of either metoclopramide 20 mg (Group M) or ondansetron 8 mg (Group O), intravenously from identical syringes. A nurse, not participating in the evaluation of the patients, prepared the study drugs from instructions"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were interviewed by the attending nurse (who was blind to the study drug)"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "in all, 122 patients were recruited for the study. Of these, 15 patients were excluded from the analyses: six because of more extensive surgery performed, five because of inadvertent violation to the study protocol, three due to re-operations due to postoperative hemorrhage during the study period and one patient because of renal failure. Thus, 107 patients were left for analyses: 51 in the metoclopramide group (Group M) and 56 in the ondansetron group,,," Judgement comment: reason for missing outcome data described and not related to outcomes of interest

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Quaynor 2002 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Rajeeva 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 26 • *Received treatment (n)*: 26 • *Analysed (n)*: 26 • *Age (mean ± SD, median (IQR), median (range))*: 28.85 ± 5.29 • *Weight (mean ± SD, median (IQR), median (range))*: 48.88 ± 6.38 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 26/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 28.54 • *Use of perioperative opioids (if yes, which?)*: 1 mg/kg meperidine intraoperative • *Type of surgery*: gynaecological diagnostic laparoscopy Ondansetron + dexamethasone (group II) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 28.72 ± 4.46 • *Weight (mean ± SD, median (IQR), median (range))*: 50.84 ± 6.92 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 25/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 29.00 • *Use of perioperative opioids (if yes, which?)*: 1 mg/kg meperidine intraoperative

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Rajeeva 1999 *(Continued)*

- *Type of surgery*: gynaecological diagnostic laparoscopy

Included criteria: ASA I, female, 20 to 40 years of age, undergoing elective diagnostic laparoscopy under general anaesthesia

Excluded criteria: obese (BW 20% more than expected for their age), pregnant, history of motion sickness or PONV, had received antiemetics within 24 hours of surgery, needing long-term steroid therapy, diabetes mellitus, intestinal obstruction or hiatus hernia

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group I) • *Dose*: 4 mg • *Time point of administration*: soon after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.15 mg/kg metoclopramide; the need for rescue antiemetics did not differ between the 2 groups Ondansetron + dexamethasone (group II) • *Dose*: ondansetron 4 mg + dexamethasone 8 mg • *Time point of administration*: soon after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.15 mg/kg metoclopramide; the need for rescue antiemetics did not differ between the 2 groups
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** NA, single-centre **Author's name:** Neerja Bhardwaj **Institution:** Departments of Anaesthesia and Obstetrics and Gynaecology, Post Graduate Institute of Medical Education and Research, Chandigarh **Email:** NA **Address:** Flat No. 124-C, Sector 24-A, Chandigarh, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA

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Rajeeva 1999 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomly divided by random number chart into two groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the two groups were comparable regarding age, weight, last menstrual period (LMI'), duration of procedure, and duration of insufflation" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Raphael 1993

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: 61 • *Analysed (n)*: 61 • *Age (mean ± SD, median (IQR), median (range))*: 35 (16 to 44) • *Weight (mean ± SD, median (IQR), median (range))*: 68.0 ± 12.1

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Raphael 1993 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 22.95/14.75
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 14
- *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl, 10 patients received morphine postoperatively
- *Type of surgery*: gynaecological laparoscopic surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: 62
- *Analysed (n)*: 62
- *Age (mean ± SD, median (IQR), median (range))*: 33 (23 to 57)
- *Weight (mean ± SD, median (IQR), median (range))*: 67.3 ± 9.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 22.58/16.13
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 13.6
- *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl, 8 patients received morphine postoperatively
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: undergoing elective day-case gynaecological laparoscopic surgery

Excluded criteria: pregnant, breastfeeding, taking any medication other than the oral contraceptive pill, currently being treated for nausea or vomiting

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Metoclopramide • *Dose*: 10 mg • *Time point of administration*: immediately before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Vomiting (0 to 6 hours)*

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Raphael 1993 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (6 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this study was funded by a grant from Pullmaflex UK Ltd. **Country:** England **Setting:** outpatient, single-centre **Author's name:** J.H. Raphael **Institution:** Department of Anaesthetics, Pilgrim Hospital, Boston, Lincolnshire PE21 9QS **Email:** NA **Address:** Department of Anaesthetics, Pilgrim Hospital, Boston, Lincolnshire PE21 9QS **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the study was conducted in a double-blind manner with coded ampoules and restricted and stratified randomization was used" Judgement comment: no detailed information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "the study was conducted in a double-blind manner with coded ampoules and restricted and stratified randomization was used, with sealed envelopes, to ensure treatment groups of the same size and an equal number of patients with previous PONV in each group" Judgement comment: not stated; "sequentially numbered, opaque" envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")

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Raphael 1993 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred and six patients (86%) completed the questionnaire: 50 in the ondansetron group and 56 in the metoclopramide group. Of the patients who failed to complete the questionnaire, the proportion in each group with no nausea and vomiting in the first 6 h was similar to that found in those who did complete the questionnaire" Quote: "sixty-one patients received ondansetron and 62 received metoclopramide. One patient was excluded from the study after randomization because additional atropine was administered during operation to correct a bradycardia"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the groups in age, body weight, previous history of PONV, history of motion sickness, grade of anaesthetist, duration of anaesthesia or administration of postoperative opioid drugs" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Reeve 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Diclectin • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 71 • *Received treatment (n)*: NA • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 34.8 ± 5.5 • *Weight (mean ± SD, median (IQR), median (range))*: 70.7 ± 17.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 33.85/15.38 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia • *Type of surgery*: laparoscopic tubal ligation Placebo

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Reeve 2005 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 75
- *Received treatment (n)*: NA
- *Analysed (n)*: 62
- *Age (mean ± SD, median (IQR), median (range))*: 33.8 ± 5.8
- *Weight (mean ± SD, median (IQR), median (range))*: 72.0 ± 14.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 13.43/16.42
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia
- *Type of surgery*: laparoscopic tubal ligation

Included criteria: non-pregnant females scheduled for elective laparoscopic tubal ligation, ASA I to III

Excluded criteria: on oral contraceptives, did not know the date of their last menstrual period, had not resumed menses postpartum, had Parkinson's disease, declined consent

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, history of motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear; (history of PONV): yes

Interventions	**Intervention characteristics** Diclectin • *Dose*: diclectin (doxylamine succinate 10 mg, pyridoxine hydrochloride 10 mg) • *Time point of administration*: patients were instructed to take 2 pills with fluid before retiring to bed on the night before surgery. Upon awakening the morning of surgery, they took 1 more tablet with a sip of water and any other preoperative medications as instructed by the anaesthesiologist. The fourth tablet was taken postoperatively, before discharge from the short stay unit (SSU) • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: placebo tablets • *Time point of administration*: patients were instructed to take 2 pills with fluid before retiring to bed on the night before surgery. Upon awakening the morning of surgery, they took 1 more tablet with a sip of water and any other preoperative medications as instructed by the anaesthesiologist. The fourth tablet was taken postoperatively, before discharge from the short stay unit (SSU) • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Duchesnay Pharmaceuticals provided the drugs, the placebo and $1000 **Country:** Canada

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Reeve 2005 *(Continued)*

Setting: outpatient, single-centre

Author's name: B.K. Reeve

Institution: Department of Anesthesia, St. Joseph's Hospital, Hamilton, Canada

Email: acescholes@yahoo.com

Address: Department of Anesthesia, St. Joseph's Hospital, 50 Charlton Avenue East, Hamilton, Ontario L8N 4A6, Canada

Duration of study: October 1998 to December 2000

Language: English

Study's primary outcome: PONV

Trial registry number: NA

Notes	Repetitive doses of antiemetic drugs (before discharge of SSU). Outcomes are eligible only before discharge of SSU (vomiting only in PACU relevant)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Parkinson's disease, or declined consent. Study design Patients were allocated to DCL or placebo using a computer-generated random number table kept in the pre-operative assessment clinic.Because of a previous study"
Allocation concealment (selection bias)	Low risk	Quote: "because of a previous study done at our institution which showed a difference in the incidence of nausea and vomiting according to the phase in the menstrual cycle, the study design had patients stratified into two groups with respect to the phase in the menstrual cycle at the time of their surgical procedure (group 1: day one to eight, vs group 2: day nine or greater). Drug allocation was determined by a sealed opaque package containing four pills (four tablets of DCL, or four placebo tablets)"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "drug allocation was determined by a sealed opaque package containing four pills (four tablets of DCL, or four placebo tablets)"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "data collectors were blinded to treatment allocation throughout the study" Quote: "strengths of this study design include the randomized, stratified, concealed design, using a placebo comparison with DCL. Blinding of the patients, clinicians, data collectors, investigators and biostatistician was assured until our analysis was complete"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "a total of 146 patients were recruited in the study period (Figure 1). This was less than our calculated target of 200. Patients were stratified according to the timing of their menstrual cycle, such that 44 patients were in day zero to eight, and 102 patients were in day nine or later in their cycle. Of 146 patients enrolled in the study, 132 patients underwent tubal ligation, and surgery was cancelled in 14 patients. Of 132 patients, data were unavailable for four patients, one patient withdrew consent and one withdrew because she was breastfeeding, leaving 126 patients with full data sets for the effectiveness analysis. This population contributed to the primary effectiveness analysis. A break in protocol occurred in 11 patients in the DCL group and 13 in the placebo group; the reasons for this break in protocol were that patients

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Reeve 2005 *(Continued)*

		did not take all four tablets (DCL = 10, placebo = 9), or the anesthesiologist administered preoperative antiemetics (DCL = 1, placebo = 4). Thus, 102 patients contributed to the efficacy analysis (Figure 2). The clinical and demographic characteristics" Judgement comment: dropout rate about 30%
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the clinical and demographic characteristics of patients undergoing tubal ligation and receiving DCL and placebo were similar, except for a greater proportion reporting a history of PONV in patients receiving DCL (Table I)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, history of motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear; (history of PONV): yes

Reihner 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 72 • *Received treatment (n)*: NA • *Analysed (n)*: 71 • *Age (mean ± SD, median (IQR), median (range))*: 54 (21 to 78) • *Weight (mean ± SD, median (IQR), median (range))*: 66 (45 to 100) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 49.30/21.13 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 100 • *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia, ketobemidone for postoperative pain • *Type of surgery*: breast surgery Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 72 • *Received treatment (n)*: NA • *Analysed (n)*: 69

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Reihner 2000 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 53 (30 to 80)
- *Weight (mean ± SD, median (IQR), median (range))*: 66 (45 to 100)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 33.33/21.74
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 110
- *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia, ketobemidone for postoperative pain
- *Type of surgery*: breast surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 72
- *Received treatment (n)*: NA
- *Analysed (n)*: 67
- *Age (mean ± SD, median (IQR), median (range))*: 55 (18 to 74)
- *Weight (mean ± SD, median (IQR), median (range))*: 66 (45 to 100)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 47.76/22.39
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95
- *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia, ketobemidone for postoperative pain
- *Type of surgery*: breast surgery

Included criteria: women, 18 to 80 years of age, ASA I or II, scheduled for breast surgery

Excluded criteria: pregnancy, body weight > 100 kg, ongoing corticosteroid medication

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: 0.9% saline
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 49% (prochlorperazine 10 mg IM)

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 30% (prochlorperazine 10 mg IM)

Ondansetron

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Reihner 2000 *(Continued)*

- *Dose*: 8 mg
- *Time point of administration*: immediately after induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 39% (prochlorperazine 10 mg IM)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** supported by grants from the Karolinska Institute, The Swedish Society of Medicine, and the Swedish Cancer Fund (3948-B97-01XAB). Glaxo AB, Mölndal, Sweden provided ondansetron **Country:** Sweden **Setting:** inpatient, single-centre **Authors name:** E. Reihnér **Institution:** Department of Surgery, Karolinska Institute at Huddinge University Hospital, Huddinge, Sweden **Email:** NA **Address:** Department of Surgery, Karolinska Institute at Huddinge University Hospital, Huddinge, Sweden **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response as defined by no nausea, emesis, or need to administer rescue antiemetics during the 24-hour postoperative period (designated as 'no PONV') **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomization was carried out according to a randomization list and split into three equally sized groups" Judgement comment: no information on sequence generation provided

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Reihner 2000 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "the treatment allocation codes were not disclosed until the study was finished" Quote: "randomization was carried out according to a randomization list and split into three equally sized groups" Quote: "numbered vials, with the study drugs diluted in saline to equal volumes, were prepared by the hospital pharmacy according to the randomization list" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "numbered vials, with the study drugs diluted in saline to equal volumes, were prepared by the hospital pharmacy according to the randomization list" Quote: "the treatment allocation codes were not disclosed until the study was finished" Quote: "the objective of the present investigation was to compare the efficacy of droperidol and ondansetron in the prevention of PONV in a prospective, double-blind, randomized placebo-controlled trial of patients undergoing breast surgery" Judgement comment: vials not specified as "identical"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the objective of the present investigation was to compare the efficacy of droperidol and ondansetron in the prevention of PONV in a prospective, double-blind, randomized placebo-controlled trial of patients undergoing breast surgery" Quote: "the treatment allocation codes were not disclosed until the study was finished" Judgement comment: it is unclear who performed outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...considered for P < 0.05. Nine out of a total of 216 patients were excluded (six required corticosteroids during anaesthesia as a result of difficulties at intubation or bronchial asthma, and three patients received premedication and anaesthesia diverging from the protocol), one in the placebo, three in the droperidol and five in the ondansetron group. Thus, 207 women were included in the analysis"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no differences in age, weight, type or duration of surgery and duration of anaesthesia" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Reinhart 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial

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Reinhart 1994 *(Continued)*

Study grouping: 2 groups, monoprophylaxis

Participants	**Baseline characteristics** Scopolamine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 45.2 ± 19.2 • *Weight (mean ± SD, median (IQR), median (range))*: 78.7 ± 15.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 12/4/0/0 • *Gender (female in %)*: 56.25 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, codeine • *Type of surgery*: exploratory tympanostomy, mastoidectomy, or endolymphatic sac and oval and round window surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 15.7 • *Weight (mean ± SD, median (IQR), median (range))*: 82.6 ± 16.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 11/5/0/0 • *Gender (female in %)*: 56.25 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, codeine • *Type of surgery*: exploratory tympanostomy, mastoidectomy, or endolymphatic sac and oval and round window surgery **Included criteria:** ASA I and II; for exploratory tympanostomy, mastoidectomy, or endolymphatic sac and oval and round window surgery; 18 to 65 years of age, weighed 45 to 100 kg **Excluded criteria:** sensitive to anticholinergic medication, current therapy with anticholinergics or antihistamines, narrow-angle glaucoma, gastrointestinal obstruction, urinary tract obstruction, pregnancy, nursing **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics**

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Reinhart 1994 *(Continued)*

	Scopolamine • *Dose*: scopolamine patch 140 µg delivered initially, 5 µg/h thereafter • *Time point of administration*: 2 hours before surgery • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: promethazine 12.5 mg IV Placebo • *Dose*: placebo patch • *Time point of administration*: 2 hours before surgery • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: promethazine 12.5 mg IV
Outcomes	*Visual disturbances (blurred vision, post discharge until 26 hours postoperative)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, single-centre **Comments:** none **Author's name:** Douglas J. Reinhart **Institution:** University of Utah, McKay-Dee Hospital **Email:** NA **Address:** Douglas J. Reinhart, MD, Department of Anesthesiology, University of Utah, McKay-Dee Hospital, 3939 Harrison Blvd., Box 9370, Ogden, UT 84409-0370, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized fashion". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Low risk	Judgement comment: described as "double-blind"; patches (scopolamine and placebo) were identical

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Reinhart 1994 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were observed by a trained, blinded monitor who recorded the incidence of nausea, vomiting, and length of stay in the postanesthesia care unit (PACU) and day surgery unit (DSU) and discharge time"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "...overall average VAS scores. Thirty-nine patients were enrolled in the study and 32 patients completed it. Three patients (one from the active patch group and two from the placebo group) were omitted from the results due to failure to return the diary sent home with them. One patient from the placebo group was admitted to the hospital due to uncontrollable vomiting postoperatively and was discontinued from the study. Three other patients failed to wear the patch throughout the study. In two of these patients" Judgement comment: exclusion of 1 patient from the control group due to uncontrollable vomiting. Reason for exclusion related to the outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Rennemo 1982

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Levomepromazine + scopolamine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 44.9 ± 2.3 • *Weight (mean ± SD, median (IQR), median (range))*: 69.2 ± 2.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 56.6 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced (N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 154.7 • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine • *Type of surgery*: upper abdominal surgery Droperidol + scopolamine • *Assessed for eligibility (n)*: -

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Rennemo 1982 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 47.5 ± 2.1
- *Weight (mean ± SD, median (IQR), median (range))*: 72.5 ± 2.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced (N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 141.0
- *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine
- *Type of surgery*: upper abdominal surgery

Included criteria: undergoing elective upper abdominal surgery, ASA I or II, 24 to 68 years of age

Excluded criteria: took analgesics or psychotropic drugs

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Levomepromazine + scopolamine • *Dose*: levomepromazine 0.1 mg/kg, scopolamine 0.4 mg • *Time point of administration*: levomepromazine at induction of anaesthesia, scopolamine 1 hour before induction • *Route of administration*: levomepromazine IV, scopolamine SC • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IV Droperidol + scopolamine • *Dose*: droperidol 0.15 mg/kg, scopolamine 0.4 mg • *Time point of administration*: droperidol at induction of anaesthesia, scopolamine 1 hour before induction • *Route of administration*: droperidol IV, scopolamine SC • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IV
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** levomepromazine was supplied by Rhone-Poulene, Oslo **Country:** Norway **Setting:** inpatient, single-centre **Author's name:** Fred Rennemo **Institution:** Regional Hospital of Trondheim, Norway **Email:** NA

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Rennemo 1982 *(Continued)*

	Address: Fred Rennemo, Department of Anesthesiology, Regional Hospital of Trondheim, Norway **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized ... according to the envelope method." No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "neither the patient, nor the investigators or nurses taking part in the anaesthesia and postoperative care knew what kind of neuroleptic drug was used"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "neither the patient, nor the investigators or nurses taking part in the anaesthesia and postoperative care knew what kind of neuroleptic drug was used"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Rettori 2011

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA

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Rettori 2011 *(Continued)*

- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 53.8 ± 14.73
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 77
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 84.40
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction
- *Type of surgery*: lobectomy or total thyroidectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 57.37 ± 13.25
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 74
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88.65
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction
- *Type of surgery*: lobectomy or total thyroidectomy

Included criteria: undergoing thyroid surgery for benign disease, ASA I or II, weight between 50 and 100 kg

Excluded criteria: younger than 18 years of age, previous neoplasm and/or thyroid and neck surgery, received antiemetic therapy within 48 hours before surgery, chronic pain, insulin-dependent diabetes mellitus, history of PONV after minor surgery, pregnant women

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, peri-operative opioids): unclear

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: 20 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg (first line), ondansetron 4 mg (second line)

Placebo

- *Dose*: 2 mL of NaCl 0.9%
- *Time point of administration*: 20 minutes before induction of anaesthesia
- *Route of administration*: IV

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Rettori 2011 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg (first line), ondansetron 4 mg (second line)
Outcomes	*Mortality (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** F. Feroci **Institution:** General Surgery Unit, Misericordia and Dolce Hospital, Prato, Italy **Email:** fferoci@yahoo.it **Address:** Ospedale Misericordia e Dolce, Piazza dell´Ospedale 5, 59100 Prato, Italy **Duration of study:** January to December 2009 **Language:** Italian (translated by Insa Backhaus) **Study's primary outcome:** NA **Trial registry number:** NCT00888303
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "randomization was performed with a computer-generated list ..." (translated)
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "... and personnel not involved in the study prepared the syringes with the drugs." "...Patients (after signing informed consent), the anaesthetist during surgery and to those who collected postoperative data were blinded to the study....." (translated)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "... and personnel not involved in the study prepared the syringes with the drugs"; "...patients (after signing informed consent), the anaesthetist during surgery and to those who collected postoperative data were blinded to the study....." (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "two patients in group B were excluded from the statistical analysis because they were involved in urgent reoperation for postoperative bleeding" (translated)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00888303 (retrospective registration)

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Rettori 2011 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Rho 2001-1

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 105 • *Use of perioperative opioids (if yes, which?)*: 1 mg butorphanol intraoperative, no postoperative opioids • *Type of surgery*: laparoscopic hysterectomy, ovarian tumour removal Droperidol (group 3) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 40 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 132 • *Use of perioperative opioids (if yes, which?)*: 1 mg butorphanol intraoperative, no postoperative opioids • *Type of surgery*: laparoscopic hysterectomy, ovarian tumour removal

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Rho 2001-1 *(Continued)*

	Included criteria: healthy female patients 20 to 60 years of age, scheduled to undergo laparoscopic hysterectomy and ovarian tumour removal, ASA I or II **Excluded criteria:** history of recurrent respiratory disease, endocrine system/nervous system disease, pregnancy, obesity (> 50% of normal body weight) **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, peri-operative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia): yes
Interventions	**Intervention characteristics** Control (group 1) • *Dose*: normal saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (group 3) • *Dose*: 1 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (3 to 6 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (at recovery room, during 30 minutes postoperative, 30 minutes to 1 hour, 1 to 3 hours, 3 to 6 hours, 6 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Shi Youn Rho **Institution:** Department of Anesthesiology, Chungnam National University Hospital, Daejeon, Korea **Email:** NA **Address:** NA

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Rho 2001-1 *(Continued)*

	Duration of study: April 2000 to July 2000 **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Study with 4 groups split into 2 sub-studies (Rho 2005-1, Rho 2005-2), with 2 groups each due to different anaesthesia regimens (TIVA vs inhalational)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly assigned". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "observed by a familiar nurse who was trained for this study" (translated). No information on blinding of outcome assessors provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia): yes

Rho 2001-2

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA

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Rho 2001-2 *(Continued)*

- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 111
- *Use of perioperative opioids (if yes, which?)*: 1 mg butorphanol intraoperative, no postoperative opioids
- *Type of surgery*: laparoscopic hysterectomy, ovarian tumour removal

Droperidol (group 4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 10
- *Weight (mean ± SD, median (IQR), median (range))*: 55 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105
- *Use of perioperative opioids (if yes, which?)*: 1 mg butorphanol intraoperative, no postoperative opioids
- *Type of surgery*: laparoscopic hysterectomy, ovarian tumour removal

Included criteria: healthy female patients 20 to 60 years of age, scheduled to undergo laparoscopic hysterectomy and ovarian tumour removal, ASA I or II

Excluded criteria: history of recurrent respiratory disease, endocrine system/nervous system disease, pregnancy, obesity (> 50% of normal body weight)

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Control (group 2) • *Dose*: normal saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (group 4) • *Dose*: 1 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV

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Rho 2001-2 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (3 to 6 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (at recovery room, during 30 minutes postoperative, 30 minutes to 1 hour, 1 to 3 hours, 3 to 6 hours, 6 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Shi Youn Rho **Institution:** Department of Anesthesiology, Chungnam National University Hospital, Daejeon, Korea **Email:** NA **Address:** NA **Duration of study:** April 2000 to July 2000 **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Study with 4 groups split into 2 sub-studies (Rho 2005-1, Rho 2005-2), with 2 groups each due to different anaesthesia regimens (TIVA vs inhalational)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly assigned". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Rho 2001-2 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "observed by a familiar nurse who was trained for this study" (translated). No information on blinding of outcome assessors provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia): yes

Riley 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 80 • *Age (mean ± SD, median (IQR), median (range))*: 44 • *Weight (mean ± SD, median (IQR), median (range))*: 78 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 36/31 • *Type of general anaesthesia*: balanced (isoflurane, fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA but no difference between groups was stated • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine, meperidine • *Type of surgery*: total abdominal hysterectomy Placebo + droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Riley 1998 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: 44
- *Weight (mean ± SD, median (IQR), median (range))*: 75
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 38/39
- *Type of general anaesthesia*: balanced (isoflurane, fentanyl, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA but no difference between groups was stated
- *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine, meperidine
- *Type of surgery*: total abdominal hysterectomy

Included criteria: non-pregnant, ASA I or II, women scheduled for total abdominal hysterectomy

Excluded criteria: 30 to 45 years of age; ASA III, IV, V; ingestion of any antiemetic drugs; vomiting in the 24 hours preceding surgery; history of drug abuse

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron + droperidol • *Dose*: ondansetron 4 mg, droperidol 1.25 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo + droperidol • *Dose*: placebo, droperidol 1.25 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre

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Riley 1998 *(Continued)*

Author's name: Theodore J. Riley

Institution: Magee-Womens Hospital, Pittsburg

Email: NA

Address: Ray McKenzie, Department of Anesthesia, Magee-Womens Hospital, 300 Halket St, Pittsburg, PA 15213-3180, USA

Duration of study: NA

Language: English

Study's primary outcome: proportion of patients having a complete response (no emesis and no administration of rescue antiemetics 24 hours postoperatively)

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was accomplished with a computer-generated random numbers table. Identical syringes containing either ondansetron 4 mg (Group 1) or saline (Group 2)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...were prepared by personnel not involved in the study and administered intravenously after droperidol according to the random numbers table. The 24 hour study period began on entry"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Rimaitis 2010

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis

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Rimaitis 2010 *(Continued)*

Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 51 • *Received treatment (n)*: NA • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 4 • *ASA I/II/III/IV (n)*: 28/23/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (fentanyl, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 45 • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: laparoscopic gynaecological surgery Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 51 • *Received treatment (n)*: NA • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 2 • *BMI (mean ± SD, median (IQR), median (range))*: 25 ± 5 • *ASA I/II/III/IV (n)*: 29/22/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (fentanyl, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: laparoscopic gynaecological surgery **Included criteria:** ASA I or II, undergoing laparoscopic gynaecological surgery **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA

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Rimaitis 2010 *(Continued)*

	Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Lithuania **Setting:** inpatient, single-centre **Author's name:** Kęstutis Rimaitis **Institution:** Department of Gynecology and Obstetrics, Kaunas University of Medicine, Kaunas, Lithuania **Email:** estutis.rimaitis@kmuk.lt **Address:** Eivenių 2, 50009 Kaunas, Lithuania **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (ketorolac)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "...use of opioids, were registered. All the study groups were coded; therefore, neither study patients nor investigators knew group dependence. Data were analyzed using the..." Judgement comment: no placebo treatment in the control group. Participants and personnel were able to uncover the group allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "use of opioids, were registered. All the study groups were coded; therefore, neither study patients nor investigators knew group dependence. Data were analyzed using..."

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Rimaitis 2010 *(Continued)*

		Judgement comment: not clear whether outcome assessors were blinded (no placebo treatment in the control group)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic data of the study population are presented in Table 1. There were no significant differences between the study groups with respect to age, weight, height, ASA status, and body mass index (BMI)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Rodrigo 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 24 ± 5.1 • *Weight (mean ± SD, median (IQR), median (range))*: 53 ± 8.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced (fentanyl, N_2O, isoflurane) • *Duration of anaesthesia (in min; as mean or median)*: 48 • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine • *Type of surgery*: removal of impacted third molar teeth Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 26 ± 7.6

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Rodrigo 1994 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 55 ± 9.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 56.4
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced (fentanyl, N_2O, isoflurane)
- *Duration of anaesthesia (in min; as mean or median)*: 47
- *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine
- *Type of surgery*: removal of impacted third molar teeth

Included criteria: 18 to 48 years of age, ASA I or II, scheduled to undergo minor oral surgery (removal of impacted third molar teeth) that could not be carried out under local anaesthesia

Excluded criteria: males weighing more than 120 kg, females weighing more than 100 kg, pregnant, breastfeeding, allergic to ondansetron

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 6.25 mg prochlorperazine IM Placebo • *Dose*: 2 mL saline • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 6.25 mg prochlorperazine IM
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Glaxo (Hong Kong Ltd) supplied ondansetron **Country:** Hong Kong **Setting:** inpatient, single-centre

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Rodrigo 1994 *(Continued)*

	Author's name: M.R.C. Rodrigo **Institution:** Department of Maxillofacial Surgery, Dental Faculty, University of Hong Kong **Email:** NA **Address:** Block 1, Flat A8, 23 Sha Wan Drive, Pokfulam, Hong Kong **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "random allocation chart"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind study" Judgement comment: quote: "the test drug was drawn up by the nursing officer of the operating theatre and was given by the anaesthetist, thus making it blind to patients, the anaesthetist and the surgeons"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "eighty patients were included in the study. Of these results, three patients were eliminated as instead of paracetamol two had been given oral difluisal and one Panadeine..." Reasons for exclusion described and unrelated to the outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Rodrigo 1996

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis

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Rodrigo 1996 *(Continued)*

Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 42.0 ± 13.7 • *Weight (mean ± SD, median (IQR), median (range))*: 57.4 ± 10.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 37.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced (N_2O, enflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 212 • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine • *Type of surgery*: maxillofacial operation Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 36.7 ± 15.4 • *Weight (mean ± SD, median (IQR), median (range))*: 54.6 ± 10.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 31.3 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced (N_2O, enflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 198.8 • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine • *Type of surgery*: maxillofacial operation **Included criteria:** 19 to 68 years of age, undergoing maxillofacial operation longer than 1 hour, insertion of nasogastric tube, male weighing less than 120 kg, female weighing less than 100 kg **Excluded criteria:** scheduled to receive dexamethasone, pregnant, breastfeeding **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately before induction • *Route of administration*: IV

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Rodrigo 1996 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: 6.25 mg prochlorperazine IM

Placebo

- *Dose*: 2 mL normal saline
- *Time point of administration*: immediately before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 6.25 mg prochlorperazine IM

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Glaxo (Hong Kong) for supplied ondansetron **Country:** Hong Kong **Setting:** inpatient, single-centre **Author's name:** Chandra Rodrigo **Institution:** Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Hong Kong **Email:** NA **Address:** Block 1 Flat A8, Sha Wan Drive, Pokfulam, Hong Kong **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "random allocation chart"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Rodrigo 1996 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind" Quote: "...of a random allocation chart. Immediately before induction of anesthesia, the test agent was drawn into a syringe by the nurse in the operating room and was given intravenously by an anesthetist, thus making it unknown to the patients, anesthetists, and surgeons. The systolic and diastolic blood..."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the results of 2 of the 34 patients were eliminated because the duration of the operation was less than 1 hour"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Rothenberg 1991

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 33 • *Age (mean ± SD, median (IQR), median (range))*: 32 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 64 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl • *Type of surgery*: gynaecological laparoscopy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Rothenberg 1991 *(Continued)*

- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 59
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Included criteria: ASA I or II, undergoing outpatient gynaecological laparoscopy

Excluded criteria: history of hypertension or organic heart disease, being treated preoperatively with medications with potential antiemetic effects (e.g. benzodiazepines, steroids, droperidol, scopolamine, antihistamines, metoclopramide)

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 0.9% saline • *Time point of administration*: before reversal of neuromuscular blockade • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 0.04 mg/kg • *Time point of administration*: before reversal of neuromuscular blockade • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (discharge to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (PACU)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, single-centre **Author's name:** David M. Rothenberg

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Rothenberg 1991 *(Continued)*

Institution: Department of Anesthesiology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL, USA

Email: NA

Address: Department of Anesthesiology, Rush-Presbyterian-St. Luke's Medical Center, 739 Jelke, 1750 West Congress Parkway, Chicago, IL 60612, USA

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	Two out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized fashion" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "all doses were prepared in equal volumes" Quote: "anesthesia for outpatient gynecologic laparoscopy. Patients were assigned in a double-blind randomized fashion to receive a standardized general anesthetic followed by an intramuscular dose of either ephedrine (0.5 mg/kg), droperidol (0.04 mg/kg), or saline before the conclusion of surgery. Nausea, retching, or vomiting..." Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "in the recovery room the patients were evaluated every 5-10 min for nausea, retching, or vomiting by a nurse not directly involved in the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 100 patients studied, three patients required laparotomy and were therefore excluded from the study. Of the remaining 97 patients..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no differences in regard to age, weight, amount of IV fluids administered, or duration of anesthesia between the three groups..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Rothenberg 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 47 • *Age (mean ± SD, median (IQR), median (range))*: 32 (17 to 45) • *Weight (mean ± SD, median (IQR), median (range))*: 66 (45 to 95) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 8.5/14.9 • *Type of general anaesthesia*: combined anaesthesia (N_2O, propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 40 • *Use of perioperative opioids (if yes, which?)*: 2.9 mg morphine, 1.5 µg/kg fentanyl • *Type of surgery*: gynaecological laparoscopy Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 48 • *Age (mean ± SD, median (IQR), median (range))*: 32 (18 to 48) • *Weight (mean ± SD, median (IQR), median (range))*: 65 (47 to 100) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 6.3/14.6 • *Type of general anaesthesia*: combined anaesthesia (N_2O, propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 41.5 • *Use of perioperative opioids (if yes, which?)*: 3.4 mg morphine, 1.5 µg/kg fentanyl • *Type of surgery*: gynaecological laparoscopy **Included criteria:** ASA I or II, requiring outpatient gynaecological laparoscopy **Excluded criteria:** currently receiving antiemetic or corticosteroid therapy; history of immunosuppression, peptic ulcer disease, diabetes mellitus, hypertension, recent tuberculosis, Cushing's syndrome, or cataracts **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics**

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Rothenberg 1998 *(Continued)*

	Droperidol • *Dose*: 0.02 mg/kg • *Time point of administration*: before abdominal incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide, ondansetron, prochlorperazine, droperidol, or ephedrine, alone or in combination Dexamethasone • *Dose*: 0.17 mg/kg • *Time point of administration*: before abdominal incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide, ondansetron, prochlorperazine, droperidol, or ephedrine, alone or in combination
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (discharge to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, single-centre **Author's name:** David M. Rothenberg **Institution:** Department of Anesthesiology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois, USA **Email:** NA **Address:** Department of Anesthesiology, Rush-Presbyterian-St. Luke's Medical Center, 1653 W. Congress Parkway, Chicago, Illinois, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Rothenberg 1998 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "the purpose of this randomized..." Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "unlabeled numbered aliquots of the study drugs were prepared in equal volumes by an operating room pharmacist without knowledge of the study design"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "within 24 h a blinded observer telephoned each patient to inquire about additional postoperative complications" Quote: "...by a nurse not directly participating in the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "five patients (5%) were excluded from data analysis due to the need to perform surgical laparotomy (2 patients) and failure to achieve telephone contact (3 patients). Of the remaining 95 patients, 47 were assigned to the droperidol group, and 48 were assigned to the dexamethasone group"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...assigned to the dexamethasone group. There were no differences between the two groups in relationship to patient age, weight, prior episodes of PONV, preoperative history of motion sickness, timing of menses, duration of surgery, amount of IV fluid or vecuronium administered or propofol maintenance dosage (Table 1)..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Rudra 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 40 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0

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Rudra 2005 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction, pethidine 1.5 mg/kg IM, if VAS > 5 for postoperative pain
- *Type of surgery*: laparoscopic cholecystectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction, pethidine 1.5 mg/kg IM, if VAS > 5 for postoperative pain
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 10
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction, pethidine 1.5 mg/kg IM, if VAS > 5 for postoperative pain
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: women 20 to 60 years of age, ASA I or II

Excluded criteria: gastrointestinal disease, history of motion sickness and/or previous PONV, pregnancy or menstruation, had taken antiemetics within 24 hours before operation

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Rudra 2005 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Droperidol • *Dose*: 20 µg/kg • *Time point of administration*: NA • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 40 µg/kg Metoclopramide • *Dose*: 0.2 mg/kg • *Time point of administration*: NA • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 40 µg/kg Placebo • *Dose*: saline • *Time point of administration*: NA • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 40 µg/kg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** A. Rudra **Institution:** Calcutta National Medical College, Kolkata **Email:** NA **Address:** NA **Language:** English **Duration of study:** NA

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Rudra 2005 *(Continued)*

	Trial registry number: NA **Study's primary outcome:** complete control (no emesis, no rescue) in 24 hours
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "after extubation, based on the randomization table, patients were allocated in equal numbers into 3 groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind manner" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients and investigators who collected postoperative data were blinded to the study drug administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Ruiz 1999

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 29 • *Received treatment (n)*: NA • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 20 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Ruiz 1999 *(Continued)*

- *ASA I/II/III/IV (n)*: 10/19/0/0
- *Gender (female in %)*: 28
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 85
- *Use of perioperative opioids (if yes, which?)*: 0.6 mg fentanyl intraoperative
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 27
- *Received treatment (n)*: NA
- *Analysed (n)*: 23
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 16
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 10/13/0/0
- *Gender (female in %)*: 22
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 78
- *Use of perioperative opioids (if yes, which?)*: 0.6 mg fentanyl intraoperative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: scheduled for laparoscopic cholecystectomy to treat uncomplicated cholelithiasis, ASA I or II

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 15 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: saline • *Time point of administration*: 15 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Headache (postoperative follow-up)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA

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Ruiz 1999 *(Continued)*

Country: Spain

Setting: inpatient, single-centre

Author's name: J.C. Ruiz de Adana

Institution: General Surgery and Digestive System Service, Getafe University Hospital, Madrid, Spain

Email: NA

Address: Avda. Europa, 4. 28224 Pozuelo (Madrid), Spain

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "prophylaxis with first generation cephalosporin. The Pharmacy Department randomly assigned the patients to the treatment or placebo group with a computerized system. One group received 4 mg..."
Allocation concealment (selection bias)	Low risk	Quote: "randomization and blinded conditions were maintained throughout the clinical trial" Judgement comment: central randomization by pharmacy
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...prophylaxis with first generation cephalosporin. The Pharmacy Department randomly assigned the patients to the treatment or placebo group with a computerized system. One group received 4 mg of ondansetron in 50 mL saline solution intravenously 15 min before surgery, and patients in the placebo group were given 50 mL saline solution intravenously. Randomization and blinded conditions were maintained throughout the clinical trial. The same anesthetic technique..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "an independent, blinded observer collected information about every patient..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "a total of 56 patients were enrolled in the study, 29 in the ondansetron group and 27 in the control group. Four patients in the control group were excluded from study because of conversion to open surgery necessitated by scleroatrophic cholecystitis and choledocholithiasis (2 patients each)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear

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Rusch 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Dolasetron (Group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 32 • *Age (mean ± SD, median (IQR), median (range))*: 35 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 50 • *History of PONV/motion sickness (%)*: 21.88 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 87 • *Use of perioperative opioids (if yes, which?)*: 0.16 mg fentanyl intraoperative, 3 patients received piritramide as rescue analgesic • *Type of surgery*: elective laparoscopic surgery Metoclopramide (Group M) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 33 • *Age (mean ± SD, median (IQR), median (range))*: 33 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 60.61 • *History of PONV/motion sickness (%)*: 27.27 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 99 • *Use of perioperative opioids (if yes, which?)*: 0.16 mg fentanyl intraoperative, 1 patient received piritramide as rescue analgesic • *Type of surgery*: elective laparoscopic surgery Placebo (Group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA

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Rusch 1999 *(Continued)*

- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 32 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 50
- *History of PONV/motion sickness (%)*: 18.75
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104
- *Use of perioperative opioids (if yes, which?)*: 0.17 mg fentanyl intraoperative, 6 patients received piritramide as rescue analgesic
- *Type of surgery*: elective laparoscopic surgery

Included criteria: ASA I and II, women 18 to 55 years of age, scheduled for elective laparoscopic (pelviscopy) surgery

Excluded criteria: pregnancy or breastfeeding, known allergy to one of the used drugs, gastrointestinal infection during the last 2 weeks, intake of antiemetic drugs within the past 24 hours, extreme underweight or overweight (± 30% of the Broca-Index), communication problems (e.g. lack of German language skills)

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dolasetron (Group D) • *Dose*: 12.5 mg • *Time point of administration*: 20 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (1) 62.5 mg dimenhydrinate 12.5%; (2) 10 mg metoclopramide 3.125%; (3) 1.25 mg droperidol Metoclopramide (Group M) • *Dose*: 10 mg • *Time point of administration*: 20 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (1) 62.5 mg dimenhydrinate 15.15%; (2) 10 mg metoclopramide 3.03%; (3) 1.25 mg droperidol Placebo (Group P) • *Dose*: NaCl • *Time point of administration*: 20 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (1) 62.5 mg dimenhydrinate 31.25%; (2) 10 mg metoclopramide 9.375%; (3) 1.25 mg droperidol.
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)*

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Rusch 1999 *(Continued)*

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Dirk Rüsch **Institution:** Klinik für Anästhesiologie und Operative Intensivmedizin der Christian-Albrechts-Universität zu Kiel **Email:** wulf@anaesthesie.uni-kiel.de **Address:** Klinik für Anästhesiologie und Operative Intensivmedizin der Christian-Albrechts-Universität zu Kiel, Schwanenweg 21, D-24105 Kiel **Duration of study:** NA **Language:** German (2 German reviewers) **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "erfolgte gemäß Randomisierungsliste" Judgement comment: random number table
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("doppel-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "ohne Kenntnis des jeweils applizierten Antiemetikums – folgende Parameter erfaßt" Judgement comment: outcome assessment was done by blinded observers
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "patientinnen pro Gruppe angestrebt. Von den ursprünglich 40 Patientinnen jeder Studiengruppe konnten infolge Wechselns auf offene Laparotomie, Abweichens der Narkoseführung von dem im Studienprotokoll vorgesehenen Procedere, unvollständig oder fehlerhaft ausgefüllter Studienprotokolle und Entlassung der Patientinnen vor Ende des Beobachtungszeitraums letzlich nur 32 (Gruppe D und -P) bzw. 33 (Gruppe M) Patientinnen in die

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Rusch 1999 *(Continued)*

		Auswertung einbezogen werden. Verglichen mit der durchschnittlich vorausgesagten" Judgement comment: high rate of missing data (19%). Reasons described and probably unrelated to the outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "antiemetika widerspiegelte (s. Tabelle 2). Wie aus Tabelle 1 ersichtlich, waren die Studiengruppen bezüglich ihrer biometrischen Daten und der prä- und intraoperativ erhobenen Variablen mit Einfluß auf PONV vergleichbar. Bezüglich der Häufigkeit von post..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Rusch 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 36 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 52.78 • *History of PONV/motion sickness (%)*: 19.44 • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 103 • *Use of perioperative opioids (if yes, which?)*: 0.17 mg fentanyl intraoperative, 6 patients received piritramide as rescue analgesic • *Type of surgery*: diagnostic or surgical gynaecological laparoscopy Droperidol (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 33

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Rusch 2002 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 36 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 63.64
- *History of PONV/motion sickness (%)*: 24.24
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 109
- *Use of perioperative opioids (if yes, which?)*: 0.19 mg fentanyl intraoperative, 6 patients received piritramide as rescue analgesic
- *Type of surgery*: diagnostic or surgical gynaecological laparoscopy

Metoclopramide (group M)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 33
- *Age (mean ± SD, median (IQR), median (range))*: 34 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 33.33
- *History of PONV/motion sickness (%)*: 36.36
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 99
- *Use of perioperative opioids (if yes, which?)*: 0.17 mg fentanyl intraoperative, 5 patients received piritramide as rescue analgesic
- *Type of surgery*: diagnostic or surgical gynaecological laparoscopy

Included criteria: women 18 to 50 years of age, ASA I or II, scheduled for elective diagnostic or surgical gynaecological laparoscopy, additional inclusion criteria for Group X: risk for postoperative vomiting > 25% (according to Apfel's risk score), duration of anaesthesia at least 1 hour

Excluded criteria: pregnancy, breastfeeding, known allergy to used drugs, intake of antiemetic drugs during the last 24 hours, gastrointestinal infection in the past 2 weeks, extreme underweight or overweight (30% of the Broca-Index), difficulties in communication or other reason for giving a non-valid consent

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): yes

Interventions	**Intervention characteristics** Placebo (group P) • *Dose*: NaCl • *Time point of administration*: 20 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (1) dimenhydrinate 62.5 mg; (2) metoclopramide 10 mg; (3) droperidol 1.25 mg Droperidol (group D)

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Rusch 2002 *(Continued)*

- *Dose*: 2.5 mg
- *Time point of administration*: 20 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: (1) dimenhydrinate 62.5 mg; (2) metoclopramide 10 mg; (3) droperidol 1.25 mg

Metoclopramide (group M)

- *Dose*: 10 mg
- *Time point of administration*: 20 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: (1) dimenhydrinate 62.5 mg; (2) metoclopramide 10 mg; (3) droperidol 1.25 mg

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Dirk Rüsch **Institution:** Klinik für Anästhesiologie und Operative Intensivmedizin der Christian-Albrechts-Universität zu Kiel **Email:** ruesch@anaesthesie.uni-kiel.de **Address:** Klinik für Anästhesiologie und Operative Intensivmedizin der Christian-Albrechts-Universität zu Kiel, Schwanenweg 21, 24105 Kiel **Duration of study:** NA **Language:** German (2 German reviewers) **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	Two studies (only study part I with 3 groups eligible)

Risk of bias

Bias	Authors' judgement	Support for judgement

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Rusch 2002 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "Zuordnung gemäß Randomisierungsliste" Judgement comment: random number table
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("untersucherblind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperativ wurden untersucherblind folgende Parameter erfasst" Judgement comment: outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "von den ursprünglich 40 Patientinnen jeder Studiengruppe des ersten Teils der Untersuchung sowie von den ursprünglich 50 Patientinnen des zweiten Teils der Untersuchung wurden jeweils 33 (Gruppe D und M) bzw. 36 (Gruppe P) bzw. 43 (Gruppe X) Patientinnen in die Auswertung einbezogen. Gründe für den Ausschluss einiger Patientinnen von der Auswertung waren: Wechsel des Operationsverfahrens auf eine offene Laparotomie, Abweichen der Narkoseführung von dem im Studienprotokoll vorgesehenen Prozedere, unvollständig oder fehler"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "die Studiengruppen waren bezüglich ihrer biometrischen Daten vergleichbar (Tab. 1). Unterschiede existierten jedoch zwischen den Gruppen bezüglich der PONV-relevanten Risikofaktoren Nichtraucherstatus und Reisekrankheit bzw. PONV in der Anamnese. Betrachtet man allerdings die Scores zur Bestimmung der Wahrscheinlichkeit für postoperatives Erbrechen [2] bzw. für PONV [9], welche beide zuvor genannten Risikofaktoren miteinbeziehen, so zeigt sich, dass die Gruppen durchaus als homogen hinsichtlich ihres PONV-Risikos zu betrachten sind" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): yes

Rust 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 204 • *Received treatment (n)*: 204

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Rust 1994 *(Continued)*

- *Analysed (n)*: 204
- *Age (mean ± SD, median (IQR), median (range))*: 45
- *Weight (mean ± SD, median (IQR), median (range))*: 67
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31/23
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104 to 111
- *Use of perioperative opioids (if yes, which?)*: morphine, fentanyl, alfentanil
- *Type of surgery*: major gynaecological surgery

Ondansetron (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 201
- *Received treatment (n)*: 201
- *Analysed (n)*: 201
- *Age (mean ± SD, median (IQR), median (range))*: 47
- *Weight (mean ± SD, median (IQR), median (range))*: 67
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31/25
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104 to 111
- *Use of perioperative opioids (if yes, which?)*: morphine, fentanyl, alfentanil
- *Type of surgery*: major gynaecological surgery

Ondansetron (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 201
- *Received treatment (n)*: 201
- *Analysed (n)*: 201
- *Age (mean ± SD, median (IQR), median (range))*: 45
- *Weight (mean ± SD, median (IQR), median (range))*: 67
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 32/27
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104 to 111
- *Use of perioperative opioids (if yes, which?)*: morphine, fentanyl, alfentanil
- *Type of surgery*: major gynaecological surgery

Ondansetron (16 mg group)

- *Assessed for eligibility (n)*: -

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Rust 1994 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 207
- *Received treatment (n)*: 207
- *Analysed (n)*: 207
- *Age (mean ± SD, median (IQR), median (range))*: 45
- *Weight (mean ± SD, median (IQR), median (range))*: 67
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31/23
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104 to 111
- *Use of perioperative opioids (if yes, which?)*: morphine, fentanyl, alfentanil
- *Type of surgery*: major gynaecological surgery

Included criteria: female inpatients 18 to 75 years of age (European study), ASA grade I to III, due to undergo surgery under general anaesthesia, were to remain in hospital for at least 24 hours postoperatively, major gynaecological surgery (European study)

Excluded criteria: pregnant or breastfeeding, weighing more than 100 kg (European study), had received a drug considered to have antiemetic properties or experienced emesis in the 24 hours before study drug administration, were due to have intraoperative gastric suctioning or would require an intragastric tube postoperatively, had participated in another study with an investigational drug including ondansetron 30 days before the start of these studies, were to participate in other clinical trials during these studies, had abnormal hepatic or renal function

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: placebo
- *Time point of administration*: 1 hour before induction
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: droperidol, metoclopramide, prochlorperazine

Ondansetron (4 mg group)

- *Dose*: 4 mg
- *Time point of administration*: 1 hour before induction
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: droperidol, metoclopramide, prochlorperazine

Ondansetron (8 mg group)

- *Dose*: 8 mg
- *Time point of administration*: 1 hour before induction
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: droperidol, metoclopramide, prochlorperazine

Ondansetron (16 mg group)

- *Dose*: 16 mg
- *Time point of administration*: 1 hour before induction

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Rust 1994 *(Continued)*

	• *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: droperidol, metoclopramide, prochlorperazine
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Germany, Belgium, Denmark, France, The Netherlands, Norway, Sweden, Siwtzerland, United Kingdom, United States of America **Setting:** inpatient, multi-centre (34) **Author's name:** M. Rust **Institution:** Institut fur Anaesthesie, Technische Universität, Klinikum Rechts der Isar, Munich, Germany **Email:** NA **Address:** Institut fur Anaesthesie, Technische Universität, Klinikum Rechts der Isar, Ismaningerstrasse 22, Munich 80, Germany **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** no emesis and no nausea in 24 hours
Notes	Only data from European studies were extracted (wrong age range in US studies, with ages 12 to 75)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomised" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding

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Rust 1994 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "nausea and emesis assessments were made by study investigators or nurses over the full 24-h post recovery period" Judgement comment: no statement on whether outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 813 and 1345 patients were included in the European and US studies, respectively" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "treatment stratification and demography for the two studies show that both patient populations were comparable across all treatment groups with respect to age, weight, history of PONV and motion sickness, and surgery" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Ryoo 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 94 • *Age (mean ± SD, median (IQR), median (range))*: 50.6 ± 10.8 • *Weight (mean ± SD, median (IQR), median (range))*: 60.2 ± 8.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 97.87 • *History of PONV/motion sickness (%)*: 7.45/21.28 • *Type of general anaesthesia*: inhalational anaesthesia (des-/sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 168 • *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperatively, postoperatively via PCA • *Type of surgery*: general, orthopaedic, gynaecological surgery Palonosetron + dexamethasone (group PD) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Ryoo 2015 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 99
- *Age (mean ± SD, median (IQR), median (range))*: 51.6 ± 12.2
- *Weight (mean ± SD, median (IQR), median (range))*: 59.8 ± 9.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 93.94
- *History of PONV/motion sickness (%)*: 4.04/25.25
- *Type of general anaesthesia*: inhalational anaesthesia (des-/sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 151
- *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperatively, postoperatively via PCA
- *Type of surgery*: general, orthopaedic, gynaecological surgery

Included criteria: healthy female, 20 to 70 years of age, ASA I or II, scheduled for elective surgery under general anaesthesia and wanted to receive IV-PCA for postoperative pain control

Excluded criteria: pregnancy; body weight > 30% above ideal body weight; vomiting or retching within 24 hours before the operation; administration of antiemetics, steroids, or psychoactive medications within 24 hours before the operation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 5 mg, saline • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (33%) metoclopramide 10 mg IV Palonosetron + dexamethasone (group PD) • *Dose*: palonosetron 0.075 mg, dexamethasone 5 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (21%) metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome

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Ryoo 2015 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Soon Im Kim **Institution:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Hospital Seoul, Seoul, Korea **Email:** soonnim@schmc.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Soonchunhyang University Hospital Seoul, 59, Daesagwan-ro, Yongsan-gu, Seoul 140-743, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV during the 0 to 24 hours postoperative period **Trial registry number:** KCT0000581
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated to one of the two groups according to a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the patients and the investigator who collected the postoperative data were blinded to the randomization" Judgement comment: no information on blinding of anaesthesiologists provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...investigator who collected the postoperative data were blinded to the randomization" Quote: "evaluation was made by the investigator blinded to the treatment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...(SD), numbers, or percentages. Among the 204 patients enrolled in this study, 11 were withdrawn from the study for insufficient data collection due to them being discharged before 48 hours after the operation. Data obtained from the remaining 193 patients were analyzed, with 94 patients in the D group and 99 patients in the PD group. There were no significant differences"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: KCT0000581 (retrospective registration)
Other bias	Unclear risk	Quote: "there were no significant differences between the groups with respect to patient characteristics, motion sickness, previous PONV history, smoking status, duration of surgery, duration of anesthesia, and type of surgery (Table 1)"

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Ryoo 2015 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Ryu 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 2.9 • *Weight (mean ± SD, median (IQR), median (range))*: 59.8 ± 5.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 270.5 • *Use of perioperative opioids (if yes, which?)*: none (only ketorolac for analgesia was used) • *Type of surgery*: tympanomastoidectomy Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 40.6 ± 3.4 • *Weight (mean ± SD, median (IQR), median (range))*: 60.2 ± 5.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 56.6 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 265.0 • *Use of perioperative opioids (if yes, which?)*: none (only ketorolac for analgesia was used) • *Type of surgery*: tympanomastoidectomy Dexamethasone + ondansetron (group DO)

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Ryu 2007 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 39.8 ± 3.5
- *Weight (mean ± SD, median (IQR), median (range))*: 58.7 ± 6.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 56.6
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 270.5
- *Use of perioperative opioids (if yes, which?)*: none (only ketorolac for analgesia was used)
- *Type of surgery*: tympanomastoidectomy

Included criteria: healthy adults, ASA I or II, scheduled tympanomastoidectomy under general anaesthesia

Excluded criteria: patients with substance abuse or hypersensitivity reactions to drugs in the past, patients with a history of nausea or motion sickness, vomiting within 24 hours before surgery, or receiving antiemetics, pregnant women, patients with kidney disease and liver disease

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 5 mg • *Time point of administration*: 30 minutes before end of operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: 30 minutes before end of operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone + ondansetron (group DO) • *Dose*: dexamethasone 5 mg, ondansetron 4 mg • *Time point of administration*: 30 minutes before end of operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 days)*

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Ryu 2007 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 48 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Lee Jung-sam **Institution:** Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Geumjeong-gu, Busan, Korea **Email:** shdo@snu.ac.kr **Address:** 374-75 Namsan-dong, Geumjeong-gu, Busan, Korea **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the patient's visit and recording is done by a doctor who does not know the type of medication the patient is taking" (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Ryu 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Ondansetron (group O4) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 26/14/0/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 80 • *Use of perioperative opioids (if yes, which?)*: 0.12 µg/kg/min remifentanil intraoperative • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group O8) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 49 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 27/13/0/0 • *Gender (female in %)*: 55 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 78 • *Use of perioperative opioids (if yes, which?)*: 0.12 µg/kg/min remifentanil intraoperative • *Type of surgery*: laparoscopic cholecystectomy Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 40

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Ryu 2010 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/16/0/0
- *Gender (female in %)*: 47.5
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 78
- *Use of perioperative opioids (if yes, which?)*: 0.12 µg/kg/min remifentanil intraoperative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, 25 to 65 years of age, scheduled for elective laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: gastrointestinal disease, pregnant or menstruating, history of motion sickness or postoperative emesis, had taken antiemetics within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron (group O4) • *Dose*: 4 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (5%) metoclopramide 10 mg IV Ondansetron (group O8) • *Dose*: 8 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (5%) metoclopramide 10 mg IV Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (0%) metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 2 hours, 2 to 24 hours, 24 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 2 hours, 2 to 24 hours, 24 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)*

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Ryu 2010 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Sang-Hwan Do **Institution:** Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital **Email:** shdo@snu.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, 166 Kumi-ro, Bundang-gu, Seongnam-si, Kyonggi-do 463-707, South Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response 24 hours after surgery **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomization was conducted using the sealed envelope method" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "using the sealed envelope method" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications were prepared by a blinded nurse in identical 5-ml syringes and administered according to the list"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the incidence of nausea and vomiting was recorded during three assessment periods (0–2 h, 2–24 h, and 24–48 h) by a nursing staff blinded to the treatment drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one of the 121 patients enrolled the study was withdrawn because the patient underwent conversion to open cholecystectomy. Consequently, 120 patients (59 men and 61 women) were included in the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the three groups were comparable in terms of patient characteristics, operation time, anesthesia time, and administered anesthetics (Table 1)"

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Ryu 2010 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Ryu 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 38 • *Received treatment (n)*: 38 • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 44 (20 to 65) • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 23/13/0/0 • *Gender (female in %)*: 56 • *Non-smoker (%)*: 83 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: combined anaesthesia (desflurane and remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 80 • *Use of perioperative opioids (if yes, which?)*: 0.14 µg/kg/min remifentanil intraoperative, no postoperative opioids • *Type of surgery*: laparoscopic cholecystectomy Ramosetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 38 • *Received treatment (n)*: 38 • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 45 (24 to 64) • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 22/14/0/0 • *Gender (female in %)*: 47 • *Non-smoker (%)*: 81 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: combined anaesthesia (desflurane and remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 82 • *Use of perioperative opioids (if yes, which?)*: 0.11 µg/kg/min remifentanil intraoperative, no postoperative opioids • *Type of surgery*: laparoscopic cholecystectomy

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Ryu 2013 *(Continued)*

Included criteria: ASA I and II, 25 to 65 years of age, scheduled for elective LC under general anaesthesia

Excluded criteria: gastrointestinal disease, obesity (more than 50% greater than ideal body weight), pregnancy or menstruation, history of motion sickness and/or postoperative emesis, diabetes mellitus, use of steroids or antiemetics within 1 month of surgery, history of allergy to any study medication

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ramosetron • *Dose*: 0.3 mg, saline 0.9% • *Time point of administration*: saline immediately after induction, ramosetron at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 36% (metoclopramide 10 mg) Ramosetron + dexamethasone • *Dose*: ramosetron 0.3 mg, dexamethasone 8 mg • *Time point of administration*: dexamethasone immediately after induction, ramosetron at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 2 hours, 2 to 24 hours, 24 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** departmental funding only **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Sang-Hwan Do **Institution:** Department of Anesthesiology Pain Medicine, Seoul National University Bundang Hospital, Korea **Email:** shdo@snu.ac.kr **Address:** Department of Anesthesiology Pain Medicine, Seoul National University Bundang Hospital, 166 Kumi-ro, Bundang-gu, Seongnam-si, Kyonggi-do 463-707, Republic of Korea **Language:** English **Duration of study:** October 2011 to January 2012 **Trial registry number:** KCT0000267

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Ryu 2013 *(Continued)*

	Study's primary outcome: incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated randomization code (Random Allocation Software Version 1.0) with block size 4"
Allocation concealment (selection bias)	Low risk	Quote: "randomization was performed before the induction of anesthesia by an independent anesthesiologist who is responsible for patient allocation and not otherwise involved in this study. Study medications were prepared by an anesthetic nurse not involved in this study. Study medications consisted of (1) an identical syringe with 2 ml solution with normal saline for group R or 8 mg dexamethasone (Dexamethasone Ò; Daewon Pharm., Seoul, Korea) for group D, administered immediately after the induction of anesthesia and (2) a syringe with 2 ml solution with 0.3 mg ramosetron (Nasea Ò injectable; Astellas Pharma Inc., Tokyo, Japan) which was injected at the end of surgery. Syringes were labeled with the patient's inclusion number and passed to the anesthesiologist"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, anesthesiologists, and outcome assessors were blinded to group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...and outcome assessors were blinded to group assignment" Quote: "by a nursing staff blinded to treatment assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "seventy six patients were randomized. Three patients (2 patients from R group and 1 patient from D group) were eliminated due to conversion to open cholecytectomy and 1 patient was excluded from the analysis due to protocol violation (ondansetron administration instead of metoclopramide as a rescue antiemetic)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: KCT0000267 (retrospective registration)
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Sadhasivam 1999

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo

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Sadhasivam 1999 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 27
- *Received treatment (n)*: 27
- *Analysed (n)*: 27
- *Age (mean ± SD, median (IQR), median (range))*: 46.5 ± 11.2
- *Weight (mean ± SD, median (IQR), median (range))*: 54.7 ± 10.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 19/8/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 3.70/18.52
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 147.3
- *Use of perioperative opioids (if yes, which?)*: 59.1 mg meperidine
- *Type of surgery*: modified radical mastectomy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 27
- *Received treatment (n)*: 27
- *Analysed (n)*: 27
- *Age (mean ± SD, median (IQR), median (range))*: 44.9 ± 11.1
- *Weight (mean ± SD, median (IQR), median (range))*: 56.9 ± 8.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 21/6/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 7.41/18.52
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 157.8
- *Use of perioperative opioids (if yes, which?)*: 58.9 mg meperidine
- *Type of surgery*: modified radical mastectomy

Included criteria: ASA I or II, adult female patients undergoing modified radical mastectomy for carcinoma of the breast

Excluded criteria: morbid obesity, gastrointestinal disease with gastric outlet obstruction, had received drugs with an antiemetic effect within 24 hours before anaesthesia

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 59% (150 µg/kg metoclopramide IV, ondansetron 4 mg IV) Ondansetron

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Sadhasivam 1999 *(Continued)*

- *Dose*: 4 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 15% (150 µg/kg metoclopramide IV, ondansetron 4 mg IV)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Abha Saxena **Institution:** Department of Anesthesiology, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India **Email:** saxenas@medinst.ernet.in **Address:** Department of Anesthesiology, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were allocated to receive, in a randomized, double-blinded manner, a single dose of either ondansetron 4 mg (4 mL) IV or saline at an equal volume (4 mL) as a placebo at the end of the surgery" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "patients were allocated to receive, in a randomized, double-blinded manner, a single dose of either ondansetron 4 mg (4 mL) IV or saline at an equal volume (4 mL) as a placebo at the end of the surgery"

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Sadhasivam 1999 *(Continued)*

All outcomes		Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded manner")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences between the groups with regard to age, weight, ASA physical status, duration of anesthesia, and intraoperative and postoperative analgesic requirements (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Safae 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 32 • *Received treatment (n)*: NA • *Analysed (n)*: 32 • *Age (mean ± SD, median (IQR), median (range))*: 57.1 ± 14.1 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 27.41 ± 3.1 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: postoperative analgesia with pethidine • *Type of surgery*: elective cholecystectomy Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 32

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Safae 2011 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 57.1 ± 13.6
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 27.8 ± 3.4
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: postoperative analgesia with pethidine
- *Type of surgery*: elective cholecystectomy

Included criteria: women over 40 years of age weighing less than 90 kg undergoing elective cholecystectomy

Excluded criteria: background illness such as diabetes, hypertension, hyperlipidaemia, asthma, motion sickness, internal ear disorder, and immunodeficiency and digestive problems such as gastritis, peptic ulcer, and/or clear reflux before surgery; had used antiemetic drugs or nausea and vomiting drugs 24 hours before surgery; did not agree to the study; were not included in the study

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, history of motion sickness): no; (history of PONV, non-smoker, duration of anaesthesia, perioperative opioids): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 10 minutes before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 4 mg • *Time point of administration*: 10 minutes before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 8 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Sara Safi **Institution:** Isfahan University of Medical Sciences, Isfahan, Iran

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Safae 2011 *(Continued)*

Email: dr.s_safi@yahoo.com

Address: NA

Duration of study: NA

Language: Persian (Google Translator)

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were divided randomly". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, history of motion sickness): no; (history of PONV, non-smoker, duration of anaesthesia, perioperative opioids): unclear

Sah 2009

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + scopolamine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Sah 2009 *(Continued)*

- *Randomized (n)*: 63
- *Received treatment (n)*: NA
- *Analysed (n)*: 61
- *Age (mean ± SD, median (IQR), median (range))*: 38.4 ± 12.2
- *Weight (mean ± SD, median (IQR), median (range))*: 67.7 ± 16.02
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 88.52
- *History of PONV/motion sickness (%)*: 47.54/36.07
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 219.63
- *Use of perioperative opioids (if yes, which?)*: intraoperative and postoperative fentanyl (µg), oral opioids (%) (NA, 49, 48)
- *Type of surgery*: plastic surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 63
- *Received treatment (n)*: NA
- *Analysed (n)*: 58
- *Age (mean ± SD, median (IQR), median (range))*: 43.7 ± 12.0
- *Weight (mean ± SD, median (IQR), median (range))*: 70.0 ± 17.02
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 98.28
- *Non-smoker (%)*: 89.66
- *History of PONV/motion sickness (%)*: 53.44/32.76
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 208.21
- *Use of perioperative opioids (if yes, which?)*: intraoperative and postoperative fentanyl (µg), oral opioids (%) (NA, 43, 43)
- *Type of surgery*: plastic surgery

Included criteria: ASA I and II, undergoing outpatient plastic surgery, at high risk of PONV (at least 3 of the following risk factors: female gender, previous history of PONV or motion sickness, non-smoking status, use of postoperative opioids)

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ondansetron + scopolamine • *Dose*: ondansetron 4 mg, scopolamine 1.5 mg • *Time point of administration*: ondansetron approximately 30 minutes before end of surgery, scopolamine 2 hours before surgery • *Route of administration*: ondansetron IV, scopolamine transdermal • *Rescue antiemetics (if yes, which?)*: 18.03% (PACU) Ondansetron

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Sah 2009 *(Continued)*

- *Dose*: ondansetron 4 mg, placebo patch
- *Time point of administration*: ondansetron approximately 30 minutes before end of surgery, placebo patch 2 hours before surgery
- *Route of administration*: ondansetron IV, placebo transdermal
- *Rescue antiemetics (if yes, which?)*: 25.86% (PACU)

Outcomes	*Vomiting (3 to 4 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (visual change, 0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported in party by Baxter HealthCare, Deerfield, IL, which provided the transdermal scopolamine and placebo patches used int his study **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Neera Sah **Institution:** Department of Anesthesiology, Magee Womens Hospital and the University of Pittsburgh, Pittsburgh, USA **Email:** sahxnb@anes.upmc.edu **Address:** Department of Anesthesia, St. Margaret'sHospital, Pittsburgh, PA 15215 USA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "all patients were randomized via computer-generated table of random numbers, to receive either a TDS or placebo patch two hours before surgery"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the placebo and TDS patches were dispensed by a pharmacist who was not directly involved in patient care"

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Sah 2009 *(Continued)*

		Judgement comment: no statement on identical appearance of the placebo patch
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...were recorded preoperatively, on admission to recovery, and every hour thereafter until discharge from the hospital by anesthesia and recovery room personnel" Judgement comment: no information on blinding of outcome assessors provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...chi-square analysis. A total of 126 patients, 63 in each group, were enrolled in the study. Two patients in the TDS group and one in the placebo group were excluded from the study for lack of follow-up. Another 4 patients in the placebo group were excluded from the study: one patient did not require general anesthesia, one had a positive pregnancy test, the trachea of one patient could not be intubated, and one patient scratched off the patch. Both groups were similar..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "both groups were similar with respect to demographic data, number of risk factors, duration of surgery, and duration of hospital stay, as summarized in Table 1" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Sanchez Rodriguez 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 105 • *Received treatment (n)*: NA • *Analysed (n)*: 105 • *Age (mean ± SD, median (IQR), median (range))*: 36.3 ± 7.3 • *Weight (mean ± SD, median (IQR), median (range))*: 70.5 ± 7.7 • *BMI (mean ± SD, median (IQR), median (range))*: 26.2 ± 3.0 • *ASA I/II/III/IV (n)*: 63/42/0/0 • *Gender (female in %)*: 61.90 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 105.3

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Sanchez Rodriguez 2010 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 3 µg/kg to 5 µg/kg fentanyl at induction, 23.9 (number of additional buprenorphine doses was significantly lower in the study group)
- *Type of surgery*: laparoscopic cholecystectomy

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 105
- *Received treatment (n)*: NA
- *Analysed (n)*: 105
- *Age (mean ± SD, median (IQR), median (range))*: 37.7 ± 7.7
- *Weight (mean ± SD, median (IQR), median (range))*: 72.3 ± 7.4
- *BMI (mean ± SD, median (IQR), median (range))*: 26.7 ± 3.0
- *ASA I/II/III/IV (n)*: 63/42/0/0
- *Gender (female in %)*: 53.33
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 104.8
- *Use of perioperative opioids (if yes, which?)*: 3 µg/kg to 5 µg/kg fentanyl at induction, 18.6 (number of additional buprenorphine doses was significantly lower in the study group)
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: undergoing laparoscopic cholecystectomy

Excluded criteria: ASA III and IV; over 80 years of age; pregnancy; treatment with steroids; severe diabetes mellitus (haemoglobin A1c (HbA1c) > 8%); use of opioids, sedatives, or any kind of analgesic 1 week before LC; history of alcohol or drug abuse; preoperative diagnosis of acute cholecystitis, acute pancreatitis, choledocholithiasis, gallbladder carcinoma; conversion of the LC to an open procedure

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: placebo • *Time point of administration*: 60 minutes before skin incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 36.19% (ondansetron 4 mg to 8 mg IV) Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 60 minutes before skin incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 15.24% (ondansetron 4 mg to 8 mg IV)
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (PACU to 6 hours)* • Outcome type: dichotomous outcome

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Sanchez Rodriguez 2010 *(Continued)*

Postoperative wound infection (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Mexico **Setting:** inpatient, single-centre **Author's name:** A. González-Ojeda **Institution:** Research Unit in Clinical Epidemiology, Specialties Hospital, Western Medical Center, Mexican Institute of Social Security, Guadalajara, Jalisco, Mexico **Email:** avygail5@yahoo.com.mx **Address:** Calle Jose ́E. Rodo #2558, Colonia Prados Providencia,Guadalajara, Jalisco 44670, Mexico **Duration of study:** from January 2007 to August 2008 **Language:** English **Study's primary outcome:** incidence of nausea and vomiting. **Trial registry number:** NCT01030614
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomized to receive intravenous dexamethasone (8 mg) or homologated placebo 60 min before skin incision, using an equal number of blind envelopes" Judgement comment: shuffling envelopes
Allocation concealment (selection bias)	Unclear risk	Quote: "...using an equal number of blind envelopes" Judgement comment: not stated; "sequentially numbered, opaque, sealed" envelopes (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 105 patients were randomized to receive intravenous dexamethasone (8 mg) and 105 to be given a placebo. All patients were admitted the day of the scheduled surgical procedure and stayed in the hospital for at least one night after LC"

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Sanchez Rodriguez 2010 *(Continued)*

		Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT01030614 (retrospective registration)
Other bias	High risk	Quote: "there were no significant differences between the two groups with regard to mean age, sex, BMI, ASA score, previous surgical procedures (Table 1), during of surgical procedures and length of anesthesia, hospital stay, or postoperative morbidity (Table 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Sandhu 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 29 • *Received treatment (n)*: NA • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 32 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 35 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: gynaecological laparoscopy Dimenhydrinate • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 28 • *Received treatment (n)*: NA • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 33 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Sandhu 1999 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 28
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological laparoscopy

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 33 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 15
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anasthesia or surgery (in min; as mean or median)*: 36
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: gynaecological laparoscopy

Included criteria: ASA I or II, women scheduled for elective gynaecological laparoscopy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: placebo • *Time point of administration*: post induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dimenhydrinate • *Dose*: 50 mg • *Time point of administration*: post induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 8 mg • *Time point of administration*: post induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (PACU)*

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Sandhu 1999 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (discharge to the following day)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** Canada **Setting:** outpatient, single-centre **Author's name:** Carol A. Stockall **Institution:** Departments of Anesthesia, London Health Sciences Centre and St.Joseph's Health Centre, University of Western Ontario, London, Canada **Email:** NA **Address:** Departments of Anesthesia, London Health Sciences Centre and St.Joseph's Health Centre, 339 Windermere Rd., University of Western Ontario, London, ON N6A5A5 Canada **Duration of study:** NA **Language:** English **Study's primary outcome:** VAS for PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomization and preparation of study drugs were completed by the hospital pharmacy" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Low risk	Quote: "randomization and preparation of study drugs were completed by the hospital pharmacy" Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the study design was double blind and randomized with a placebo control group" Judgement comment: no detailed information on blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "postoperative nausea, drowsiness and satisfaction were evaluated by a blinded observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Sandhu 1999 *(Continued)*

Other bias	Unclear risk	Quote: "demographic data was similar in all groups (Table 1), and there was no difference in PONV risk due to menstrual cycle, motion sickness or prior PONV" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Sandhu 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 52.45 ± 12.54 • *Weight (mean ± SD, median (IQR), median (range))*: 58.42 ± 11.77 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 75 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 75.25 • *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl for induction, 6.85 mg morphine intraoperative • *Type of surgery*: laparoscopic cholecystectomy Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 52.98 ± 11.01 • *Weight (mean ± SD, median (IQR), median (range))*: 58.93 ± 12.63 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 67.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 78.50

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Sandhu 2008 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 1 µg/kg fentanyl for induction, 7.05 mg morphine intraoperative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, 18 to 75 years of age, scheduled for elective cholecystectomy

Excluded criteria: pregnancy, breastfeeding, over 100 kg in weight, nausea, vomiting or use of antiemetics within 24 hours before surgery, insulin-dependent diabetes mellitus, conversion to open cholecystectomy, allergy to any protocol medication, development of intraoperative complications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: at discretion of the doctor Metoclopramide • *Dose*: 10 mg • *Time point of administration*: at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: at discretion of the doctor
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Thailand **Setting:** inpatient, single-centre **Author's name:** Trichak Sandhu **Institution:** Departments of Surgery and, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand **Email:** tsandhu@mail.med.cmu.ac.th **Address:** Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand **Duration of study:** NA **Language:** English **Study's primary outcome:** complete control of PONV

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Sandhu 2008 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly selected into one of two groups to receive the study drug at the end of surgery. Randomization was performed with sealed envelops containing the study assignment and kept by the pharmacist who prepared the drugs" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "sealed envelops containing the study assignment and kept by the pharmacist who prepared the drugs" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the pharmacy supplied syringes in a blinded fashion and they were diluted in normal swine serum of equal volume, so that the patients and the investigator were unaware of which of the two drugs was being administered"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...by research nurses who were blinded to the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "eighty patients were randomized into the study with no patients being removed for protocol violation"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic data were similar in the two groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Sandhya 1994

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Sandhya 1994 *(Continued)*

- *Randomized (n)*: 11
- *Received treatment (n)*: NA
- *Analysed (n)*: 11
- *Age (mean ± SD, median (IQR), median (range))*: 25.00 ± 4.88
- *Weight (mean ± SD, median (IQR), median (range))*: 47.91 ± 6.39
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 11/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, thiopentone)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 8.82
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: voluntary termination of pregnancy

Promethazine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 11
- *Received treatment (n)*: NA
- *Analysed (n)*: 11
- *Age (mean ± SD, median (IQR), median (range))*: 24.36 ± 4.60
- *Weight (mean ± SD, median (IQR), median (range))*: 49.82 ± 5.04
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 11/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, thiopentone)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 7.18
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: voluntary termination of pregnancy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 10
- *Received treatment (n)*: NA
- *Analysed (n)*: 10
- *Age (mean ± SD, median (IQR), median (range))*: 22.40 ± 2.50
- *Weight (mean ± SD, median (IQR), median (range))*: 49.10 ± 6.02
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 10/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, thiopentone)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 9.40
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: voluntary termination of pregnancy

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Sandhya 1994 *(Continued)*

	Included criteria: ASA I, undergoing voluntary termination of pregnancy during first trimester under general anaesthesia **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: 1 mL saline • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Promethazine • *Dose*: 0.5 mg/kg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 0.2 mg/kg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (until discharge which was about 150 minutes after anaesthesia)* • Outcome type: dichotomous outcome *Sedation/drowsiness (until discharge which was about 150 minutes after anaesthesia)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** outpatient, single-centre **Author's name:** Yaddanapudi L.N. Sandhya **Institution:** All India Institute of Medical Sciences New Delhi **Email:** NA **Address:** D-4, CSRE Quarters, Hillside IIT, Powai, Bombay 400076, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA

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Sandhya 1994 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "...were divided randonly". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Sanduende 2007

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Haloperidol + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 57 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 64

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Sanduende 2007 *(Continued)*

- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: 4/NA
- *Type of general anaesthesia*: TIVA (remifentanil, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93
- *Use of perioperative opioids (if yes, which?)*: 1640 µg remifentanil intraoperative, 0.8 mg morphine postoperative 0 to 6 hours, 0.4 mg morphine postoperative 6 to 24 hours
- *Type of surgery*: laparoscopic cholecystectomy

Droperidol + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 59 ± 17
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 88
- *Non-smoker (%)*: 92
- *History of PONV/motion sickness (%)*: 20/NA
- *Type of general anaesthesia*: TIVA (remifentanil, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 84
- *Use of perioperative opioids (if yes, which?)*: 1351 µg remifentanil intraoperative, 1.0 mg morphine postoperative 0 to 6 hours, 0.0 mg morphine postoperative 6 to 24 hours
- *Type of surgery*: laparoscopic cholecystectomy

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 51 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 76 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 68
- *Non-smoker (%)*: 76
- *History of PONV/motion sickness (%)*: 8/NA
- *Type of general anaesthesia*: TIVA (remifentanil, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 88
- *Use of perioperative opioids (if yes, which?)*: 1928 µg remifentanil intraoperative, 2.9 mg morphine postoperative 0 to 6 hours, 0.0 mg morphine postoperative 6 to 24 hours
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I to III, 18 to 75 years of age, undergoing elective laparoscopic cholecystectomy

Excluded criteria: pregnancy, Parkinson's disease, history of adverse reactions with neuroleptics, prolonged QT in the preoperative electrocardiogram (ECG) or prolonged pecibility (hypokalaemia, hypocalcaemia, cerebrovascular disease, anorexia; treatment with antiarrhythmic, macrolide, or antagonist of 5-HT3 receptors), obesity (weight superior to 40% of the ideal person), slowed gastric emptying, neuropathy, amyloidosis, allergy to study drugs

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Sanduende 2007 *(Continued)*

	Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (history of PONV, duration of anaesthesia, non-smoker): no; (history of motion sickness): unclear; (perioperative opioids, gender): yes
Interventions	**Intervention characteristics** Haloperidol + dexamethasone • *Dose*: haloperidol 10 µg/kg, dexamethasone 8 mg • *Time point of administration*: dexamethasone after anaesthetic induction, haloperidol 15 minutes before end of surgical intervention • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg IV Droperidol + dexamethasone • *Dose*: droperidol 10 µg/kg, dexamethasone 8 mg • *Time point of administration*: dexamethasone after anaesthetic induction, droperidol 15 minutes before end of surgical intervention • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg IV Dexamethasone • *Dose*: 8 mg • *Time point of administration*: dexamethasone after anaesthetic induction, saline 15 minutes before end of surgical intervention • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Spain **Setting:** inpatient, single-centre **Author's name:** Yolanda Sanduende Otero **Institution:** Secrvicio de Anestesiología y Reanimación, Complejo Hospitalario Universitario Juan Canalejo, A Coruña **Email:** prmaceiras@wanadoo.es **Address:** Secrvicio de Anestesiología Reanimación, Complejo Hospitalario Universitario Juan Canalejo, Xubias de Arriba 84, 15006 A Coruña **Duration of study:** NA **Language:** Spanish (translated by Insa Backhaus) **Study's primary outcome:** NA

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Sanduende 2007 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "prospective, randomized double-blind trial"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the syringes with the study drugs were previously prepared by an anesthesiologist unrelated to the anesthetic procedure..." (translated)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (history of PONV, duration of anaesthesia, non-smoker): no; (history of motion sickness): unclear; (perioperative opioids, gender): yes

Sarkar 2006

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 38.3 • *Weight (mean ± SD, median (IQR), median (range))*: 38.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0

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Sarkar 2006 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: obstetrical laparoscopic surgery

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 38.5
- *Weight (mean ± SD, median (IQR), median (range))*: 38.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: obstetrical laparoscopic surgery

Included criteria: 18 to 65 years of age, ASA I or II, laparoscopic surgery

Excluded criteria: severe medical illness classifying them as ASA III and IV, history of drug reaction to any of the drugs used in this study, history of PONV, history of motion sickness, has received antiemetics in the previous 24 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 10 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)*

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Sarkar 2006 *(Continued)*

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** M. Sarkar **Institution:** Departement of Anesthesiology, Seth G.S. Medical College **Email:** NA **Address:** NA **Duration of study:** January 2007 to June 2007 **Language:** English **Study's primary outcome:** number of emetic episodes **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "60 patients randomized into two groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Satomoto 2017

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 17 • *Analysed (n)*: 17 • *Age (mean ± SD, median (IQR), median (range))*: 58 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 53 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 10/7/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 142 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil • *Type of surgery*: mastectomy, quadrantectomy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 18 • *Analysed (n)*: 18 • *Age (mean ± SD, median (IQR), median (range))*: 64 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 5/13/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 131 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil • *Type of surgery*: mastectomy, quadrantectomy **Included criteria:** women 38 to 77 years of age with ASA I or II who underwent a mastectomy or a quadrantectomy **Excluded criteria:** abuse of alcohol or drugs, psychiatric disease, hypersensitivity to droperidol or desflurane

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Satomoto 2017 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Control • *Dose*: saline • *Time point of administration*: 30 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 20 µg/kg • *Time point of administration*: 30 minutes after induction of anesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours, measured on postoperative day 1)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours, measured on postoperative day 1)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Maiko Satomoto **Institution:** Department of Anesthesiology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan **Email:** satomoto.mane@tmd.ac.jp **Address:** Department of Anesthesiology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan **Duration of study:** March to September 2014 **Language:** English **Study's primary outcome:** saving effect of droperidol on desflurane consumption **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were allocated randomly to the DHB or saline group" Judgement comment: no further information on sequence generation provided

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Satomoto 2017 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study drugs were drawn into identical 2 ml syringes, labelled “anti-emetic” (DHB was diluted to 2 ml in normal saline) by a nurse who was not part of the study, and handed to the anesthesiologist. The patient and investigators were blinded to the study medication" Judgement comment: anaesthesiologist also stated as blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the patient and the investigators were blinded to the study medication"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "(Number Cruncher Statistical Systems). Seven patients were excluded from the investigation (two for long surgery due to reconstructive procedures, one for epilepsy and mental retardation, and four for inaccurate BIS values due to electromyography without rocuronium throughout surgery) (Fig. 1). Thus, data from 35 patients were analyzed. The patients’ demographic characteristics, duration..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the patients’ demographic characteristics, duration of surgery and anesthesia, and blood circulatory parameters before DHB administration did not differ between the groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Savant 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 38.0 ± 14.9 • *Weight (mean ± SD, median (IQR), median (range))*: 59.2 ± 13.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 33 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0

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Savant 2016 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 150.4
- *Use of perioperative opioids (if yes, which?)*: pentazocine (0.5 mg/kg) as premedication
- *Type of surgery*: oral and maxillofacial surgery

Granisetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 31.8 ± 11.1
- *Weight (mean ± SD, median (IQR), median (range))*: 56.0 ± 11.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 23
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 166.4
- *Use of perioperative opioids (if yes, which?)*: pentazocine (0.5 mg/kg) as premedication
- *Type of surgery*: oral and maxillofacial surgery

Included criteria: 18 to 70 years of age, weighing more than 40 kg, ASA I or II, scheduled for oral and maxillofacial surgery under general anaesthesia

Excluded criteria: unable or unwilling to give informed consent, documented hypersensitivity to any of the study drugs, history of motion sickness or previous PONV, had taken antiemetic drugs within 24 hours before surgery, history of neurological or renal disease, medically compromised and not considered fit for surgery under general anaesthesia, history of adverse reactions to study drugs

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: ondansetron before induction, dexamethasone during surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 3.3% (metoclopramide 10 mg) Granisetron + dexamethasone • *Dose*: granisetron 2 mg, dexamethasone 8 mg • *Time point of administration*: granisetron before induction, dexamethasone during surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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Savant 2016 *(Continued)*

	Complete response (no PONV) in 24 hours • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Rakshit Vijay Sinai Khandeparke **Institution:** Oral and Maxillofacial Surgery, Richardsons Dental and Craniofacial Hospital, Nagercoil, India **Email:** rockdotcom1386@gmail.com **Address:** Oral and Maxillofacial Surgery, Richardsons Dental and Craniofacial Hospital, #71 Trivandrum Highway, Parvathipuram, Nagercoil, Tamil Nadu 629003, India, TEL: +91-7868096436 **Language:** English **Duration of study:** October 2011 to October 2012 **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated to the two study drug groups (A and B) and in a double blind manner" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on whether outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Savant 2016 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Scholz 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 296 • *Received treatment (n)*: 296 • *Analysed (n)*: 296 • *Age (mean ± SD, median (IQR), median (range))*: 46.5 (mean) (18.2 to 75.5) • *Weight (mean ± SD, median (IQR), median (range))*: 71.4 (mean) (42.0 to 120.0) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 129/139/28/0 • *Gender (female in %)*: 74 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 25/21 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, sufentanil • *Type of surgery*: abdominal and non-abdominal (ENT, eye, breast) surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 271 • *Received treatment (n)*: 271 • *Analysed (n)*: 271 • *Age (mean ± SD, median (IQR), median (range))*: 45.3 (mean) (18.1 to 74.5) • *Weight (mean ± SD, median (IQR), median (range))*: 71.0 (mean) (46.0 to 110.0) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 109/132/30/0 • *Gender (female in %)*: 72 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 29/21 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl, sufentanil • *Type of surgery*: abdominal and non-abdominal (ENT, eye, breast) surgery Placebo

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Scholz 1998 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 275
- *Received treatment (n)*: 275
- *Analysed (n)*: 275
- *Age (mean ± SD, median (IQR), median (range))*: 44.7 (mean) (18.1 to 73.8)
- *Weight (mean ± SD, median (IQR), median (range))*: 70.7 (mean) (42.0 to 114.0)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 123/124/24/0
- *Gender (female in %)*: 73
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 25/20
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl, sufentanil
- *Type of surgery*: abdominal and non-abdominal (ENT, eye, breast) surgery

Included criteria: ASA I to III, 18 to 75 years of age, abdominal and non-abdominal (ENT, eye, breast) surgery with general anaesthesia

Excluded criteria: ASA IV or V, women of childbearing age who were pregnant or lactating, or who might be pregnant (women of childbearing potential were required to test negative using a sensitive pregnancy test in the 24 hours before surgery); hypersensitivity to tropisetron or any other components of the formulations; expected to have a gastric tube in situ after surgery; vomiting in the 24 hours before surgery and/or concomitant medication known to influence gastrointestinal motility or vomiting or motion sickness (benzamides, phenothiazines, butyrophenones, corticosteroids, antihistamines, anticholinergics, other 5-HT3 antagonists); history of alcohol or drug abuse; co-existing medical conditions that might interfere with evaluation of the study drug or put the patient at risk (e.g. severe cardiac insufficiency, known hypersensitivity reaction); receiving any non-registered drug or drug under investigation in the 4 weeks before surgery or planning to receive any such drugs in the 4 weeks after study drug administration; dementia or altered mental status and not able to fully understand, therefore not competent to give informed consent; history of sub-ileus or ileus

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

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Interventions

Intervention characteristics

Tropisetron

- *Dose*: 2 mg
- *Time point of administration*: 3 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: tropisetron 2 mg

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: 3 minutes before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: tropisetron 2 mg

Placebo

- *Dose*: placebo
- *Time point of administration*: 3 minutes before induction
- *Route of administration*: IV

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Scholz 1998 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: tropisetron 2 mg
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (PACU discharge to 6 hours, 6 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (postoperative events before tropisetron rescue treatment)* • Outcome type: dichotomous outcome *Subjects with any AE (postoperative events before tropisetron rescue treatment)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Novartis Pharma Ltd. **Country:** Germany **Setting:** inpatient, multi-centre (10) **Author's name:** J. Scholz **Institution:** Department of Anaesthesiology, University Hospital Eppendorf, Hamburg **Email:** NA **Address:** Department of Anaesthesiology, University Hospital Eppendorf, Martinistrasse 52, D-20246 Hamburg **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response in 24 hours (absence of vomiting: absence of emetic episodes (vomiting or retching), regardless of the treatment received)
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were enrolled over an 8-month inclusion period, according to a stratified central randomization scheme"

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Scholz 1998 *(Continued)*

		Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the person administering the study medication was unaware of the identity of the drug being given" Judgement comment: no further information on blinding of participants and anaesthesiologists provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...less than 1 min. 5. Information on post-operative nausea and vomiting was obtained from the nursing staff by direct observation during the stay in the recovery room and on the ward, patient questionnaire for self-assessment of post-operative nausea and vomiting or patient interview by the investigator 6 h and 24 h after administration of the study drug. Rescue treatment Administration of rescue" Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "thus, significant differences were not observed between the groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Schuh 1987

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol (DHB) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 13.9 • *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 13.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 85 • *Non-smoker (%)*: NA

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Schuh 1987 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (enflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80
- *Use of perioperative opioids (if yes, which?)*: 0.33 mg intraoperative fentanyl, tramadol postoperative
- *Type of surgery*: cholecystectomy

TTS-Scopalamine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 50 ± 12.3
- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 12.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 70
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (enflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 71
- *Use of perioperative opioids (if yes, which?)*: 0.35 mg intraoperative fentanyl, tramadol postoperative
- *Type of surgery*: cholecystectomy

Included criteria: ASA I or II, cholecystolithiasis undergoing cholecystectomy under standardized balanced anaesthesia

Excluded criteria: over 70 years of age, glaucoma, micturition disturbance, intake of anticholinergics, history of psychiatric therapy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Droperidol (DHB) • *Dose*: 7.5 mg, placebo patch • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 15% (metoclopramide) TTS-Scopalamine • *Dose*: NA • *Time point of administration*: on the evening before surgery • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: 60% (metoclopramide)
Outcomes	*Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, observation until the afternoon on the first postoperative day)* • Outcome type: general notes on side effects

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Schuh 1987 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Rainer Schuh **Institution:** Anästhesieabteilung, Elisabethenstift, Darmstadt **Email:** NA **Address:** Anästhesieabteilung, Elisabethenstift, Landgraf-Georg-Straße 100, 6100 Darmstadt **Duration of study:** 1985 to 1986 **Language:** German (2 German reviewers) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Ppatienten wurden prospektiv mit einer Zufallszahlentabelle zwei Gruppen randomisiert zugeordnet. Mit..." Judgement comment: random number table
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "tabelle zwei Gruppen randomisiert zugeordnet. Mit der Anwendung eines Placebopflasters in der DHB-Gruppe wurde die Untersuchung einfach blind durchgeführt. Die angewendeten statistischen Methoden richteten" Judgement comment: personnel was not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "hinsichtlich der anthropometrischen Daten (Tab. 1) ergaben sich - auch bei der Geschlechtsverteilung - keine signifikanten Unterschiede" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Schultz 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 50.2 ± 13.7 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (Isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 197 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: vaginal or total abdominal hysterectomy, laparoscopy, tubal ligation, tubal re-anastomosis, bladder suspension, Burch procedure, anterior-posterior repair or myomectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 47.7 ± 12.3 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (Isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 153 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: vaginal or total abdominal hysterectomy, laparoscopy, tubal ligation, tubal re-anastomosis, bladder suspension, Burch procedure, anterior-posterior repair or myomectomy **Included criteria:** over 18 years of age, able to read and write English, low risk of anaesthesia issues, scheduled for inpatient surgery after gynaecological surgery **Excluded criteria:** pregnancy, surgery for cancer within previous 5 years, chemotherapy or radiation therapy within 5 years, antiemetic within 24 hours before surgery, previous use of acupressure bands, peripheral neuropathy

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Schultz 2003 *(Continued)*

	Pretreatment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear; (duration of anaesthesia): yes
Interventions	**Intervention characteristics** Droperidol • *Dose*: 1.25 mg • *Time point of administration*: before or with induction, "an anesthesiologist gave the study drug and documented the time of administration" • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: NA • *Time point of administration*: before or with induction, "an anesthesiologist gave the study drug and documented the time of administration" • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Seabands UK Ltd contributed the Seabands for the study **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Alyce A. Schultz **Institution:** New England Rehabilitation Hospital of Portland **Email:** Schula@mmc.org **Address:** Alyce A. Schultz, RN, PhD, Nurse Researcher, Maine Medical Center, 22 Bramhall Street, Portland, ME 04102, USA **Duration of study:** July 1999 to August 2000 **Language:** English **Study's primary outcome:** nausea **Trial registry number:** NA
Notes	Two out of 4 groups relevant (acupressure bands)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "random table number"

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Schultz 2003 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: quote: "study envelopes ... were prepared by the principal investigator and the study pharmacist..." Not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE). Unclear who performed randomization
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: quote: "the envelope containing the study group designation was opened by the admitting nurse and placed on the front of the subject's chart" "An anesthesiologist gave the study drug". Study personnel probably was not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: quote: "one hundred and forty-three women consented the study. One hundred and three women completed the hospital phase of the study...the most frequent reason for attrition was non-administration of the study drug". High rate of missing outcome data (> 15%)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear; (duration of anaesthesia): yes

Scuderi 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 285 • *Received treatment (n)*: NA • *Analysed (n)*: 285 • *Age (mean ± SD, median (IQR), median (range))*: 37.5 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 175 ± 46 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 63.5 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (99.3% fentanyl, 93% N_2O, 45.7% isoflurane, 54% sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 62

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Scuderi 1999 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 283 patients received intraoperative fentanyl, 1 patient received morphine
- *Type of surgery*: "outpatient surgery"

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 290
- *Received treatment (n)*: NA
- *Analysed (n)*: 290
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 174 ± 48
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 63.1
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (99.7% fentanyl, 96.2% N_2O, 46.2% isoflurane, 53.8% sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 67
- *Use of perioperative opioids (if yes, which?)*: 289 patients received intraoperative fentanyl, no patients received morphine
- *Type of surgery*: "outpatient surgery"

Included criteria: men and women, 18 to 65 years of age, ASA I to III, undergoing outpatient surgery or for short stay (23 hours or less)

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear (however -> stratification to eight subgroups on the presence of PONV risk factors)

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: randomized to 1 mg ondansetron or saline Placebo • *Dose*: saline • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: randomized to 1 mg ondansetron or saline
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** financial support was received from the Department of Anesthesiology, Wake Forest University School of Medicine **Country:** USA

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Scuderi 1999 *(Continued)*

Setting: outpatient, single-centre

Author's name: Phillip E. Scuderi

Institution: Wake Forest University School of Medicine, North Carolina, USA

Email: pscuderi@wfubmc.edu

Address: Department of Anesthesiology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, North Carolina 27157-1009, USA

Duration of study: NA

Language: English

Study's primary outcome: patient satisfaction with management of PONV, time to discharge from PACU

Trial registry number: NA

Notes	There is a second randomization for participants who require treatment of PONV (ondansetron vs placebo)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "...by random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear (however -> stratification to eight subgroups on the presence of PONV risk factors)

Scuderi 2000

Study characteristics

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Scuderi 2000 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 42 • *Received treatment (n)*: 42 • *Analysed (n)*: 42 • *Age (mean ± SD, median (IQR), median (range))*: 32.5 • *Weight (mean ± SD, median (IQR), median (range))*: 160 ± 44 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced inhalational anaesthesia (fentanyl, sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 66.5 • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: gynaecological laparoscopy Placebo • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 37 • *Received treatment (n)*: 37 • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 33.1 • *Weight (mean ± SD, median (IQR), median (range))*: 155 ± 44 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced inhalational anaesthesia (fentanyl, sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 69.4 • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: gynaecological laparoscopy **Included criteria:** female; 18 to 50 years of age; ASA I, II, or III; undergoing outpatient gynaecological laparoscopy under general anaesthesia; with or without history of PONV or motion sickness **Excluded criteria:** over 150% of ideal body weight **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Ondansetron

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Scuderi 2000 *(Continued)*

- *Dose*: 4 mg
- *Time point of administration*: before emergence form anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg

Placebo

- *Dose*: saline
- *Time point of administration*: before emergence form anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 1 mg

Outcomes

Vomiting (0 to 2 hours, PACU)

- Outcome type: dichotomous outcome

Identification

Sponsorship source: NA

Country: USA

Setting: outpatient, single-centre

Author's name: Phillip E. Scuderi

Institution: Department of Anesthesiology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA

Email: pscuderi@wfubmc.edu

Address: Department of Anesthesiology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1009, USA

Duration of study: NA

Language: English

Study's primary outcome: the primary aim of the study was to demonstrate a 100% complete response rate, defined as no vomiting and no need for rescue antiemetics

Trial registry number: NA

Notes

Two out of 3 groups relevant. Group I (TIVA/multi-modal prophylactic regimen) was excluded

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized to one of three groups" Judgement comment: no statement on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement on allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: study described as "double-blind" but no information on blinding of intraoperative personnel provided
Blinding of outcome assessment (detection bias)	Low risk	Quote: "it can possibly be. On admission to the postanesthesia care unit (PACU) the patients were monitored by study personnel, blinded as to the

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Scuderi 2000 *(Continued)*

All outcomes		anesthetic technique used, for both efficacy and outcomes. All patients were admitted"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Scuderi 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 327 • *Received treatment (n)*: NA • *Analysed (n)*: 327 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 0.8 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 0.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 39/24 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 144 • *Use of perioperative opioids (if yes, which?)*: 99% of patients received opioids for anaesthesia, 94% received postoperative opioids • *Type of surgery*: gynaecological and non-gynaecological surgery Ondansetron (4 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 337 • *Received treatment (n)*: NA • *Analysed (n)*: 337 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 0.8 • *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 0.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Scuderi 2001 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 40/25
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 144
- *Use of perioperative opioids (if yes, which?)*: 99% of patients received opioids for anaesthesia, 95% received postoperative opioids
- *Type of surgery*: gynaecological and non-gynaecological surgery

Ondansetron (8 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 338
- *Received treatment (n)*: NA
- *Analysed (n)*: 338
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 0.7
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 0.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 39/20
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 146
- *Use of perioperative opioids (if yes, which?)*: 99% of patients received opioids for anaesthesia, 94% received postoperative opioids
- *Type of surgery*: gynaecological and non-gynaecological surgery

Ondansetron (16 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 343
- *Received treatment (n)*: NA
- *Analysed (n)*: 343
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 0.8
- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 0.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 39/21
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 136
- *Use of perioperative opioids (if yes, which?)*: 99% of patients received opioids for anaesthesia, 93% received postoperative opioids
- *Type of surgery*: gynaecological and non-gynaecological surgery

Included criteria: non-pregnant; female; 12 years of age or older; ASA I, II, or III; scheduled to undergo surgery under general anaesthesia requiring hospital admission for at least 24 hours postoperatively

Excluded criteria: pregnant or breastfeeding; > 100% over ideal body weight; had received an investigational drug within 30 days; had received any drug with antiemetic properties within 24 hours; had ex-

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Scuderi 2001 *(Continued)*

	perienced any vomiting or retching within 24 hours before administration of study drug; history of gastroparesis or a similar condition; scheduled to undergo craniotomy, termination of pregnancy, or hepatic, gastrointestinal, or intrathoracic surgery; serum creatinine > 2.0 mg/dL; serum alanine aminotransferase (ALT) or aspartate transaminase (AST) > 2× the upper limit of normal; scheduled to undergo gastric suctioning intraoperatively; would require a nasogastric tube postoperatively **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: placebo • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 58% (left to discretion of the investigator) Ondansetron (4 mg group) • *Dose*: 4 mg • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 50% (left to discretion of the investigator) Ondansetron (8 mg group) • *Dose*: 8 mg • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 48% (left to discretion of the investigator) Ondansetron (16 mg group) • *Dose*: 16 mg • *Time point of administration*: 1 hour before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: 38% (left to discretion of the investigator)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Arrhythmia (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)*

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Scuderi 2001 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this study was supported in part by Glaxo-Wellcome, Inc. **Country:** USA **Setting:** inpatient, multi-centre (29) **Author's name:** Phillip Scuderi **Institution:** Department of Anesthesiology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC, USA **Email:** NA **Address:** Department of Anesthesiology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1009, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** number of emetic episodes **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized to receive" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Segelman 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Betamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 34 • *Received treatment (n)*: 33 • *Analysed (n)*: 33 • *Age (mean ± SD, median (IQR), median (range))*: 44.2 ± 13.0 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 32 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, morphine or oxycodone) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 25.5 • *Use of perioperative opioids (if yes, which?)*: 0.1 mg fentanyl, 3.5 mg morphine and oxycodone intraoperatively • *Type of surgery*: arthroscopic knee surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 38.9 ± 12.0 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 35 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, morphine, or oxycodone) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 24.5 • *Use of perioperative opioids (if yes, which?)*: 0.1 mg fentanyl, 3.3 mg morphine and oxycodone intraoperatively • *Type of surgery*: arthroscopic knee surgery **Included criteria:** elective outpatient arthroscopic knee surgery, ASA I or II **Excluded criteria:** over 18 years of age; inability to provide informed consent due to linguistic problems or cognitive dysfunction; planned cruciate ligament repair; locked knee due to a torn meniscus with a subsequent planned meniscus reinsertion; use of a tourniquet; diabetes mellitus; bleeding disorder; atrial fibrillation; ongoing corticosteroid medication; intake of non-steroidal anti-inflammatory drugs within 2 days before surgery; pregnancy; Apfel score > 2

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Segelman 2016 *(Continued)*

	Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Betamethasone • *Dose*: 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: sodium chloride 9 mg/mL • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Subjects with any AE (within 3 days)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** financial support was provided through the Regional Agreement on Medical Training and Clinical Research (ALF) between the Stockholm Community Council and Karolinska Institutet and by the Bengt Ihre Foundation. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript **Country:** Sweden **Setting:** outpatient, single-centre **Author's name:** Jerker Segelman **Institution:** Section of Anaesthesiology and Intensive Care, Department of Clinical Science and Education, Karolinska Institutet **Email:** jerker.segelman@sodersjukhuset.se **Address:** Karolinska Institutet, Södersjukhuset, 118 81,Stockholm, Sweden **Duration of study:** May 2011 to February 2013 **Language:** English **Study's primary outcome:** pain day 1 evaluated by a verbal descriptor scale **Trial registry number:** EUCTR2009-014717-27
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed with a 1:1 ratio using a computer-generated, random allocation"

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Segelman 2016 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "sequence concealed in consecutively numbered sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "at the time of inclusion, an envelope was opened and a syringe with the intervention substance was prepared by a nurse not otherwise involved in data collection or care of the patients. The patients, care providers, and data collectors were blinded to the drug in use"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "data collectors were blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "thus, 74 patients were randomized. All patients were operated with an arthroscopic partial meniscus resection without any perioperative complications. The clinical characteristics are presented in Table 1. Thirty-three patients received betamethasone and 40 received placebo. One patient randomized to the betamethasone group did not receive the study drug due to the start of surgery being delayed. Follow-up was possible for all patients except for one in the placebo group. In total, 33 patients in the betamethasone group and 39 in the placebo group were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: EUCTR2009-014717-27 (prospective registration). The prospectively registered primary outcome (pain) was reported in the final study. No time frame for outcome assessment was prespecified within the protocol. The primary outcome was not PONV-related
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Sekhavat 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 5.6 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 23 ± 3.1 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Sekhavat 2015 *(Continued)*

- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 87
- *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine
- *Type of surgery*: abdominal hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 5.1
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 4.5
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol), N_2O
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 89
- *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine
- *Type of surgery*: abdominal hysterectomy

Included criteria: women undergoing abdominal hysterectomy for various indications

Excluded criteria: known allergy/hypersensitivity to dexamethasone, nausea or vomiting within 24 hours before the operation, had received an antiemetic within 48 hours before surgery, any gastrointestinal disorder (e.g. esophagitis, gastritis)

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

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Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 18% (metoclopramide 10 mg IV)

Placebo

- *Dose*: saline
- *Time point of administration*: at end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 24% (metoclopramide 10 mg IV)

Outcomes

Vomiting (0 to 2 hours)

- Outcome type: dichotomous outcome

Vomiting (12 to 24 hours)

- Outcome type: dichotomous outcome

PONV (0 to 24 hours)

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Sekhavat 2015 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Robab Davar **Institution:** Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Sciences, Yazd, Iran **Email:** sekhavat@ssu.ac.ir, lsekhavat@yahoo.com **Address:** Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Sciences, Yazd, Iran **Duration of study:** June 2009 to September 2010 **Language:** English **Study's primary outcome:** VAS score for nausea **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed with a computer-driven random"
Allocation concealment (selection bias)	Low risk	Quote: "number sequence and sealed in opaque envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "prior to each operation, the set was prepared with identical syringes containing dexamethasone or saline for injection with the purpose of maintaining blindness in the study"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the postoperative nausea, vomiting and medications required were evaluated and recorded by a second-year resident and were collected every 4 h during the first 24 h after surgery" Judgement comment: no information on blinding of the outcome assessor
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Sekhavat 2015 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Seki 2005

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 10 • *Received treatment (n)*: NA • *Analysed (n)*: 10 • *Age (mean ± SD, median (IQR), median (range))*: 70 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 4/6/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: 80 • *History of PONV/motion sickness (%)*: 10/0 • *Type of general anaesthesia*: combined anaesthesia (TIVA + sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 236 • *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 2 µg/kg fentanyl, 1.3 mg/kg morphine, 2 patients used PCA • *Type of surgery*: spinal surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 10 • *Received treatment (n)*: NA • *Analysed (n)*: 10 • *Age (mean ± SD, median (IQR), median (range))*: 63 ± 16 • *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 4/6/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: 60 • *History of PONV/motion sickness (%)*: 10/10 • *Type of general anaesthesia*: combined anaesthesia (TIVA + sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 257 • *Use of perioperative opioids (if yes, which?)*: 1 µg/kg to 2 µg/kg fentanyl, 1.3 mg/kg morphine, 5 patients used PCA • *Type of surgery*: spinal surgery

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Seki 2005 *(Continued)*

	Included criteria: scheduled for spinal surgery under general anaesthesia, over 20 years of age, ASA I or II **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness, non-smoker): no
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo • *Dose*: saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (0 to 48 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Hiroyuki Seki **Institution:** Department of Anesthesiolgy, Keio University, School of Medicine, Tokyo **Email:** NA **Address:** Department of Anesthesiolgy, Keio University, School of Medicine, Tokyo 160-8582 **Duration of study:** NA **Language:** Japanese (translated by Simone Schneider and Kota Amamoto) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided

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Seki 2005 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness, non-smoker): no

Semira 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 8.2 • *Weight (mean ± SD, median (IQR), median (range))*: 60.4 ± 7.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/6/0/0 • *Gender (female in %)*: 70 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O/isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 75.2 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic cholecystectomy Dexamethasone • *Assessed for eligibility (n)*: -

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Semira 2013 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 43.9 ± 10.4
- *Weight (mean ± SD, median (IQR), median (range))*: 57.9 ± 8.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 23/7/0/0
- *Gender (female in %)*: 77
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O/isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 75.5
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 39.6 ± 8.6
- *Weight (mean ± SD, median (IQR), median (range))*: 60.3 ± 8.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 24/6/0/0
- *Gender (female in %)*: 63
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O/isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79.4
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: USG diagnosed cholelithiasis scheduled for laparoscopic cholecystectomy under general anaesthesia, both sexes, ASA I and II

Excluded criteria: patients with 18 or above 60 years of age; unable to cooperate or epileptic; impaired kidney or liver function; history of hypersensitivity to any drug; history of peptic ulcer disease; taking psychotropic drugs, calcium channel blockers, or antidepressants; for whom laparoscopic cholecystectomy was converted into open cholecystectomy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 10 to 15 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 1 mg IV Dexamethasone

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Semira 2013 *(Continued)*

	• *Dose*: 8 mg • *Time point of administration*: 10 to 15 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 1 mg IV Placebo • *Dose*: 2 mL saline • *Time point of administration*: 10 to 15 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: granisetron 1 mg IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Semira **Institution:** SKIMS Medical College, Bemina Kashmir **Email:** NA **Address:** Department of Pharmacology, SKIMS medical college, Bemina Kashmir, India 190001 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Three out of 4 groups relevant (gabapentin)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "the table of random numbers..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Semira 2013 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Semple 1992

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Hyoscine patch • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 46 (28 to 64) • *Weight (mean ± SD, median (IQR), median (range))*: 68.5 (49 to 86) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane/N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 72 • *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, 77.5 mg morphine postoperatively • *Type of surgery*: abdominal hysterectomy Placebo • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 45.5 (31 to 63) • *Weight (mean ± SD, median (IQR), median (range))*: 68 (54 to 97) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane/N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 62

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Semple 1992 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction, 82.5 mg morphine postoperatively
- *Type of surgery*: abdominal hysterectomy

Included criteria: 18 to 65 years of age, ASA I or II, requiring general anaesthesia for abdominal hysterectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Hyoscine patch • *Dose*: NA • *Time point of administration*: 2 hours before operation • *Route of administration*: transdermal patch • *Rescue antiemetics (if yes, which?)*: cyclizine 50 mg IM Placebo • *Dose*: NA • *Time point of administration*: 2 hours before operation • *Route of administration*: transdermal patch • *Rescue antiemetics (if yes, which?)*: cyclizine 50 mg IM
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (day 1 after PACU)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (first postoperative day, day 2, day 3)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 3 days' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** inpatient, single-centre **Author's name:** P. Semple **Institution:** York District Hospital **Email:** NA **Address:** Department of Anaesthesia, York District Hospital, Wigginton Road, York YO3 7HE, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA

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Semple 1992 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly allocated". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the placebo was a standard waterproof dressing (Johnson and Johnson) and each hyoscine patch was covered by a similar dressing, so that its identity could not be distinguished from placebo by patient or assessor. The patches were applied by a nurse who was not involved with subsequent assessment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the placebo was a standard waterproof dressing (Johnson and Johnson) and each hyoscine patch was covered by a similar dressing, so that its identity could not be distinguished from placebo by patient or assessor. The patches were applied by a nurse who was not involved with subsequent assessment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "seventy-two patients were recruited into the trial but five were later withdrawn: two patients had problems with the PCA (one severe itching, one was unable to operate it) and both were converted to intramuscular analgesia, one patient was inadequately followed up, one patch was accidentally removed and one patient developed an allergy to the dressing. Of the remaining 67 subjects, 37 were in the active group and 30 in the placebo group"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Senthil 2007

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Granisetron • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: NA • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: NA

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Senthil 2007 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: NA

Granisetron + dexamethasone

- *Assessed for eligibility (n)*: NA
- *Enrolled (n)*: NA
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: NA

Included criteria: both sexes, 20 to 60 years of age, ASA I and II, to undergo general anaesthesia and to remain in the hospital for at least 24 hours postoperatively

Excluded criteria: GIT disease, received antiemetic medication (or) experienced nausea and vomiting before surgery, pregnant (or) menstruating

Pretreatment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Granisetron • *Dose*: 40 µg/kg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg Granisetron + dexamethasone • *Dose*: granisetron 40 µg/kg, dexamethasone 8 mg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg
Outcomes	*Vomiting (0 to 3 hours)*

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Senthil 2007 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (3 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Kumar S. Senthil **Institution:** Kasturba Medical College Hospital, Mangalore, INDIA **Email:** NA **Address:** Department of Anaesthesiology, Kasturba Medical College Hospital, Mangalore, INDIA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated" Judgement comment: no detailed information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "each drug combination [was] prepared and administered by personnel blind to the drugs" Judgement comment: no statement on patients
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...and 3-24 hrs in ward, all the episodes of PONV (nausea, retching, vomiting) were recorded every 3 hrs by blinded nursing staff. NAUSEA defined as the unpleasant"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Senthil 2007 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Seo 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 43.7 ± 14.9 • *Weight (mean ± SD, median (IQR), median (range))*: 60.3 ± 8.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 82.86 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 215.1 • *Use of perioperative opioids (if yes, which?)*: 0.2 mg fentanyl intraoperatively • *Type of surgery*: thyroidectomy Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 38 • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 46.9 ± 14.9 • *Weight (mean ± SD, median (IQR), median (range))*: 63.5 ± 8.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 81.58 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 228.1 • *Use of perioperative opioids (if yes, which?)*: 0.2 mg fentanyl intraoperatively • *Type of surgery*: thyroidectomy **Included criteria:** underwent thyroidectomy, 20 to 72 years of age, ASA I or II, normal thyroid function

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Seo 2003 *(Continued)*

	Excluded criteria: history of nausea and vomiting after surgery, carcinoma, gastrointestinal disorder, diabetes mellitus, cataracts, hypertension, steroids, immunosuppressive agents, recent TB **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Dexamethasone • *Dose*: 5 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Kyung-Han Kim **Institution:** Department of Anesthesiology and Pain Medicine, Kosin University School of Medicine, Korea **Email:** kimkh@kosinmed.or.kr **Address:** 34 Aman-dong, Seo-gu, Busan, KoreaDepartment of Anesthesiology and Pain Medicine, Kosin University School of Medicine, Postal Code: 602-702 **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None
Risk of bias	

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Seo 2003 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Shadangi 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 41.4 ± 12.7 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl for induction

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Shadangi 2013 *(Continued)*

- *Type of surgery*: major elective surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 36.6 ± 10.93
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction
- *Type of surgery*: major elective surgery

Palonosetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 39.9 ± 9.68
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 43.3
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction
- *Type of surgery*: major elective surgery

Included criteria: ASA I and II, of either sex, 20 to 60 years of age, scheduled for major elective surgery under general anaesthesia

Excluded criteria: difficulty in communicating; prone to nausea, vomiting, or motion sickness; on opioid analgesics or antiemetics within 24 hours before anaesthesia; requiring continuous gastric suction for 24 hours in postoperative period; having Mallampatti grade II or above

Pretreatment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, perioperative opioids, history of motion sickness): no; (history of PONV, duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 4 mL saline • *Time point of administration*: 10 minutes before induction

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Shadangi 2013 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 8 mg • *Time point of administration*: 10 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: 10 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** none declared **Country:** India **Setting:** inpatient, single-centre **Author's name:** Bijaya Kumar Shadangi **Institution:** DepartmentofAnesthesiology, Medanta-Medicity, Gurgaon **Email:** drbijayakumars@gmail.com **Address:** Flat no 107, Atulya Apartments, Sector-18B, Dwarka, NewDelhi-110078, India **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

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Shadangi 2013 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "by coded envelope technique" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "randomization of the patients was carried out by coded envelop technique" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind study" Quote: "drugs were loaded in identical syringes with the code by the personnel not participating in the study"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, perioperative opioids, history of motion sickness): no; (history of PONV, duration of anaesthesia, non-smoker): unclear

Shah 1972

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Metoclopramide + hyoscine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: 41 • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 36 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Shah 1972 *(Continued)*

- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: minor gynaecological surgery

Hyoscine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 41
- *Received treatment (n)*: 41
- *Analysed (n)*: 41
- *Age (mean ± SD, median (IQR), median (range))*: 33.9
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: minor gynaecological surgery

Included criteria: patients for minor gynaecological surgery

Excluded criteria: patients with severe cardiovascular or respiratory disease

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide + hyoscine • *Dose*: metoclopramide 10 mg, hyoscine 0.4 mg • *Time point of administration*: 1 hour before anaesthesia • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA Hyoscine • *Dose*: saline, hyoscine 0.4 mg • *Time point of administration*: 1 hour before anaesthesia • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 6 hours)*

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Shah 1972 *(Continued)*

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 6 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 6 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** the coded ampoules of metoclopramide and placebo were kindly supplied by Beecham Research Laboratories **Country:** England **Setting:** outpatient, single-centre **Author's name:** Z.P. Shah **Institution:** United Leeds Hospitals, Leeds **Email:** NA **Address:** University Department of Anaesthesia, Leeds LS2 9LN **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly allocated" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the ampoules of the trial drug and the placebo were identical, their contents being unknown to the nurses and anaesthetists; a code was available in the event of emergency, but this did not arise"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Shah 1972 *(Continued)*

Other bias	Unclear risk	Quote: "the age distribution, duration of anaesthesia and mean recovery rime were similar for the two groups" Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Sharma 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 48.5 ± 19 • *Weight (mean ± SD, median (IQR), median (range))*: 55.4 ± 17 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 174 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: major gynaecological surgery Droperidol (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 50.5 ± 17 • *Weight (mean ± SD, median (IQR), median (range))*: 56.4 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 160 • *Use of perioperative opioids (if yes, which?)*: NA

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Sharma 2000 *(Continued)*

- *Type of surgery*: major gynaecological surgery

Metoclopramide (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: 49.7 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 58.2 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 170
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major gynaecological surgery

Placebo (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: NA
- *Analysed (n)*: 24
- *Age (mean ± SD, median (IQR), median (range))*: 51.2 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 54.7 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 168
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: major gynaecological surgery

Included criteria: women undergoing major gynaecological surgery, ASA I or II, 16 to 70 years of age

Excluded criteria: taking drugs with antiemetic effects

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group A) • *Dose*: 4 mg • *Time point of administration*: 10 minutes before the neuromuscular blockade was antagonized at the end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM

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Sharma 2000 *(Continued)*

	Droperidol (group B) • *Dose*: 2.5 mg • *Time point of administration*: 10 minutes before the neuromuscular blockade was antagonized at the end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Metoclopramide (group C) • *Dose*: 10 mg • *Time point of administration*: 10 minutes before the neuromuscular blockade was antagonized at the end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Placebo (group D) • *Dose*: saline • *Time point of administration*: 10 minutes before the neuromuscular blockade was antagonized at the end of the procedure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 6 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Malaysia **Setting:** inpatient, single-centre **Author's name:** S. Sharma **Institution:** Department of Anaesthesia and Critical Care Medicine School of Medical Studies University Science Malaysia **Email:** ssharma@pc.jaring.my **Address:** Department of Anaesthesia and Critical Care Medicine, School of Medical Studies, University Science Malaysia, Kubang Kerian, Kelantan, Malaysia **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA

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Sharma 2000 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "100 ASA physical status I-II undergoing major gynaecological surgery were randomized to receive intravenously (IV), one of the four test drugs 10 minutes before the end of anaesthesia" Judgement comment: no details on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the observer was blinded to the study drug"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred patients were involved in the study initially; one patient each in the metoclopramide group and placebo group were excluded, because they had to be given opioid analgesic as the pain could not be controlled with keterolac"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no statistically significant difference between the groups with regard to patients' age and weight (Table I). The type of surgery performed, and the number of patients in each group who underwent abdominal or vaginal procedures was comparable" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Sharma 2015

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Palonosetron + dexamethasone (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA

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Sharma 2015 *(Continued)*

- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 37.8 ± 8.5
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, analgesic not specified)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 119.7
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic hysterectomy

Ondansetron + dexamethasone (group II)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: NA
- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 39.1 ± 8.8
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, analgesic not specified)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 118.0
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic hysterectomy

Included criteria: 30 to 50 years of age, ASA I or II, posted for elective laparoscopic hysterectomy under general anaesthesia

Excluded criteria: procedure refusal; receiving antiemetics, steroids, or psychoactive medications within 24 hours of study initiation; vomiting or retching in the 24 hours before surgery; cancer chemotherapy within the last 4 weeks; ongoing vomiting from gastrointestinal disease; allergy to NSAIDs; bronchial asthma

Pretreatment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Palonosetron + dexamethasone (group I) • *Dose*: palonosetron 0.075 mg, dexamethasone 8 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (4%) metoclopramide 10 mg IV Ondansetron + dexamethasone (group II) • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: before induction of anaesthesia

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Sharma 2015 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (20%) metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Mortality (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** no funding was received for this work **Country:** India **Setting:** inpatient, single-centre **Author's name:** Anish N.G. Sharma **Institution:** Department of Anaesthesiology, KVG Medical College and Hospital, Karnataka, India **Email:** anish84guthu@gmail.com **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of nausea and vomiting during the first 24 hours after anaesthesia and up to 48 hours **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized into two groups of 45 patients each according to the sealed envelope technique" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "according to the sealed envelope technique" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")

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Sharma 2015 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "no patients were later excluded from the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients in the two groups had a similar demographic profile, and no patients were later excluded from the study. Baseline hemodynamic data were also similar in both groups. Table 1 and 2 shows age distribution and duration of surgery in both groups" Judgement comment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Shirdashtzadeh 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Promethazine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 27 ± 5.3 • *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 6.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 25/0/0/0 • *Gender (female in %)*: 0 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 44 • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: appendectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25

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Shirdashtzadeh 2011 *(Continued)*

- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 23.5 ± 5.8
- *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 5.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 25/0/0/0
- *Gender (female in %)*: 0
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 27
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: appendectomy

Included criteria: ASA I, 15 to 40 years of age, listed for elective appendectomy

Excluded criteria: female, younger than 15 and older than 40 years of age, systematic disease (diabetes), took any drugs before surgery, haemodynamic disturbance within surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Promethazine • *Dose*: 1 mg/kg • *Time point of administration*: 5 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: placebo • *Time point of administration*: 5 minutes before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Azadeh Eshraghi

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Shirdashtzadeh 2011 *(Continued)*

Institution: Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

Email: eshraghi_a82@yahoo.com

Address: Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	Two out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly allocated to receive one of the three regimens" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the intravenous medications were coded and given 5 minutes prior to surgery" Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "24 hours (every 6 hours) after anesthesia were gathered and recorded by a trained investigator with no knowledge of which treatment the patients had received..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the characteristics of the patients in the three treated groups are shown in table 1" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, non-smoker, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia): yes

Shora 2007

Study characteristics

Methods	**Study design:** randomized controlled trial

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Shora 2007 *(Continued)*

Study grouping: 2 groups, monoprophylaxis and combination prophylaxis

Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 33.27 ± 8.53 • *Weight (mean ± SD, median (IQR), median (range))*: 52.90 ± 7.27 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 65.27 • *Use of perioperative opioids (if yes, which?)*: morphine for induction • *Type of surgery*: laparoscopic cholecystectomy Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 32.47 ± 10.18 • *Weight (mean ± SD, median (IQR), median (range))*: 52.70 ± 7.47 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 66.67 • *Use of perioperative opioids (if yes, which?)*: morphine for induction • *Type of surgery*: laparoscopic cholecystectomy **Included criteria:** female, 18 to 55 years of age, ASA I or II, undergoing laparoscopic cholecystectomy under general anaesthesia **Excluded criteria:** history of motion sickness, migraine, PONV during previous surgery, pregnant or lactating **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 1 minute before induction of anaesthesia

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Shora 2007 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 0.1 mg/kg Ondansetron + dexamethasone • *Dose*: ondansetron 4 mg, dexamethasone 4 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 0.1 mg/kg
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (12 to 18 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Asaf Nazir Shora **Institution:** Sher-i-Kashmir Institute of Medical Sciences **Email:** NA **Address:** Soura, Bemina, Srinagar, Jammu and Kashmir 190011 **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated into two groups of 30 patients each" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Shora 2007 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "patients included in the study. In the preoperative holding area, patients were randomly allocated into two groups of 30 patients each and received study medications prepared by a single person in identical 5 ml syringe and all study medications were diluted up to 4 ml in 0.9 % saline in order to ensure blinding" Judgement comment: it is unclear whether the person preparing the syringes was further involved in the study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "after surgery patients were observed for a period of 24 hours by the same anaesthetist" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Simpson 1988

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: 21 • *Randomized (n)*: 21 • *Received treatment (n)*: NA • *Analysed (n)*: 21 • *Age (mean ± SD])*: 44.1 ± 8.7 • *Weight (mean ± SD, median (IQR), median (range))*: 62.9 ± 16.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery: mean(SD)*: 81.6 +/-30.3 • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine, papaveretum • *Type of surgery*: major gynaecological surgery

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Simpson 1988 *(Continued)*

	Hyoscine • *Assessed for eligibility (n)*: NA • *Enrolled (n)*: 20 • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD])*: 42.5 ± 67 • *Weight (mean ± SD, median (IQR), median (range))*: 68.4 ± 12.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery: mean(SD)*: 75.3 +/-22.7 • *Use of perioperative opioids (if yes, which?)*: fentanyl, morphine, papaveretum • *Type of surgery*: major gynaecological surgery **Included criteria:** undergoing major gynaecological surgery, healthy women, ASA I or II, 25 to 60 years of age **Excluded criteria:** analgesic or psychotropic medication **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: placebo • *Time point of administration*: 2 hours before surgery • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Hyoscine • *Dose*: 0.6 mg • *Time point of administration*: 2 hours before surgery • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM
Outcomes	*Sedation/drowsiness (0 to 3 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** Napp Laboratories, for support, provision of MST used during the study and organisation of the morphine assay. Also staff of the Yorkshire Regional Drug Information Centre for providing the placebo and randomising the tablets for the study **Country:** United Kingdom **Setting:** inpatient, single-centre **Author's name:** K.H. Simpson **Institution:** University Deparment of Anaesthesia, St James's University Hospital

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Simpson 1988 *(Continued)*

	Email: NA **Address:** General Infirmary, Great George Street, Leeds **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	Two out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized manner" Judgement comment: no statement on sequence generation
Allocation concealment (selection bias)	Low risk	Quote: "staff of the Yorkshire Regional Drug Information Centre for providing the placebo and randomizing the tablets for the study" Judgement comment: central allocations
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "in a double-blind randomized manner" Judgement comment: insufficient information on blinding (who was blinded?)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the same anaesthetist recorded sedation, anxiety, mood and emesis scores immediately after the patient was admitted to the recovery room" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data assumed (61 participants were reported in all tables and figures)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Singla 2010

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics**

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Singla 2010 *(Continued)*

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 140
- *Received treatment (n)*: NA
- *Analysed (n)*: 140 (efficacy)/ 130 (safety)
- *Age (mean ± SD, median (IQR), median (range))*: 39.3 ± 8.15
- *Weight (mean ± SD, median (IQR), median (range))*: 75.1 ± 18.27
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 52/76
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77.2
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/remifentanil/morphine, postoperative at discretion of investigator
- *Type of surgery*: laparoscopic/laparotomy gynaecological procedure, laparoscopic cholecystectomy

Casopitant 50 mg + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 140
- *Received treatment (n)*: NA
- *Analysed (n)*: 140 (efficacy)/ 135 (safety)
- *Age (mean ± SD, median (IQR), median (range))*: 38.1 ± 8.24
- *Weight (mean ± SD, median (IQR), median (range))*: 75.1 ± 17.32
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 54/71
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77.0
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic/laparotomy gynaecological procedure, laparoscopic cholecystectomy

Casopitant 100 mg + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 140
- *Received treatment (n)*: NA
- *Analysed (n)*: 140 (efficacy)/ 134 (safety)
- *Age (mean ± SD, median (IQR), median (range))*: 39.5 ± 8.58
- *Weight (mean ± SD, median (IQR), median (range))*: 73.8 ± 19.66
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 58/72
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane, N_2O)

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Singla 2010 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80.5
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/remifentanil/morphine, postoperative at discretion of investigator
- *Type of surgery*: laparoscopic/laparotomy gynaecological procedure, laparoscopic cholecystectomy

Casopitant 150 mg + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 140
- *Received treatment (n)*: NA
- *Analysed (n)*: 140 (efficacy)/ 131 (safety)
- *Age (mean ± SD, median (IQR), median (range))*: 39.3 ± 7.84
- *Weight (mean ± SD, median (IQR), median (range))*: 74.6 ± 17.40
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 54/69
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77.8
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/remifentanil/morphine, postoperative at discretion of investigator
- *Type of surgery*: laparoscopic/laparotomy gynaecological procedure, laparoscopic cholecystectomy

Casopitant

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 142
- *Received treatment (n)*: NA
- *Analysed (n)*: 140 (efficacy)/132 (safety)
- *Age (mean ± SD, median (IQR), median (range))*: 38.5 ± 8.33
- *Weight (mean ± SD, median (IQR), median (range))*: 74.5 ± 17.84
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 58/67
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane/desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79.1
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl/remifentanil/morphine, postoperative at discretion of investigator
- *Type of surgery*: laparoscopic/laparotomy gynaecological procedure, laparoscopic cholecystectomy

Included criteria: premenopausal or perimenopausal, non-smoking, female, 18 to 55 years of age, history of PONV and/or motion sickness, undergoing a laparoscopic or laparotomy gynaecological surgical procedure or laparoscopic cholecystectomy with general anaesthesia

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics**

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Singla 2010 *(Continued)*

	Ondansetron • *Dose*: 4 mg, placebo • *Time point of administration*: placebo 60 minutes before induction of anaesthesia, ondansetron immediately before induction of anaesthesia • *Route of administration*: placebo PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: NA Casopitant 50 mg + ondansetron • *Dose*: casopitant 50 mg, ondansetron 4 mg • *Time point of administration*: casopitant 60 minutes before induction of anaesthesia, ondansetron immediately before induction of anaesthesia • *Route of administration*: casopitant PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: NA Casopitant 100 mg + ondansetron • *Dose*: casopitant 100 mg, ondansetron 4 mg • *Time point of administration*: casopitant 60 minutes before induction of anaesthesia, ondansetron immediately before induction of anaesthesia • *Route of administration*: casopitant PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: NA Casopitant 150 mg + ondansetron • *Dose*: casopitant 150 mg, ondansetron 4 mg • *Time point of administration*: casopitant 60 minutes before induction of anaesthesia, ondansetron immediately before induction of anaesthesia • *Route of administration*: casopitant PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: NA Casopitant • *Dose*: 150 mg, placebo • *Time point of administration*: casopitant 60 minutes before induction of anaesthesia, placebo immediately before induction of anaesthesia • *Route of administration*: casopitant PO, placebo IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 120 hours)* • Outcome type: dichotomous outcome *Mortality (0 to 120 hours)* • Outcome type: dichotomous outcome *Headache (0 to 120 hours)*

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Singla 2010 *(Continued)*

- Outcome type: dichotomous outcome

Constipation (0 to 120 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 120 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** funding for this study was provided by GlaxoSmithKline (NCT00108095), Research Triangle Park, North Carolina, and Endo Pharmaceuticals, Chadds Ford, Pennsylvania **Country:** USA **Setting:** NA, multi-centre (53) **Author's name:** Neil K. Singla **Institution:** Lotus Clinical Research Inc., Huntington Hospital, Pasadena, California, USA **Email:** neil@lotuscr.com **Address:** Lotus Clinical Research Inc., 100 West California Boulevard, Pasadena, California 91105, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response during 24 hours **Trial registry number:** NCT00108095
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned to one of five treatments" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "approximately 90% of the patients completed the study (i.e., completed all required assessments for the 24 h after the emergence from anesthesia on postoperative day 1) (table 2). The most frequent reasons for premature withdrawal were surgery being canceled or delayed, errors in randomization or dosing, and subject's decision to withdraw. Adverse events (AEs) leading to withdrawal from the study were reported in one subject in the 100 mg casopitant plus 4 mg ondansetron arm (amnesia) and two subjects in the 150-mg

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Singla 2010 *(Continued)*

		casopitant- alone arm (nerve compression and anaphylactic shock). None of these AEs was considered to be related to the study drug by the investigators"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00108095 (retrospective registration)
Other bias	Unclear risk	Quote: "demographic characteristics, including major risk factors for PONV, were well balanced among the treatment groups (table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Sinha 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 41.0 ± 14.1 • *Weight (mean ± SD, median (IQR), median (range))*: 51.3 ± 9.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 8.57 • *Type of general anaesthesia*: balanced anaesthesia (N_2O, halothane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 232.4 • *Use of perioperative opioids (if yes, which?)*: 308.2 µg fentanyl intraoperative, no postoperative opioids • *Type of surgery*: breast surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 41.6 ± 10.3 • *Weight (mean ± SD, median (IQR), median (range))*: 54.1 ± 9.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Sinha 2004 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 11.43
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, halothane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 233.1
- *Use of perioperative opioids (if yes, which?)*: 319.6 µg fentanyl intraoperative, no postoperative opioids
- *Type of surgery*: breast surgery

Included criteria: female, ASA I and II, 25 to 65 years of age, scheduled for breast surgery under general anaesthesia

Excluded criteria: known to have history of gastrointestinal disease, hormonal therapy, vomiting during the 24 hours before surgery or had received antiemetics during the same period, history of drug abuse, allergic reaction to serotonin antagonist

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: normal saline • *Time point of administration*: approximately 1 hour before skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 42.9% (metoclopramide 10 mg IV) Ondansetron • *Dose*: 4 mg • *Time point of administration*: approximately 1 hour before skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8.6% (metoclopramide 10 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 48 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA

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Sinha 2004 *(Continued)*

Country: India

Setting: inpatient, single-centre

Author's name: Prabhat Kumar Sinha

Institution: Department of Anaesthesiology and Critical Care Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences

Email: NA

Address: Department of Anaesthesiology and Critical Care Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lueknow 226014

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "randomisation was done by tossing the coin"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the anaesthesiologist who administered the study drugs was kept blind about the nature of treatment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the observers as well as the nurses were aware of the nature of the study, but they were blinded to the drug administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV/motion sickness): no; (non-smoker): unclear

Sinha 2014

Study characteristics

Methods	**Study design:** randomized controlled trial

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Sinha 2014 *(Continued)*

Study grouping: 2 groups, monoprophylaxis and combination prophylaxis

Participants

Baseline Characteristics

Aprepitant + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 64
- *Received treatment (n)*: 64
- *Analysed (n)*: 64
- *Age (mean ± SD, median (IQR), median (range))*: 43.09 ± 12.45
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 50.11 ± 8.28
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 65.63
- *Non-smoker (%)*: 83.33
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (des-/sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 153.05
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative morphine
- *Type of surgery*: laparoscopic bariatric surgery

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 61
- *Received treatment (n)*: 61
- *Analysed (n)*: 60
- *Age (mean ± SD, median (IQR), median (range))*: 43.20 ± 12.70
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 48.07 ± 6.72
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 65
- *Non-smoker (%)*: 84.65
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (des-/sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 141.97
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative morphine
- *Type of surgery*: laparoscopic bariatric surgery

Included criteria: morbidly obese, ASA I to III, 18 years of age or older, considered at high risk for PONV to participate in this trial. Patients were considered if they had 2 or more of the following: (1) female gender, (2) non-smoker, (3) history of motion sickness or history of previous PONV, (4) planned use of perioperative opioids

Excluded criteria: known allergy to ondansetron or aprepitant, pregnant or breastfeeding, substance abuse or significant psychiatric disease, history of chronic nausea/vomiting, taking any medication with known antiemetic properties or known interaction with the study drugs (pimozide, terfenadine, cisapride, etc.)

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

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Sinha 2014 *(Continued)*

Interventions	**Intervention characteristics** Aprepitant + ondansetron • *Dose*: aprepitant 80 mg, ondansetron 4 mg • *Time point of administration*: aprepitant 1 hour before scheduled time of surgery, ondansetron before cessation of surgery • *Route of administration*: aprepitant PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: (42.18%) 4 mg ondansetron, 4 mg dexamethasone, 10 mg metoclopramide, 0.625 mg droperidol Ondansetron • *Dose*: 4 mg, placebo • *Time point of administration*: placebo 1 hour before scheduled time of surgery, ondansetron before cessation of surgery • *Route of administration*: placebo PO, ondansetron IV • *Rescue antiemetics (if yes, which?)*: (42.33%) 4 mg ondansetron, 4 mg dexamethasone, 10 mg metoclopramide, 0.625 mg droperidol
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** Dr Ashish Sinha received a grant from “Merck, Inc., Whitehouse Station, NJ, USA” for the conduct of this study **Country:** USA **Setting:** inpatient, single-centre **Author's name:** A.C. Sinha **Institution:** Anesthesiology and Perioperative Medicine, Drexel University College of Medicine, Philadelphia, USA **Email:** Ashish.Sinha@drexelmed.edu **Address:** Anesthesiology and Perioperative Medicine, Drexel University College of Medicine, 245 N. 15th Street, MS 310, Philadelphia, PA 19102, USA **Duration of study:** August 2009 to January 2012 **Language:** English **Study's primary outcome:** incidence of vomiting within 72 hours **Trial registry number:** NCT00956215
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "were randomized using a computer-generated table into two groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Sinha 2014 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "as the placebo and study drug were identical in appearance, both the investigators and the patients were blinded to the patient's study group, eliminating any possibility of bias" Judgement comment: no information on blinding of anaesthesiologists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "in the postoperative period, a blinded observer (unaware to patient classification into groups A or P) recorded VRS nausea score for all the patients at 30 min, 1, 2, 6, 24, 48, and 72 h after the surgery"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of 125 participating patients, 124 were able to complete the study. One case in the placebo group was cancelled due to technical surgical difficulties and was a surgical decision"
Selective reporting (reporting bias)	High risk	Judgement comment: NCT00956215 (prospective registration). The prospectively registered primary outcome was changed from "preventing post operative nausea or vomiting" to "incidence of vomiting" (significant result). Nausea was not a primary endpoint in the final published article (no significant result)
Other bias	Unclear risk	Quote: "all included patients were morbidly obese (body mass index (BMI) > 40 kg/m 2) with a mean BMI of 49.12±7.60 kg/m 2. On statistical analysis, the patients were evenly distributed for age, gender, race, BMI, smoking status, and type as well as length of surgery (Table 1)" Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Sistla 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 40 ± 13.7 • *Weight (mean ± SD, median (IQR), median (range))*: 57.9 ± 12.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 75 • *Non-smoker (%)*: 11.1 • *History of PONV/motion sickness (%)*: 13.89/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 63

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Sistla 2009 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 11.9 mg morphine intraoperative, 22.9 mg morphine post-operative
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 34
- *Received treatment (n)*: NA
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 10.9
- *Weight (mean ± SD, median (IQR), median (range))*: 57.7 ± 12.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 76.47
- *Non-smoker (%)*: 5.88
- *History of PONV/motion sickness (%)*: 17.65/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 57
- *Use of perioperative opioids (if yes, which?)*: 11.7 mg morphine intraoperative, 29.9 mg morphine post-operative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: undergoing elective laparoscopic cholecystectomy for symptomatic gallstone

Excluded criteria: acute cholecystitis, those for whom the procedure required conversion, when steroids were contraindicated, those already on steroids, patients who could not be trained to use the visual analog scale (VAS)

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 90 minutes before skin incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16.67% (ondansetron 4 mg IV) Placebo • *Dose*: saline • *Time point of administration*: 90 minutes before skin incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 29.41% (ondansetron 4 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)*

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Sistla 2009 *(Continued)*

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Sarath Sistla **Institution:** Jawaharlal Institute of Postgraduate Medical, Education and Research, Pondicherry, India **Email:** sarathsistla@hotmail.com **Address:** Jawaharlal Institute of Postgraduate Medical, Education and Research, Pondicherry 605006, India **Duration of study:** NA **Language:** English **Study's primary outcome:** morphine consumption **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized to either the dexamethasone, or the placebo group on the day of surgery by a sealed envelope method" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "by a sealed envelope method" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "dexamethasone or placebo was administered by the ward nurse, and the patient and clinician were blinded to this group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "nine patients were excluded, due to conversion to open procedure in 6, due to contraindications to morphine in 2, and due to difficulty in assessing pain scores because of paraparesis in 1 patient"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Sistla 2009 *(Continued)*

Other bias	Unclear risk	Quote: "patient characteristics, operative variables, and variables that can influence the incidence of PONV such as sex, duration of surgery, anesthesia technique, past history of PONV, smoking, motion sickness, and perioperative opioid were well matched in both the groups" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

Smith 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 71 • *Age (mean ± SD, median (IQR), median (range))*: 44.5 ± 16.2 • *Weight (mean ± SD, median (IQR), median (range))*: 78.9 ± 16.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 37/34/0/0 • *Gender (female in %)*: 32.39 • *Non-smoker (%)*: 77.46 • *History of PONV/motion sickness (%)*: 15.49/20.83 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 40.5 • *Use of perioperative opioids (if yes, which?)*: 100 µg fentanyl, alfentanil 0.25 mg, co-codamol • *Type of surgery*: breast surgery, hernia repair, open urology, circumcision, other Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 72 • *Age (mean ± SD, median (IQR), median (range))*: 42.3 ± 13.5 • *Weight (mean ± SD, median (IQR), median (range))*: 80.5 ± 16.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 41/31/0/0 • *Gender (female in %)*: 29.17 • *Non-smoker (%)*: 69.44 • *History of PONV/motion sickness (%)*: 18.06/22.22 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)

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Smith 2008 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 39.7
- *Use of perioperative opioids (if yes, which?)*: 100 µg fentanyl, alfentanil 0.25 mg, co-codamol
- *Type of surgery*: breast surgery, hernia repair, open urology, circumcision, other

Included criteria: over 16 years of age, undergoing elective non-endoscopic day-case surgery

Excluded criteria: known or suspected adverse reaction to sevoflurane or any of the other study medications, patients for whom tracheal intubation and/or controlled ventilation was required

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 23.94 (NA) Dexamethasone • *Dose*: 4 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 30.56 (NA)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (PACU)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was supported, in part, by an educational grant from Abbott Laboratories **Country:** UK **Setting:** outpatient, single-centre **Author's name:** Ian Smith **Institution:** University Hospital of North Staffordshire, Departments of Anaesthesia, Postgraduate Medicine, Stoke-on-Trent, Staffordshire, UK **Email:** damsmith@btinternet.com **Address:** University Hospital ofNorth Staffordshire, Newcastle Road, Stoke-on-Trent, Staffordshire ST4 6QG, UK **Duration of study:** NA **Language:** English

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Smith 2008 *(Continued)*

	Study's primary outcome: incidence of PONV **Trial registry number:** NA
Notes	Two out of 3 relevant groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were then randomly allocated to receive VIMA supplemented by fentanyl (Group 1), or supplemented by fentanyl and dexamethasone (Group 2) or without i.v. supplement (Group 3). To ensure the even distribution of other causes of PONV, randomization was performed in two strata according to whether patients had either zero or one risk factor or two or more risk factors" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement on allocation concealment (randomization occurred after eligibility screening and before anaesthesia)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all anaesthetics were delivered by the senior author (IS) who was unaware of the group allocation" Quote: "these study medications were prepared in two syringes by an anaesthetist not involved with the clinical care of the patient using the sealed opaque envelope technique and were identified only by study number"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "room and the day unit. Patients were assessed by a dedicated research nurse (who was unaware of intraoperative events or group allocation) at 1 and 2 h after the end of surgery and at discharge from the day unit. At each of these times"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "there were no differences in the patient characteristics and risk factors for PONV of the three treatment groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Sniadach 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics**

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Sniadach 1997 *(Continued)*

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: 80
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: 33 (18 to 49)
- *Weight (mean ± SD, median (IQR), median (range))*: 70 (43 to 128)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane or desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 52
- *Use of perioperative opioids (if yes, which?)*: 206 µg fentanyl
- *Type of surgery*: laparoscopic gynaecological surgery

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: 78
- *Analysed (n)*: 76
- *Age (mean ± SD, median (IQR), median (range))*: 32 (19 to 50)
- *Weight (mean ± SD, median (IQR), median (range))*: 68 (46 to 110)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane or desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 53
- *Use of perioperative opioids (if yes, which?)*: 178 µg fentanyl
- *Type of surgery*: laparoscopic gynaecological surgery

Included criteria: women undergoing outpatient laparoscopic gynaecological surgery under general anaesthesia, ASA I or II, 18 to 50 years of age, anaesthesia time less than 2 hours

Excluded criteria: known hypersensitivity to any antiemetic

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics**

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: during induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: "anaesthesiologists were instructed to treat nausea as needed to ensure patient comfort in the PACU"

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Sniadach 1997 *(Continued)*

	Droperidol • *Dose*: 20 µg/kg • *Time point of administration*: during induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: "anaesthesiologists were instructed to treat nausea as needed to ensure patient comfort in the PACU"
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** funded by a grant from Kaiser Permanente of Colorado **Country:** USA **Setting:** outpatient, single-centre **Author's name:** M. Steve Sniadach **Institution:** Department of Anesthesiology, Saint Joseph Hospital, Kaiser Permanente Medical Center, Denver, USA **Email:** NA **Address:** Department of Anesthesiology, Saint Joseph Hospital, Kaiser Permanente Medical Center, 2045 Franklin St., Denver, CO 80205 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "prospectively randomized to receive either droperidol..." Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...mg) during induction of anesthesia. Study medications were prepared by a single pharmacist in identical syringes, with identical volumes, to ensure blind administration by the anesthesiologist and preoperative nurses. No other antiemetics were given"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...within 3 days after surgery. The first two assessments were made by 1 of a group of 10 PACU nurses blinded to the medication each patient had received, who asked the subjects about..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the original 160 subjects, 2 were excluded from the study because of failure to receive the study medication at induction, and 2 were excluded because they had received an extra intraoperative antiemetic dose. All four ex-

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Sniadach 1997 *(Continued)*

		cluded patients had been assigned to receive droperidol. Therefore, data from 156 patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...groups. Neither were differences found between groups in variables that could have potentially influenced nausea and sedation outcomes, including average operation time, average anesthesia time, average PACU time, and average fentanyl dose. No difference in group distribution among types of surgery was noted" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

So 2002

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: 36 • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 52 (21 to 82) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 1 • *ASA I/II/III/IV (n)*: 25/11/0/0 • *Gender (female in %)*: 61 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/0 • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 67 • *Use of perioperative opioids (if yes, which?)*: intravenous morphine (0.1 mg/kg to 0.2 mg/kg), postoperative pethidine IM • *Type of surgery*: laparoscopic cholecystectomy Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 32 • *Received treatment (n)*: 32 • *Analysed (n)*: 32 • *Age (mean ± SD, median (IQR), median (range))*: 45 (27 to 78) • *Weight (mean ± SD, median (IQR), median (range))*: NA

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So 2002 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 0
- *ASA I/II/III/IV (n)*: 19/13/0/0
- *Gender (female in %)*: 44
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/1
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 82
- *Use of perioperative opioids (if yes, which?)*: intravenous morphine (0.1 mg/kg to 0.2 mg/kg), postoperative pethidine IM
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, scheduled for elective laparoscopic cholecystectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10/36 (promethazine IM.) Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: 11/32 promethazine IM
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Republic of Singapore **Setting:** outpatient, single-centre **Author's name:** J.B.Y. So **Institution:** Department of Surgery, National University Hospital, Republic of Singapore **Email:** NA **Address:** Department of Surgery, National University Hospital, Lower Kent Ridge Road, Singapore 119072, Republic of Singapore **Language:** English

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So 2002 *(Continued)*

	Duration of study: NA **Trial registry number:** NA **Study's primary outcome:** incidence of nausea and vomiting
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomized, by using sealed envelopes, to receive either intravenous ondansetron (4 mg) or nothing at the end of the surgery" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "patients were randomized, by using sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the assistant nurse prepared the drug after randomization and the drug was given by the anesthetist. Both the anesthetist and the nurse did not participate in the postoperative assessment" Judgement comment: personnel who administered the study drug were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the degree of nausea, vomiting, and pain were assessed by a research student who was unaware of the treatment arm at 2 and 24 h in the postoperative period"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 68 patients were enrolled in the study. Thirty-six patients received intravenous ondansetron, whereas 32 patients did not received any prophylaxis" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Sodhi 2007

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Granisetron

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Sodhi 2007 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: NA ("all the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA ("all the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA ("All the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: breast surgery

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: NA ("all the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA ("all the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA ("all the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: breast surgery

Granisetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: 30
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: NA ("all the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA ("all the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *ASA I/II/III/IV (n)*: NA/NA/0/0

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Sodhi 2007 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA ("all the 3 groups were statistically comparable as regards to age, BMI and duration of anaesthesia", no data provided)
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: breast surgery

Included criteria: female, ASA I and II, 40 to 60 years of age, scheduled to undergo breast surgery

Excluded criteria: history of preoperative nausea and vomiting (24 hours before surgery), history of PONV after previous anaesthesia, taking antiemetics/opioids/hormonal therapy, disease prolonging gastric emptying like diabetes mellitus, intestinal obstruction, hiatus hernia, obese (BMI > 30), pregnant, history of motion sickness, known hypersensitivity to study drug

Pretreatment: baseline characteristics (ASA): no; (age, BMI): unclear. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Granisetron • *Dose*: 3 mg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg Granisetron + dexamethasone • *Dose*: granisetron 3 mg, dexamethasone 8 mg • *Time point of administration*: 5 minutes before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)*

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Sodhi 2007 *(Continued)*

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Kanwalpreet Sodhi **Institution:** Department of Anaesthesia, MMM, Chennai, India **Email:** NA **Address:** 4-A, Dr. J. Jayalalitha Nagar, Mogappair, Chennai, Tamil Nadu 600037, India **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "further divided randomly into three groups of 30 patients each" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "all the three groups were statistically comparable as regards to age, BMI and duration of anaesthesia and also the postoperative vitals"

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Sodhi 2007 *(Continued)*

	Judgement comment: baseline characteristics (ASA): no; (age, BMI): unclear. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Soga 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Fosaprepitant (NK1 group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 24 • *Received treatment (n)*: 24 • *Analysed (n)*: 24 • *Age (mean ± SD, median (IQR), median (range))*: 52 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 11/13/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 87.5 • *History of PONV/motion sickness (%)*: 45.83 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 246 • *Use of perioperative opioids (if yes, which?)*: 2.5 mg remifentanil intraoperative, 100 µg fentanyl, 10 patients received fentanyl via PCA • *Type of surgery*: major gynaecological surgery Ondansetron (ONS group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 52 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 55 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 9/11/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 90 • *History of PONV/motion sickness (%)*: 25 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 239 • *Use of perioperative opioids (if yes, which?)*: 2.4 mg remifentanil intraoperative, 100 µg fentanyl, 9 patients received fentanyl via PCA • *Type of surgery*: major gynaecological surgery

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Soga 2015 *(Continued)*

Included criteria: 20 to 80 years of age, ASA I or II, undergoing major gynaecological surgery under combined epidural/general anaesthesia

Excluded criteria: ASA III or IV, neuronal disease, abnormal liver and/or renal function, receiving other antiemetic drugs

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): yes

Interventions	**Intervention characteristics** Fosaprepitant (NK1 group) • *Dose*: 150 mg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Ondansetron (ONS group) • *Dose*: 4 mg • *Time point of administration*: 30 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** supported by JSPS KAKENHI Number 25861378 from Japan Society for the Promotion of Science, Tokyo **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Yasuo M. Tsutsumi **Institution:** Department of Anesthesiology, Tokushima University Graduate School, Japan **Email:** tsutsumi@tokushima-u.ac.jp **Address:** Department of Anesthesiology, Tokushima University Graduate School, 3-18-15 Kuramoto, Tokushima 770-8503, Japan **Duration of study:** 1 June 2012 to 28 April 2014 **Language:** English **Study's primary outcome:** incidence of vomiting

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Soga 2015 *(Continued)*

	Trial registry number: JPRN-UMIN000007613
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the patients were randomly allocated in a double-blind manner using computer software (Quickcalcs; Graph-Pad Inc., La Jolla, CA, USA)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: insufficient information on allocation concealment (how was the allocated group concealed for that person who enrolled participants? SNOSE?)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind") with no statement identity of syringes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of 63 randomized patients, 19 patients refused and 44 patients agreed to participate in this study. All 44 patients received the study medications and completed the trial after being randomized to the NK1 group"
Selective reporting (reporting bias)	High risk	Judgement comment: JPRN-UMIN000007613 (prospective registration). The prospectively registered primary outcome was changed from "frequency of PONV" to "incidence of vomiting" (significant result). Nausea was not a primary endpoint in the final published article (no significant result)
Other bias	High risk	Quote: "there were no significant differences in patient demographics or risk factors for PONV (Table 1). The duration of surgery, duration of anaesthesia, and intraoperative remifentanil use were not significantly different between the two groups (Table 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, perioperative opioids): no; (history of PONV/motion sickness): yes

Sohi 1994

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Scopolamine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Sohi 1994 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 40.8
- *Weight (mean ± SD, median (IQR), median (range))*: 78.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 84
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 16/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 86
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, 56% required meperidine postoperative
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 47
- *Age (mean ± SD, median (IQR), median (range))*: 41.5
- *Weight (mean ± SD, median (IQR), median (range))*: 79.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 77
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 23/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 94
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, 64% required meperidine postoperative
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: 20 to 60 years of age, scheduled to undergo elective laparoscopic cholecystectomy

Excluded criteria: pregnancy; actively nursing; narrow-angle glaucoma; gastrointestinal or urinary tract obstruction; currently taking antiemetic, anticholinergic, or antihistamine medications; patient whose laparoscopic procedure was converted to open cholecystectomy; any breach of anaesthesia protocol; any potentially antiemetic drugs given intraoperatively; any illness predisposing to nausea and vomiting (e.g. acute cholecystitis)

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Scopolamine • *Dose*: 1.5 mg • *Time point of administration*: night before surgery • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: 67% (dimenhydrinate 50 mg IM, prochlorperazine 10 mg IM) Placebo

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Sohi 1994 *(Continued)*

- *Dose*: placebo patch without medication
- *Time point of administration*: night before surgery
- *Route of administration*: transdermal
- *Rescue antiemetics (if yes, which?)*: 68% (dimenhydrinate 50 mg IM, prochlorperazine 10 mg IM)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Canada **Setting:** inpatient, single-centre **Author's name:** Murray J. Girotti **Institution:** Department of Surgery, University of Western Ontario, Victoria Hospital, London, Canada **Email:** NA **Address:** Department of Surgery, University of Western Ontario, Victoria Hospital, 375 South St., London, ON N6A4G5, Canada **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** nausea
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "[..] in a randomized, double-blind fashion." No further information on sequence generation provided
Allocation concealment (selection bias)	Low risk	Judgement comment: quote: "once enrolled, patients were assigned a study package through the pharmacy department in a randomized, double-blinded fashion. Active packages contained the Transderm V patch ...Inactive packages contained a similar patch without medication...'.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: the "similar" patches (intervention and placebo) were allocated by the pharmacy. Participants and personnel (anaesthetists) were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: the "similar" patches (intervention and placebo) were allocated by the pharmacy. Outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: quote: "over a 14-month period 125 patients were enrolled in the study. Of these, 90 patients (43 treatment versus 47 control) were included in the final analysis.Thirty-five patients were excluded because of

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Sohi 1994 *(Continued)*

		protocol violations. The most common cause was failure of proper data collection and recording (23 patients), followed by breaches of the anesthesia protocol, such as antiemetic drugs being given intraoperatively (5 patients). The other reasons for exclusion were: laparoscopic procedure converted to open cholecystectomy (five patients) and miscellaneous reasons (two patients)" High rate of missing outcome data (> 15%). Reasons explained and probably not related to the outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: quote: "there was significant difference between the patient populations in terms of sex distribution, age, weight, history of travel sickness or postoperative nausea and vomiting'' Baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker, perioperative opioids): unclear

Song 2013

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Control (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: NA • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 52.3 ± 7.5 • *Weight (mean ± SD, median (IQR), median (range))*: 60.3 ± 6.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 90.24 • *History of PONV/motion sickness (%)*: 4.9/0 • *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 139.8 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, no postoperative opioids • *Type of surgery*: thyroid surgery Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: NA • *Analysed (n)*: 41

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Song 2013 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 54.2 ± 7.7
- *Weight (mean ± SD, median (IQR), median (range))*: 58.44 ± 6.7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 92.68
- *History of PONV/motion sickness (%)*: 4.9/0
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 144.0
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, no postoperative opioids
- *Type of surgery*: thyroid surgery

Ramosetron (group R)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 41
- *Received treatment (n)*: NA
- *Analysed (n)*: 41
- *Age (mean ± SD, median (IQR), median (range))*: 55.1 ± 7.5
- *Weight (mean ± SD, median (IQR), median (range))*: 60.6 ± 5.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 92.68
- *History of PONV/motion sickness (%)*: 7.3/0
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142.2
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, no postoperative opioids
- *Type of surgery*: thyroid surgery

Included criteria: 20 to 65 years of age, ASA I or II, undergoing thyroid surgery

Excluded criteria: history of intolerance or allergy to any drugs used in the study, gastrointestinal disease, motion sickness, postoperative emesis, obesity (body mass index > 35 kg/m^2), cardiovascular or respiratory disease, alcohol or opioid dependence, renal or hepatic functional impairment, pregnant, menstruating, had taken another antiemetic drug or a systemic steroid 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions

Intervention characteristics

Control (group C)

- *Dose*: 0.9% NaCl
- *Time point of administration*: immediately after anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Dexamethasone (group D)

- *Dose*: 10 mg
- *Time point of administration*: immediately after anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

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Song 2013 *(Continued)*

	Ramosetron (group R) • *Dose*: 0.3 mg • *Time point of administration*: immediately after anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was supported by Wonkwang University 2012 **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Cheol Lee **Institution:** Department of Anesthesiology and Pain Medicine, Wonkwang University School of Medicine **Email:** ironyii@wonkwang.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Wonkwang University School of Medicine, 344-2 Sinyong-dong, Iksan 570-711, Korea **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence and severity of nausea, incidence of vomiting, and amount of rescue antiemetic administered at 5 postoperative time intervals (T1: 0–1 hour, T6: 1–6 hours, T12: 6–12 hours, T24: 12–24 hours, and T48: 24–48 hours) **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "a total of 123 patients scheduled for thyroid surgery were randomly (envelope randomization) allocated to one of three groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "(envelope randomization)" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement

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Song 2013 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the 3 groups did not differ in terms of distribution of age, weight, height, smoking status, history of PONV, duration of surgery, the amount of intravenous fluid administered, type of surgery, or tympanic temperature immediately before induction or just before extubation" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Song 2017

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 150 • *Received treatment (n)*: 150 • *Analysed (n)*: 150 • *Age (mean ± SD, median (IQR), median (range))*: NA (reported for different genotypes, no difference between groups) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA (reported for different genotypes, no difference between groups) • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA (reported for different genotypes, no difference between groups) • *Non-smoker (%)*: NA (reported for different genotypes, no difference between groups) • *History of PONV/motion sickness (%)*: NA (reported for different genotypes, no difference between groups) • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (reported for different genotypes, no difference between groups) • *Use of perioperative opioids (if yes, which?)*: remifentanil, fentanyl via PCA (reported for different genotypes, no difference between groups) • *Type of surgery*: spinal surgery Palonosetron

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Song 2017 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 150
- *Received treatment (n)*: 150
- *Analysed (n)*: 146
- *Age (mean ± SD, median (IQR), median (range))*: NA (reported for different genotypes, no difference between groups)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA (reported for different genotypes, no difference between groups)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA (reported for different genotypes, no difference between groups)
- *Non-smoker (%)*: NA (reported for different genotypes, no difference between groups)
- *History of PONV/motion sickness (%)*: NA (reported for different genotypes, no difference between groups)
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA (reported for different genotypes, no difference between groups)
- *Use of perioperative opioids (if yes, which?)*: remifentanil, fentanyl via PCA, (reported for different genotypes, no difference between groups)
- *Type of surgery*: spinal surgery

Included criteria: 20 to 85 years of age, ASA I or II, undergoing spinal surgery (type of surgery included cervical laminoplasty, cervical anterior interbody fusion, lumbar laminectomy, posterior lumbar interbody fusion, and benign spinal cord tumour removal)

Excluded criteria: administration of an antiemetic within 24 hours before surgery, regular administration of opioids or corticosteroids, history of psychiatric disorder, active drug or alcohol abuse, gastrointestinal motility disorder, severe hepatic or renal disease, uncontrolled diabetes, pregnancy, malignancy, body mass index > 35 kg/m^2, postoperative admission to an intensive care unit

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: 20 minutes before end of surgery and 24 hours after surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (19%) metoclopramide 10 mg Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: 20 minutes before end of surgery and 24 hours after surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (26%) metoclopramide 10 mg
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported solely by departmental sources

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Song 2017 *(Continued)*

Country: Korea

Setting: inpatient, single-centre

Author's name: Young Lan Kwak

Institution: Department of Anesthesiology and Pain Medicine; and Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea

Email: ylkwak@yuhs.ac

Address: Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research, Institute Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV during postoperative 48 hours for patients with ABCB1 TT and non-TT genotype who received prophylactic ramosetron or palonosetron

Trial registry number: NCT02480088

Notes	Repetitive dose of study drug after 24 hours

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were assigned to either the ramosetron or the palonosetron group according to a computer-generated randomization list"
Allocation concealment (selection bias)	Low risk	Quote: "sequentially numbered opaque envelopes containing the group assignment were opened on the day of operation by a nurse who was not involved in patients' management, and the nurse prepared the study drugs as assigned" Judgement comment: SNOSE
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...by a nurse who was not involved in patients' management, and the nurse prepared the study drugs as assigned. The group assignment was blinded to both patients and investigators until the end of the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the group assignment was blinded to both patients and investigators until the end of the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "four patients in the palonosetron group were excluded because they were transferred to the intensive care unit after surgery (Fig. 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT02480088 (retrospective registration)
Other bias	Low risk	Quote: "patient characteristics and operative data were comparable between the ramosetron and palonosetron groups, as well as between the non-TT and TT for each group (Table 1)"

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Song 2017 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Sriraman 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 30.4 ± 4.7 • *Weight (mean ± SD, median (IQR), median (range))*: 53.7 ± 9.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 10/46 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 54.8 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction, no postoperative opioids • *Type of surgery*: gynaecological laparoscopic surgery Granisetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: 50 • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 29.1 ± 4.7 • *Weight (mean ± SD, median (IQR), median (range))*: 52.2 ± 8.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 8/28 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 53.4 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction, no postoperative opioids • *Type of surgery*: gynaecological laparoscopic surgery

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Sriraman 2007 *(Continued)*

	Included criteria: female, 18 to 40 years of age, ASA I or II, undergoing gynaecological laparoscopic surgery for diagnostic or sterilization purposes, medical termination of pregnancy along with laparoscopic sterilization **Excluded criteria:** acid peptic disease, known hypersensitivity to serotonin antagonists, history of drug abuse and use of antiemetics, steroids or NSAIDs within 24 hours of onset of surgery; uneducated patients who were unable to comprehend the nature of the study and cooperate with the investigator were not evaluated **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Ondansetron + dexamethasone • *Dose*: ondansetron 100 µg/kg, dexamethasone 8 mg • *Time point of administration*: after endotracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 14% (metoclopramide 10 mg) Granisetron + dexamethasone • *Dose*: granisetron 40 µg/kg, dexamethasone 8 mg • *Time point of administration*: after endotracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours, PACU)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Headache (discharge (4h) to 24 hours)* • Outcome type: dichotomous outcome *Constipation (discharge (4h) to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (discharge (4h) to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** outpatient, single-centre **Author's name:** R. Sriraman **Institution:** Department of Anaesthesia Intensive Care, PGIMER, Chandigarh, India **Email:** NA

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Sriraman 2007 *(Continued)*

	Address: NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of postoperative emesis
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer generated randomization list"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "an anaesthesiologist not involved in the study administered the antiemetics diluted in 5ml normal saline, soon after endotracheal intubation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all observations were made by an anaesthesiologist who was not aware of the patients' group assignments"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the patients' profile and demographic data (Table 1) were comparable in both the treatment groups. Other variables like history of motion sickness, previous PONV or migraine were also similar" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Stefani 1995

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo

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Stefani 1995 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 56.3 ± 12.03
- *Weight (mean ± SD, median (IQR), median (range))*: 72.8 ± 14.66
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, Isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 68.5
- *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl at induction, ketorolac for postoperative analgesia
- *Type of surgery*: laparoscopic cholecystectomy

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 50.55 ± 10.31
- *Weight (mean ± SD, median (IQR), median (range))*: 68.95 ± 10.09
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, Isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 67.55
- *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl at induction, ketorolac for postoperative analgesia
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: female, ASA I or II

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: 15 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Tropisetron

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Stefani 1995 *(Continued)*

- *Dose*: 5 mg
- *Time point of administration*: 15 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** M. Stefani **Institution:** Servizi di Anestesia e Terapia del Dolore, Ospedale Regina Apostolorum Alabano Laziale, Roma **Email:** NA **Address:** NA **Duration of study:** NA **Language:** Italian (translated by Insa Backhaus) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "with a randomized double-blind system, the patients were randomly assigned to two groups of 20 people" (translated). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Stefani 1995 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Steinbrook 1998

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 66 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 17 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 81.8 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (desflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 67 • *Use of perioperative opioids (if yes, which?)*: 225 µg fentanyl intraoperative, 55 patients received opioids in PACU • *Type of surgery*: laparoscopic cholecystectomy Droperidol + metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 66 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 81.8 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (desflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 68

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Steinbrook 1998 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 244 µg fentanyl intraoperative, 54 patients received opioids in PACU
- *Type of surgery*: laparoscopic cholecystectomy

Perphenazine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 68
- *Age (mean +/- SD, median (IQR), median [range])*: 46 +/- 13
- *Weight (mean +/- SD, median (IQR), median [range])*: 74 +/- 16
- *BMI (mean +/- SD, median (IQR), median [range])*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 77.9
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (desflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 68
- *Use of perioperative opioids (if yes, which?)*: 230 µg fentanyl intraoperative, 51 patients received opioids in PACU
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: scheduled for laparoscopic cholecystectomy

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron + droperidol • *Dose*: ondansetron 4 mg, droperidol 0.625 mg • *Time point of administration*: immediately after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol + metoclopramide • *Dose*: droperidol 0.625 mg, metoclopramide 10 mg • *Time point of administration*: immediately after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Perphenazine • *Dose*: perphenazine 5 mg, placebo 50 ml saline • *Time point of administration*: immediately after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome

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Steinbrook 1998 *(Continued)*

	Vomiting (2 to 24 hours) • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, single-centre **Author's name:** Richard A. Steinbrook **Institution:** Brigham and Women's Hospital, Harvard Medical School, USA **Email:** NA **Address:** Department of Anesthesia, Brigham andWomen's Hospital, 75 Francis St., Boston, MA 02115, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "assign patient treatment blocks of six from a published table of random numbers; 6 patients were stratified by gender-adjusted percent ideal body weight"
Allocation concealment (selection bias)	Unclear risk	Quote: "antiemetic drug preparation and randomization were performed by an unblinded research pharmacist, using a computer program to assign patient treatment blocks of six..." Judgement comment: insufficient information on allocation concealment (unclear whether pharmacist could foresee allocation of the next patient)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "physicians, nurses, and patients were blinded to the identity of the antiemetics"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "twelve patients required conversion to open cholecystectomy and therefore were eliminated from the study; thus, 200 patients completed the protocol and are included in the analysis"

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Steinbrook 1998 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the groups were similar with respect to gender, age, weight, duration of surgery, intraoperative fentanyl dose, and numbers receiving intraoperative atropine or ephedrine (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Stromberg 1991

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Scopolamine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 101 • *Received treatment (n)*: 101 • *Analysed (n)*: NA (59 efficacy) • *Age (mean ± SD, median (IQR), median (range))*: 39.9 ± 15.5 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 31%/NA/NA/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: meperidine, codeine, oxycodone postoperative • *Type of surgery*: general, plastic, or orthopaedic surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 100 • *Received treatment (n)*: 100 • *Analysed (n)*: NA (58 efficacy) • *Age (mean ± SD, median (IQR), median (range))*: 39.4 ± 16.0 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 45%/NA/NA/0 • *Gender (female in %)*: 55 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Stromberg 1991 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: meperidine, codeine, oxycodone postoperative
- *Type of surgery*: general, plastic, or orthopaedic surgery

Included criteria: general anaesthesia; over 18 years of age; both sexes; ASA I to III; general, plastic, or orthopaedic surgery (1 to 5 hours); patch had to be applied at least 6 hours before onset of anaesthesia

Excluded criteria: procedures of the inner or middle ear; intra-abdominal procedures that would require use of a nasogastric tube or ophthalmic procedures; specific contraindication to the use of scopolamine, including a history of allergy to the drug, neurological problems, pyloric obstruction, urinary bladder neck obstruction, or narrow angle glaucoma; preoperative use of any drug with antiemetic properties or any anticholinergic drug; history of alcohol or drug abuse; psychiatric disorder

Pretreatment: baseline characteristics (age): no; (weight): unclear; (ASA): yes. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Scopolamine • *Dose*: NA • *Time point of administration*: 8 hours preoperatively until 24 hours postoperatively • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: 26% (not specified) Placebo • *Dose*: placebo • *Time point of administration*: 8 hours preoperatively until 24 hours postoperatively • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: 12% (not specified)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (overall, no time point)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** inpatient, multi-centre (2) **Author's name:** Brent V. Stromberg

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Stromberg 1991 *(Continued)*

Institution: Creighion University, Omaha, Nebraska, and the Medical University of South Carolina, Charleston, South Carolina, USA

Email: NA

Address: Division of Plastic Reconstructive Surgery, Department of Surgery, 601 N. 30th Street, Omaha, NE 68131, USA

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: quote: "two hundred and one patients were enrolled in the study and 180 successfully completed the protocol. Eighty-two of the 201 patients entered into the study were not evaluated for efficacy (42 placebo, 42 TS scopolamine). The majority of the patients removed from the study were excluded because of inadvertent use of medications, especially antihistamines" Reasons for missing data have been described in part. Nonetheless, 42% of all data for efficacy is missing
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: quote: "there was a significant difference between the two groups concerning ASA classification" Baseline characteristics (age): no; (weight): unclear; (ASA): yes. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Suen 1994

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 102 • *Age (mean ± SD, median (IQR), median (range))*: 34.4 ± 3.6 • *Weight (mean ± SD, median (IQR), median (range))*: 54.9 ± 9.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 25.1 • *Use of perioperative opioids (if yes, which?)*: 23 patients received postoperative pethidine • *Type of surgery*: laparoscopic sterilization, diagnostic laparoscopy Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 102 • *Age (mean ± SD, median (IQR), median (range))*: 34.9 ± 4.7 • *Weight (mean ± SD, median (IQR), median (range))*: 56.6 ± 9.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 23.3 • *Use of perioperative opioids (if yes, which?)*: 23 patients received postoperative pethidine • *Type of surgery*: laparoscopic sterilization, diagnostic laparoscopy **Included criteria:** ASA I or II, oriental female patients undergoing laparoscopic sterilization or diagnostic laparoscopy **Excluded criteria:** pre-existing nausea or vomiting, had received antiemetic or opioid drugs in the 24 hours before surgery; pregnant; history of gastro-oesophageal reflux **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics**

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Suen 1994 *(Continued)*

	Placebo • *Dose*: normal saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 9.80% (ondansetron 4 mg IV, prochlorperazine 12.5 mg IM) Ondansetron • *Dose*: 4 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 7.84% (ondansetron 4 mg IV, prochlorperazine 12.5 mg IM)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (5 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Glaxo Laboratories (kind of support unclear) **Country:** China **Setting:** inpatient and outpatient, single-centre **Authors name:** Tony Gin **Institution:** Department of Anaesthesia and Intensive Care, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, N.T. Hong Kong **Email:** NA **Address:** NA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None
Risk of bias	
Bias	**Authors' judgement** **Support for judgement**

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Suen 1994 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomised". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "study drugs were prepared by an investigator who was not administering the anaesthetics or making the postoperative assessment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "study drugs were prepared by an investigator who was not administering the anaesthetics or making the postoperative assessment"; "double-blind"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "six patients were excluded because laparotomy was performed and 102 patients remained in each group"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Suh 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 38.5 ± 7.8 • *Weight (mean ± SD, median (IQR), median (range))*: 59.2 ± 10.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 154 • *Use of perioperative opioids (if yes, which?)*: 5.3, 17.4, 16.2 (PCA volume used in mL at 3 hours, 24 hours, and 48 hours)

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Suh 2007 *(Continued)*

- *Type of surgery*: hysterectomy, uterine myomectomy

Ramosetron (group R)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 29
- *Age (mean ± SD, median (IQR), median (range))*: 40.8 ± 11.1
- *Weight (mean ± SD, median (IQR), median (range))*: 59.5 ± 8.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 150
- *Use of perioperative opioids (if yes, which?)*: 5.7, 20.9, 16.3 (PCA volume used in mL at 3 hours, 24 hours, and 48 hours)
- *Type of surgery*: hysterectomy, uterine myomectomy

Included criteria: underwent hysterectomy or uterine myomectomy, 30 years old and 65 years old or younger, ASA I and II

Excluded criteria: gastrointestinal symptoms such as gastritis, gastric ulcer, and cardiovascular disease; respiratory system or brain disease; kidney or liver disease; pregnant; receiving anticancer chemotherapy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 8 mg • *Time point of administration*: immediately before the end of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (14%) 10 mg metoclopramide Ramosetron (group R) • *Dose*: 0.3 mg • *Time point of administration*: immediately before the end of the operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (14%) 10 mg metoclopramide
Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 3 hours, 3 to 24 hours, 24 to 48 hours)* • Outcome type: dichotomous outcome

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Suh 2007 *(Continued)*

Constipation (0 to 3 hours, 3 to 24 hours, 24 to 48 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 3 hours, 3 to 24 hours, 24 to 48 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 48 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Sang-Hwan Do **Institution:** Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul **Email:** shdo@snu.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Postal Code: 110-744 **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly assigned" (translated). No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the preparation of the antiemetics is made by the recovery room nurse and is marked on the surface of the syringe as A or B so that the anesthesiologist can not know what kind of medicine it is" (translated)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "...an anesthesiologist who did not know the patient's group visited the patient and examined the degree of pain (visual analog scale, VAS, 0-10), nausea, area, vomiting ..." (translated)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: 60 participants were enrolled. Data for 58 participants were reported. Observations were missed by 1 person in each group

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Suh 2007 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Sun 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different time points of administration
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 76 ± 18 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 48 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 28/24 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 94 • *Use of perioperative opioids (if yes, which?)*: 1.2 µg fentanyl, 0.5 µg/kg sufentanil for induction • *Type of surgery*: ambulatory otolaryngologic surgery Ondansetron (before surgery) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 44 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 80 ± 18 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 44 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 8/36 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 93 • *Use of perioperative opioids (if yes, which?)*: 1.3 µg fentanyl, 0.5 µg/kg sufentanil for induction

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Sun 1997 *(Continued)*

- *Type of surgery*: ambulatory otolaryngologic surgery

Ondansetron (end of surgery)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 43 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 78 ± 19
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 48
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 32/20
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93
- *Use of perioperative opioids (if yes, which?)*: 0.8 µg fentanyl, 0.5 µg/kg sufentanil for induction
- *Type of surgery*: ambulatory otolaryngologic surgery

Included criteria: healthy consenting adult, ASA I and II, 20 to 70 years of age, undergoing ambulatory otolaryngologic procedures consisting of endoscopic sinus, middle ear, or mastoid surgery

Excluded criteria: received any prophylactic antiemetics within 24 hours before surgery, any pre-existing abnormalities involving major organ systems, history of drug abuse, pregnant, > 100% above ideal body weight

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (non-smoker): unclear; (history of PONV): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: first saline, second saline • *Time point of administration*: first before anaesthesia induction, second end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 64% (ondansetron 4 mg, droperidol 1.25 mg, promethazine 12.5 mg) Ondansetron (before surgery) • *Dose*: first ondansetron 4 mg, second saline • *Time point of administration*: first before anaesthesia induction, second end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 56% (ondansetron 4 mg, droperidol 1.25 mg, promethazine 12.5 mg) Ondansetron (end of surgery) • *Dose*: first saline, second ondansetron 4 mg • *Time point of administration*: first before anaesthesia induction, second end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 36% (ondansetron 4 mg, droperidol 1.25 mg, promethazine 12.5 mg)

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Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (PACU)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Paul F. White **Institution:** The Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, Dallas, Texas, USA **Email:** rsanch@mednet.swmed.edu **Address:** The Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75235-9068, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "the study medications were prepared by the pharmacy in two numbered syringes (containing 5 mL of either saline or ondansetron 4 mg) and were administered IV just before induction of anesthesia (Syringe 1) and at the end of the operation (Syringe 2). Group I received saline (Syringe 1) and saline (Syringe 2), Group II received ondansetron 4 mg (Syringe 1) and saline (Syringe 2), and Group III received saline (Syringe 1) and ondansetron 4 mg (Syringe 2). All patients received a standardized" Judgement comment: it is not stated that syringes were sequentially numbered and of identical appearance
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...treatment of their emetic symptoms. The administration of rescue antiemetic drugs was determined by the PACU nurse who was blinded to the prophylactic antiemetic treatment. A second rescue antiemetic..."

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Sun 1997 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...ambulatory surgery unit) were recorded. The incidence of PONV was assessed at 30-min intervals in the postanesthesia care unit (PACU) by an investigator who was blinded to the prophylactic antiemetic treatment. An emetic episode was defined..."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "complete 24-h follow-up data were available for 63 patients" Judgement comment: no missing outcome data for early outcomes (PACU). Overall, 16% of all patients are missing at 24 hours. Reasons for missing data at 24 hours are not described. It can be assumed that data are missing due to the ambulatory setting and because patients were lost to follow-up. All other data are reported
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (non-smoker): unclear; (history of PONV): yes

Sung 1993

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 89 • *Received treatment (n)*: 89 • *Analysed (n)*: 89 • *Age (mean ± SD, median (IQR), median (range))*: 32 ± 0.7 • *Weight (mean ± SD, median (IQR), median (range))*: 69 ± 1.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 27/0 • *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 41.8 • *Use of perioperative opioids (if yes, which?)*: fentanyl, codeine, oxycodone • *Type of surgery*: gynaecological laparoscopy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 91 • *Received treatment (n)*: 91

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Sung 1993 *(Continued)*

- *Analysed (n)*: 91
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 0.6
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 1.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 16/NA
- *Type of general anaesthesia*: balanced anaesthesia (isoflurane, N_2O, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 42.9
- *Use of perioperative opioids (if yes, which?)*: fentanyl, codeine, oxycodone
- *Type of surgery*: gynaecological laparoscopy

Included criteria: non-pregnant, ASA I and II, 18 to 65 years of age

Excluded criteria: had received any prophylactic antiemetics preceding surgery, pregnant, > 75% over ideal body weight (according to the Metropolitan Life Height and Weight Body Chart), scheduled to have gastric suction during surgery, abnormalities in clinical laboratory tests of liver function, scheduled to undergo a liver biopsy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 8 mg
- *Time point of administration*: immediately before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol 10 µg/kg IV, metoclopramide 0.15 mg/kg IV up to 10 mg

Placebo

- *Dose*: saline
- *Time point of administration*: immediately before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol 10 µg/kg IV, metoclopramide 0.15 mg/kg IV up to 10 mg

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (0 to 2 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

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Sung 1993 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** in part by Glaxo, Inc., Research Triangle Park, NC. **Country:** USA **Setting:** outpatient, multi-centre (3) **Author's name:** Yung-Fong Sung **Institution:** Emory University School of Medicine; Chief, Divison of Anaesthesiology, Ambulatory Surgical Center, The Emory Clinic, Atlanta, GA, USA **Email:** NA **Address:** Anesthesiology Division/AX, The Emory Clinic, 1327 Clifton Road, NE, Atlanta, GA 30322, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomized to" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "in a double-blind fashion" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...following previous general anesthesia. Of the 180 patients enrolled, 3 in the ondansetron group and 2 in the placebo group did not provide outpatient (diary or telephone contact) data and thus could not be included in O-24-hour data analyses. The duration of anesthesia, measured..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "as shown in Table 2, the background characteristics (race, age, weight, and height) of the 180 women enrolled were generally similar for the two study groups..."

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Sung 1993 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV): no; (history of motion sickness, non-smoker): unclear

Swaika 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 29 • *Received treatment (n)*: 29 • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 41.5 ± 14.52 • *Weight (mean ± SD, median (IQR), median (range))*: 51.93 ± 7.31 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 56.04 • *Use of perioperative opioids (if yes, which?)*: 1 mg butorphanol as premedication, no participants required opioid rescue analgesia • *Type of surgery*: laparoscopic cholecystectomy Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 29 • *Received treatment (n)*: 29 • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 38.9 ± 13.09 • *Weight (mean ± SD, median (IQR), median (range))*: 52.8 ± 6.92 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 56.08 • *Use of perioperative opioids (if yes, which?)*: 1 mg butorphanol as premedication, no participants required opioid rescue analgesia • *Type of surgery*: laparoscopic cholecystectomy

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Swaika 2011 *(Continued)*

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 29
- *Received treatment (n)*: 29
- *Analysed (n)*: 29
- *Age (mean ± SD, median (IQR), median (range))*: 45.9 ± 16.07
- *Weight (mean ± SD, median (IQR), median (range))*: 53.45 ± 9.18
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 57.08
- *Use of perioperative opioids (if yes, which?)*: 1 mg butorphanol as premedication, no participants required opioid rescue analgesia
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: female patients scheduled to undergo LC, ASA I and II

Excluded criteria: ASA III and IV; uremic; cardiovascular disease with hypotension; neurological disease; advanced liver disease and gastrointestinal disease; received antiemetic drug within the preceding 24 hours; history of alcohol or drug abuse within last 3 months; allergic to any of the study medications; body weight > 30% of ideal body weight

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: after completion of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: after completion of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV Ondansetron • *Dose*: 8 mg • *Time point of administration*: after completion of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)*

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Swaika 2011 *(Continued)*

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** departmental funding only **Country:** India **Setting:** inpatient, single-centre **Author's name:** Dr. Anirban Pal **Institution:** Department of Anesthesiology, Calcutta National Medical College (CNMC), Kolkata, West Bengal, India **Email:** pal.anirban1@gmail.com **Address:** 43/6/5 Jheel Road, Kolkata - 700 031, India **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** number of complete responders (no PONV, no rescue medication)
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized in a double-blind manner" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Swaika 2011 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Swiatkowski 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 67 • *Received treatment (n)*: NA • *Analysed (n)*: 67 • *Age (mean ± SD, median (IQR), median (range))*: 42.9 ± 14.2 • *Weight (mean ± SD, median (IQR), median (range))*: 65.2 ± 9.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 81.4 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative pethidine • *Type of surgery*: laparoscopic surgery Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 67 • *Received treatment (n)*: NA • *Analysed (n)*: 67 • *Age (mean ± SD, median (IQR), median (range))*: 46.5 ± 15.1 • *Weight (mean ± SD, median (IQR), median (range))*: 65.6 ± 10.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 75.8 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative pethidine • *Type of surgery*: laparoscopic surgery

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Swiatkowski 1999 *(Continued)*

Included criteria: ASA I and II, scheduled for laparoscopic surgery (laparoscopic cholecystectomy or minor gynaecological laparoscopic surgery)

Excluded criteria: preoperative nausea or vomiting requiring therapy; current use of antiemetics, benzodiazepines, or phenothiazine derivatives; previous dyskinetic reactions to droperidol; previous allergy to any of the drugs involved in the study; history of epilepsy; gastrointestinal reflux; liver or renal impairment; use of prostaglandins or ergometrine before or during the procedure

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions

Intervention characteristics

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: immediately after induction of anaesthesia and before surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 4.48% (droperidol 1.25 mg IV)

Droperidol

- *Dose*: 75 µg/kg
- *Time point of administration*: immediately after induction of anaesthesia and before surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 2.99% (droperidol 1.25 mg IV)

Outcomes

Vomiting (6 to 12 hours)

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (acute dyskinesia, 0 to 24 hours)

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: Glaxo Wellcome Polska supplied ondansetron

Country: Poland

Setting: inpatient, single-centre

Author's name: J. Świątkowski

Institution: University Department of Anaesthesiology and Intensive Therapy, Medical University School, Lublin, Poland

Email: NA

Address: University Department of Anaesthesiology and Intensive Therapy, Medical University School, Jaczewskiego 8, 20-090 Lublin, Poland

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

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Swiatkowski 1999 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "they were randomized to receive either ondansetron (Glaxo Wellcome Polska..." Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "neither the patient nor the observer during the post-operative period knew which drug had been administered" Quote: "...both given intravenously (i.v.) by the attending anaesthetist immediately after induction of anaesthesia and before the surgery" Judgement comment: insufficient information on blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "neither the patient nor the observer during the post-operative period knew which drug had been administered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the patients in the two groups treated with droperidol or ondansetron were comparable with regard to the demographic data shown in Table 1. There was no significant difference between two groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Talesh 2011

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Talesh 2011 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 150 to 180
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: mandibular osteotomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: NA
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 150 to 180
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: mandibular osteotomy

Included criteria: adult patients undergoing mandibular osteotomy surgery

Excluded criteria: postoperative oral or nasal bleeding, those who vomited blood

Pretreatment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, (perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 0.15 mg/kg • *Time point of administration*: 30 minutes before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: second injection of medication Metoclopramide • *Dose*: 0.5 mg/kg • *Time point of administration*: 30 minutes before extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: second injection of medication

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Talesh 2011 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Iran **Setting:** inpatient, single-centre **Author's name:** Mohammed Motamedi **Institution:** Tabriz Medical Sciences University **Email:** motamedical@lycos.com **Address:** Azad University, Giti 16, Tehran, 19667 Iran **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	Numbers of participants per group not reported (author request sent, mail not deliverable)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were allocated randomly". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "personnel not involved in the study prepared identical syringes containing the drugs"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: insufficient information on numbers of participants per group. No information on complete outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, (perioperative opioids): unclear

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Tang 1998a

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 6 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 36 • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 38.89/13.89 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 132 • *Use of perioperative opioids (if yes, which?)*: 271 µg fentanyl and 89 µg sufentanil at induction, 47 mg morphine postoperative, 283 mg meperidine • *Type of surgery*: abdominal or vaginal hysterectomy RS-25259 (0.1 µg/kg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 27 • *Received treatment (n)*: NA • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 76 ± 18 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 44.44/14.81 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 147 • *Use of perioperative opioids (if yes, which?)*: 304 µg fentanyl and 88 µg sufentanil at induction, 56 mg morphine postoperative, 273 mg meperidine • *Type of surgery*: abdominal or vaginal hysterectomy RS-25259 (0.3 µg/kg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 41 • *Received treatment (n)*: NA • *Analysed (n)*: 41

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Tang 1998a *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 16
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 34.15/7.32
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 148
- *Use of perioperative opioids (if yes, which?)*: 305 µg fentanyl and 86 µg sufentanil at induction, 46 mg morphine postoperative, 243 mg meperidine
- *Type of surgery*: abdominal or vaginal hysterectomy

RS-25259 (1.0 µg/kg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 74 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 37.14/17.14
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 146
- *Use of perioperative opioids (if yes, which?)*: 262 µg fentanyl and 78 µg sufentanil at induction, 59 mg morphine postoperative, 221 mg meperidine
- *Type of surgery*: abdominal or vaginal hysterectomy

RS-25259 (3.0 µg/kg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 14
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 37.5/12.5
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138
- *Use of perioperative opioids (if yes, which?)*: 242 µg fentanyl and 92 µg sufentanil at induction, 60 mg morphine postoperative, 217 mg meperidine
- *Type of surgery*: abdominal or vaginal hysterectomy

RS-25259 (30 µg/kg group)

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Tang 1998a *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 39
- *Received treatment (n)*: NA
- *Analysed (n)*: 39
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 71 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 30.77/5.13
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 148
- *Use of perioperative opioids (if yes, which?)*: 277 µg fentanyl and 86 µg sufentanil at induction, 56 mg morphine postoperative, 334 mg meperidine
- *Type of surgery*: abdominal or vaginal hysterectomy

Included criteria: ASA I or II, consenting women undergoing abdominal or vaginal hysterectomy with a standardized general anaesthetic technique

Excluded criteria: pregnancy; body weight > 100% of calculated ideal body weight; hypersensitivity to 5-HT, antagonists; vomiting or retching within 24 hours before the operation; administration of antiemetic or psychoactive medication within 24 hours before the operation; recent history of narcotic or alcohol abuse; pre-existing abnormalities involving the renal, hepatic, cardiovascular, metabolic, or endocrine system

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: approximately 20 to 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 75% (NA)

RS-25259 (0.1 µg/kg group)

- *Dose*: 0.1 µg/kg
- *Time point of administration*: approximately 20 to 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 67% (NA)

RS-25259 (0.3 µg/kg group)

- *Dose*: 0.3 µg/kg
- *Time point of administration*: approximately 20 to 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 61% (NA)

RS-25259 (1.0 µg/kg group)

- *Dose*: 1.0 µg/kg
- *Time point of administration*: approximately 20 to 30 minutes before end of surgery
- *Route of administration*: IV

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Tang 1998a *(Continued)*

- *Rescue antiemetics (if yes, which?)*: 54% (NA)

RS-25259 (3.0 µg/kg group)

- *Dose*: 3.0 µg/kg
- *Time point of administration*: approximately 20 to 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 53% (NA)

RS-25259 (30 µg/kg group)

- *Dose*: 30 µg/kg
- *Time point of administration*: approximately 20 to 30 minutes before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 49% (NA)

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this work was supported, in part, by a grant from Syntex, Palo Alto, CA **Country:** USA **Setting:** inpatient, multi-centre (2) **Author's name:** Paul F. White **Institution:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA **Email:** pwhite@mednet.swmed.edu **Address:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5161 Harry Hines Blvd., CS2.202, Dallas, TX 75235-9068, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA

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Tang 1998a *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "within each [stratum], patients were randomized to one of six prophylactic treatment groups: placebo (saline) or 0.1,0.3,1.0,3.0, or 30 pg/kg RS-25259" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Quote: "0.1,0.3,1.0,3.0, or 30 pg/kg RS-25259. Each dose of study medication was prepared by the hospital pharmacy in a total volume of 15 mL of isotonic sodium chloride solution and was administered IV over 30 s approximately 20-30 min before the end of surgery. In the preoperative holding area..." Quote: "...dose-ranging study, 218 healthy, consenting women were assigned to one of the six treatment groups: placebo or RS-25259 0.1, 0.3, 1.0, 3.0, or 30 pg/kg" Judgement comment: no information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "0.1,0.3,1.0,3.0, or 30 pg/kg RS-25259. Each dose of study medication was prepared by the hospital pharmacy in a total volume of 15 mL of isotonic sodium chloride solution and was administered IV over..." Judgement comment: blinding of anaesthetists assumed
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding of outcome assessors ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...+SD, numbers, or percentages. The demographic data for the six treatment groups are summarized in Table 1. The six groups were comparable with respect to age, weight, height, number of days since the start of their last menstrual cycle, percentage of patients with a history of PONV and motion sickness, and type of hysterectomy procedure (i.e., transabdominal versus vaginal). The dosages of anesthetic and analgesic drugs administered during the intraoperative and postoperative period, the duration of anesthesia and surgery, and the time to following verbal commands, and the duration of the PACU stay were also similar among all six groups. Within the first 2 h" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Tang 1998b

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, timing study
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 28.21/41.03 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 84 • *Use of perioperative opioids (if yes, which?)*: 102 µg fentanyl intraoperative, 0.8 mg hydromorphone postoperative • *Type of surgery*: laparoscopic procedure Ondansetron (split dose) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 42.11/36.84 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 86 • *Use of perioperative opioids (if yes, which?)*: 105 µg fentanyl intraoperative, 0.7 mg hydromorphone postoperative • *Type of surgery*: laparoscopic procedure Ondansetron (pre-induction) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 39

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Tang 1998b *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 35 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 30.77/28.21
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 69
- *Use of perioperative opioids (if yes, which?)*: 100 µg fentanyl intraoperative, 0.6 mg hydromorphone postoperative
- *Type of surgery*: laparoscopic procedure

Ondansetron (end of surgery)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 20/35
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 78
- *Use of perioperative opioids (if yes, which?)*: 92 µg fentanyl intraoperative, 0.7 mg hydromorphone postoperative
- *Type of surgery*: laparoscopic procedure

Included criteria: women, ASA I or II, scheduled for outpatient laparoscopic procedure

Excluded criteria: had taken an antiemetic or psychoactive medication within 24 hours before the operation, > 50% above ideal body weight, pregnant, had experienced vomiting or retching within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (non-smoker): unclear; (history of PONV): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: 2 × saline • *Time point of administration*: 2 to 3 minutes before induction of anaesthesia, at end of operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 36% (metoclopramide 10 mg to 20 mg IV) Ondansetron (split dose) • *Dose*: 2 × 2 mg • *Time point of administration*: 2 to 3 minutes before induction of anaesthesia, at end of operation • *Route of administration*: IV

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Tang 1998b *(Continued)*

- *Rescue antiemetics (if yes, which?)*: 42% (metoclopramide 10 mg to 20 mg IV)

Ondansetron (pre-induction)

- *Dose*: 4 mg
- *Time point of administration*: 2 to 3 minutes before induction of anaesthesia, saline at end of operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 32% (metoclopramide 10 mg to 20 mg IV)

Ondansetron (end of surgery)

- *Dose*: 4 mg
- *Time point of administration*: 2 to 3 minutes before induction of anaesthesia, saline at end of operation
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 20% (metoclopramide 10 mg to 20 mg IV)

Outcomes

Vomiting (0 to 24 hours)

- Outcome type: dichotomous outcome

Vomiting (PACU)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: supported in part by a grant from Glaxo Wellcome Inc., and the Ambulatory Anesthesia Research Foundation of Dallas

Country: USA

Setting: outpatient, single-centre

Author's name: Paul F. White

Institution: Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, USA

Email: pwhite@mednet.swmed.edu

Address: Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5161 Harry Hines Blvd., CS 2.126, Dallas, TX 75235-9068, USA

Duration of study: NA

Language: English

Study's primary outcome: complete response (no vomiting, no antiemetic medication, and no withdrawal from the study during the 24-hour postoperative study period) to prophylactic antiemetic medication

Trial registry number: NA

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Tang 1998b *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "subjects were randomly assigned to one of four antiemetic treatment groups using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Quote: "the study medications were prepared by the pharmacy in two numbered syringes, which were identical in appearance" Judgement comment: insufficient information on allocation concealment and time point of randomization
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind study" Quote: "the study medications were prepared by the pharmacy in two numbered syringes, which were identical in appearance"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...in the PACU were recorded. Patients were contacted 24 h and 7 days after the operation by the blind investigator, who was unaware of the type of prophylactic antiemetic medication administered. Patients were asked to report..." Quote: "...severe pain or nausea. One of the investigators (JT), who was blinded as to the treatment group, recorded all the intraoperative and recovery variables, including the incidence of PONV and the need for rescue antiemetic medication. An emetic episode was defined"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "164 patients were enrolled in the study, open surgical procedures were performed in 5 patients after laparoscopy and there were protocol violations in the treatment of 3 patients. These 8 patients were excluded from the statistical analysis" Judgement comment: "the investigator could not contact six patients (4%) by telephone after surgery (two patients in Group A, three patients in Group C, and one patient in Group D), and they were excluded from the postdischarge and 24-h analyses"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "PACU = postanesthesia care unit. The four treatment groups were comparable with respect to age, weight, height, racial background, number of days since the start of their last menstrual period, duration of anesthesia and surgery, and history of PONV and motion sickness. The doses of anesthetic drugs, including propofol, perioperative opioid analgesics, muscle relaxants, and antagonists, as well as the amount of perioperative fluid infused, were not significantly different among the four groups. The number of patients requiring..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (non-smoker): unclear; (history of PONV): yes

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Tang 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, combination prophylaxis
Participants	**Baseline characteristics** Droperidol + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 57 ± 15 • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 21/19/5/0 • *Gender (female in %)*: 64.44 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 17.78/20 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 36 • *Use of perioperative opioids (if yes, which?)*: 1 oral opioid-containing analgesic pills • *Type of surgery*: inguinal hernia repair, partial mastectomy, other Dolasetron + droperidol + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 54 ± 18 • *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 16 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 19/19/7/0 • *Gender (female in %)*: 64.44 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 22.22/22.22 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 37 • *Use of perioperative opioids (if yes, which?)*: 2 oral opioid-containing analgesic pills • *Type of surgery*: inguinal hernia repair, partial mastectomy, other Ondansetron + droperidol + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 53 ± 17 • *Weight (mean ± SD, median (IQR), median (range))*: 66 ± 14

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Tang 2003 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 20/18/7/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 15.56/17.78
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 40
- *Use of perioperative opioids (if yes, which?)*: 1 oral opioid-containing analgesic pill
- *Type of surgery*: inguinal hernia repair, partial mastectomy, other

Included criteria: outpatient, ASA I to III, undergoing superficial surgical procedures lasting 20 to 40 minutes

Excluded criteria: pregnancy; active menstruation; body weight > 50% above ideal body weight; vomiting or retching within 24 hours before the operation; administration of antiemetic or psychoactive medication within 24 hours before surgery; previous history of severe (or unstable) cardiovascular, respiratory, metabolic, endocrine, or neurological disease; alcohol or drug abuse; impaired renal or hepatic function

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Droperidol + dexamethasone • *Dose*: saline, droperidol 0.625 mg, dexamethasone 4 mg • *Time point of administration*: saline 10 to 15 minutes before end of surgery; droperidol, dexamethasone after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 4% (metoclopramide 10 mg IV) dolasetron + droperidol + dexamethasone • *Dose*: dolasetron: 12.5 mg, droperidol: 0.625 mg, dexamethasone: 4 mg • *Time point of administration*: dolasetron 10 to 15 minutes before end of surgery; droperidol, dexamethasone after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2% (metoclopramide 10 mg IV) Ondansetron + droperidol + dexamethasone • *Dose*: ondansetron: 4 mg, droperidol: 0.625 mg, dexamethasone: 4 mg • *Time point of administration*: ondansetron 10 to 15 minutes before end of surgery; droperidol, dexamethasone after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2% (metoclopramide 10 mg IV)
Outcomes	*Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (discharge to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome

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Tang 2003 *(Continued)*

	Adverse events (general notes in the publication, 24 hours' observation) • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this study was also supported by the White Mountain Institute, a not-for-profit private foundation in Los Altos, California (Dr. White is the president) **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Paul. F. White **Institution:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, Dallas, Texas, USA **Email:** paul.white@utsouthwestern.edu **Address:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, F2.208, Dallas, Texas 75390-9068, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly assigned to one of three study groups according to a computer-generated random numbers table"
Allocation concealment (selection bias)	Unclear risk	Quote: "the study medications were prepared by the local pharmacy in identical-appearing 5-ml syringes containing saline (control), dolasetron (12.5 mg), or ondansetron (4 mg) and were administered intravenously 10 –15 min prior to the end of surgery" Judgement comment: insufficient information on allocation concealment and time point of randomization
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study medications were prepared by the local pharmacy in identical-appearing 5-ml syringes containing saline (control), dolasetron (12.5 mg), or ondansetron (4 mg) and were administered intravenously 10 – 15 min prior to the end of surgery"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a trained interviewer who was blinded to the study medication contacted each patient by telephone at home approximately 24 h after discharge to inquire about postdischarge side"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Tang 2003 *(Continued)*

Other bias	Unclear risk	Quote: "...(ranges), numbers, or percentages. The three treatment groups were comparable with respect to their demographic characteristics. The duration of anesthesia and surgery, the amount of local anesthetic solution injected during the intraoperative period, and the dosage of analgesic medication administered in the recovery area were similar among the three groups (table 1). The early recovery..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Tarantino 2015

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 76 • *Received treatment (n)*: 75 • *Analysed (n)*: 76 (ITT), 65 (PP) • *Age (mean ± SD, median (IQR), median (range))*: 49.5 ± 12.0 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24.8 ± 4.1 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 81.6 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA + bilateral superficial cervical plexus block • *Duration of anaesthesia or surgery (in min; as mean or median)*: 126.2 • *Use of perioperative opioids (if yes, which?)*: 427 ± 111 µg fentanyl, 1944 ± 1197 µg remifentanil, 1.2 ± 3.3 mg morphine (protocol violation) • *Type of surgery*: hemithyroidectomy, near-total thyroidectomy, total thyroidectomy Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 76 • *Received treatment (n)*: 76 • *Analysed (n)*: 76 (ITT), 60 (PP) • *Age (mean ± SD, median (IQR), median (range))*: 48.4 ± 13.4 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.4 ± 4.6 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 76.3 • *Non-smoker (%)*: NA

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Tarantino 2015 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA + bilateral superficial cervical plexus block
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 127.5
- *Use of perioperative opioids (if yes, which?)*: 444 ± 108 µg fentanyl, 1978 ± 1111 µg remifentanil, 1.7 ± 4.0 mg morphine (protocol violation)
- *Type of surgery*: hemithyroidectomy, near-total thyroidectomy, total thyroidectomy

Included criteria: older than 18 years of age, scheduled for a primary partial or total thyroidectomy due to benign disease

Excluded criteria: history of adverse reactions to dexamethasone, polypropylene glycol, or disodium-EDTA (medication ingredients); chronic pain; necessity for sternotomy; inability to administer a cervical block; diabetes mellitus type 1 or 2 requiring medication; pregnancy (tested in all women capable of childbearing); glaucoma; administration of antiemetic therapy within 48 hours before surgery; acute pain requiring analgesics other than acetaminophen or more than a single dose of nonsteroidal anti-inflammatory drugs within 48 hours before surgery; use of antipsychotic drugs; non-compliance; proven malignancy; necessity for lateral neck dissection; re-operation

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

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Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: 30 to 60 minutes before skin incision
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol (first line, max. 3 × 0.5 mg/24 h) or ondansetron (second line, 4 mg)

Placebo

- *Dose*: 2 mL
- *Time point of administration*: 30 to 60 minutes before skin incision
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: droperidol (first line, max. 3 × 0.5 mg/24 h) or ondansetron (second line, 4 mg)

Outcomes

Vomiting (0 to 4 hours)

- Outcome type: dichotomous outcome

PONV (0 to 24 hours)

- Outcome type: dichotomous outcome

Subjects with any SAE (0 to 48 hours)

- Outcome type: dichotomous outcome

Subjects with any AE (0 to 48 hours)

- Outcome type: dichotomous outcome

Mortality (0 to 48 hours)

- Outcome type: dichotomous outcome

Postoperative wound infection (overall)

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Tarantino 2015 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this trial was supported by a grant from the Clinical Trial Unit of the Kantonsspital St. Gallen. The Clinical Trial Unit had no role in the study design, data collection and analysis, or decision to submit for publication. The final decision on content was made exclusively by study authors **Country:** Switzerland **Setting:** inpatient, single-centre **Author's name:** Ignazio Tarantino **Institution:** Department of General, Abdominal and Transplant Surgery, University of Heidelberg **Email:** ignazio.tarantino@med.uni-heidelberg.de **Address:** Department of General, Abdominal and Transplant Surgery, University of Heidelberg, Im Neuenheimer Feld 110, 69120 Heidelberg **Language:** English **Duration of study:** 1 January 2011 to 30 May 2013 **Trial registry number:** NCT01189292 **Study's primary outcome:** incidence of PONV assessed at 4, 8, 16, 24, 32, and 48 hours after surgery
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were allocated to the study arms in a 1:1 ratio based on a predefined block randomization list with blocks randomly sized between 4 and 10. The randomization list was generated by the data manager (U.B.), with the hard copy stored in a secure location and the electronic version stored within the trial management software in a password-protected, encrypted fashion. During the study, only the data manager had access to the randomization list"
Allocation concealment (selection bias)	Low risk	Quote: "two to 3 days before surgery, the data manager prepared a computer-generated study medication request form based on the patient's study number. The request contained the patient's name and the treatment allocation. The form was placed in an opaque, sealed, and signed envelope and was directly delivered to the pharmacy by study personnel. Study medication was prepared according to the request form by the hospital pharmacy"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "medication was delivered in a syringe labeled with the patient's name and study number and containing either 2 mL of saline (placebo) or 2 mL of saline with 8 mg of dexamethasone (Mephameson; Mepha Pharma, Basel, Switzerland). Syringes containing saline or dexamethasone were indistinguishable. The patients and all study personnel except for the data manager were blinded to the treatment allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "all study personnel except for the data manager were blinded to the treatment allocation"

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Tarantino 2015 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...Inc. All rights reserved. During the study period, 393 patients were eligible for inclusion. A total of 152 patients were included in the study and randomly allocated to the 2 study arms (Fig. 1). For the PP analysis, 27 patients (18%) were excluded because of protocol violations. In the treatment arm, 11 patients were excluded because of perioperative morphine administration (n ¼ 10) or failure to provide study treatment in time (n ¼ 1). In the control arm, 16 patients were excluded because of perioperative morphine (n = 14) or preoperative use of steroids (n = 2) (Fig. 1). The patient characteristics were well..."
Selective reporting (reporting bias)	Low risk	Judgement comment: NCT01189292 (prospective registration). The prospectively registered primary outcome (PONV) was reported in the pre-specified way in the final study report
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Teran 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 16 • *Received treatment (n)*: NA • *Analysed (n)*: 16 • *Age (mean ± SD, median (IQR), median (range))*: 31.18 ± 1.83 • *Weight (mean ± SD, median (IQR), median (range))*: 68.93 ± 3.46 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 82.25 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl • *Type of surgery*: laparoscopic surgical procedure Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 19 • *Received treatment (n)*: NA • *Analysed (n)*: 19 • *Age (mean ± SD, median (IQR), median (range))*: 32.10 ± 1.68

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Teran 2007 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 71.26 ± 3.17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 61.78
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: laparoscopic surgical procedure

Included criteria: women, ASA I or II, 18 to 50 years of age, elective laparoscopic surgical procedure

Excluded criteria: nausea within 24 hours before surgery that required an antiemetic; allergy to isopropyl alcohol, 5-HT3 antagonists, opioids, or promethazine; laparoscopic procedure that progressed to an open procedure; neuraxial blockade; decreased ability to breathe through the nose; history of alcoholism or disulfiram use; pregnancy; natural or surgical menopause; emergency procedure

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Interventions	**Intervention characteristics** Granisetron • *Dose*: 0.1 mg • *Time point of administration*: 15 to 30 minutes before emergence and extubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 62% (promethazine 12.5 mg) Control • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: 74% (promethazine 12.5 mg)
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Lara Teran **Institution:** 28th Combat Support Hospital, Ft Bragg, North Carolina, USA **Email:** NA **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA

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Teran 2007 *(Continued)*

	Study's primary outcome: incidence of PONV
Notes	Two out of 3 groups relevant (isopropyl alcohol)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "participants were randomly assigned using a table of random numbers to 1 of 3 groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: blinding of personnel impossible (different interventions)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the PACU nurses were blinded to subject treatment group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): unclear

Tezcan 1993

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 15 • *Received treatment (n)*: NA • *Analysed (n)*: 15 • *Age (mean ± SD, median (IQR), median (range))*: 28.0 ± 1.6 • *Weight (mean ± SD, median (IQR), median (range))*: 65.8 ± 5.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Tezcan 1993 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 33.7
- *Use of perioperative opioids (if yes, which?)*: meperidine postoperative
- *Type of surgery*: laparoscopic-gynaecological surgery

Droperidol (group D)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 15
- *Received treatment (n)*: NA
- *Analysed (n)*: 15
- *Age (mean ± SD, median (IQR), median (range))*: 30.3 ± 1.6
- *Weight (mean ± SD, median (IQR), median (range))*: 60.9 ± 2.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 24.3
- *Use of perioperative opioids (if yes, which?)*: meperidine postoperative
- *Type of surgery*: laparoscopic-gynaecological surgery

Included criteria: female, ASA I or II, undergoing planned laparoscopic-gynaecological surgery

Excluded criteria: hypertension, organic heart disease, intake of antiemetics in the pre-operation time

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear; (duration of anaesthesia): yes

Interventions	**Intervention characteristics** Placebo (group P) • *Dose*: NaCl 0.9% • *Time point of administration*: right before extubation • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: (26.6%) metoclopramide Droperidol (group D) • *Dose*: 0.04 mg/kg • *Time point of administration*: right before extubation • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: (6.7%) metoclopramide
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 12 hours)* • Outcome type: dichotomous outcome

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Tezcan 1993 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, NA **Author's name:** Cigdem Tezcan **Institution:** Ankara Oniv.Tip Fak. Anesteziyoloji Anabilim Dali, Ogretim Uyesi **Email:** NA **Address:** NA **Duration of study:** NA **Language:** Turkish (translated by Emine Yesil) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant (ephedrine)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "were randomly divided". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: a blinded clinician observed for retching, nausea, and vomiting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, perioperative opioids, non-smoker): unclear; (duration of anaesthesia): yes

Thagaard 2007

Study characteristics

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Thagaard 2007 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 62 • *Received treatment (n)*: 62 • *Analysed (n)*: 58 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 20 • *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 57/5/0/0 • *Gender (female in %)*: 47 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol, remifentanil), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 50 • *Use of perioperative opioids (if yes, which?)*: remifentanil, 1 µg/kg fentanyl at end of surgery, 57 µg fentanyl as rescue analgesic (0 to 3 hours), 26% of patients received codeine as rescue analgesic after 3 hours • *Type of surgery*: inguinal hernia repair, varicose veins, haemorrhoidectomy, minor orthopaedic surgery Betamethasone (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 57 • *Received treatment (n)*: 57 • *Analysed (n)*: 51 • *Age (mean ± SD, median (IQR), median (range))*: 48 ± 13 • *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 15 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 54/3/0/0 • *Gender (female in %)*: 49 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol, remifentanil), N_2O • *Duration of anaesthesia or surgery (in min; as mean or median)*: 58 • *Use of perioperative opioids (if yes, which?)*: remifentanil, 1 µg/kg fentanyl at end of surgery, 65 µg fentanyl as rescue analgesic (0 to 3 hours), 35% of patients received codeine as rescue analgesic after 3 hours • *Type of surgery*: inguinal hernia repair, varicose veins, haemorrhoidectomy, minor orthopaedic surgery **Included criteria:** female, admitted for minor orthopaedic surgery, haemorrhoidectomy, inguinal hernia repair or removal of varicose veins, 18 to 60 years of age, ASA I or II **Excluded criteria:** any psychiatric, neurological, or liver disease; used any regular medication with known or suspected sedative or analgesic effects; drinking alcohol more than 2 days a week; any contraindication to NSAIDs, glucocorticoids, or other drugs planned for anaesthesia

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Thagaard 2007 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 4 mg • *Time point of administration*: shortly after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 20 mg IV Betamethasone (group B) • *Dose*: 12 mg • *Time point of administration*: shortly after induction of anaesthesia • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: metoclopramide 20 mg IV
Outcomes	*Vomiting (0 to 6 hours, in hospital)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 72 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Norway **Setting:** outpatient, single-centre **Author's name:** Johan Raeder **Institution:** Departments of Anaesthesiology and Day Surgery, University of Oslo, Faculty Division, Ullevaal University Hospital, Oslo, Norway **Email:** johan.rader@medisin.uio.no **Address:** Department of Anaesthesia, Ullevaal University Hospital, N-0407 Oslo, Norway **Duration of study:** NA **Language:** English **Study's primary outcome:** number of patients with significant pain (defined as VAS pain score > 3) during the first postoperative day after discharge **Trial registry number:** NA
Notes	Two out of 3 groups relevant (ketorolac)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the sealed instructions were randomized according to a computer-generated list of random numbers and prepared by an assistant not otherwise participating in the study"

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Thagaard 2007 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "instructions in a sealed envelope administered by a nurse not participating in any other part of the study" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "administered by a nurse not participating in any other part of the study or handling of the patients. The anaesthesiologist left the room during injection and the post-operative nursing staff were also unaware of the individual patient allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the post-operative nursing staff were also unaware of the individual patient allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred and seventy-nine consecutive patients fulfilled the criteria and accepted to participate in the study, no one dropped out during the stay in the unit. One hundred and sixty-three answered the questionnaires at 24 h, and 72 h (Fig. 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the patients were evaluated for pre-operative risk factors for nausea [i.e. travel sickness, gender, smoking habits, previous PONV (11)]" Quote: "...and 72 h (Fig. 1). The patient characteristics were similar between the three groups, except for shorter duration of surgery in the ketorolac patients (Table 1). There were no significant differences between the groups in pre-operative risk factors for nausea or pain. There was significantly less severe" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Thangaswamy 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 18 • *Received treatment (n)*: 18 • *Analysed (n)*: 18 • *Age (mean ± SD, median (IQR), median (range))*: 36 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 58.3 ± 12.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0

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Thangaswamy 2010 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 146.4
- *Use of perioperative opioids (if yes, which?)*: 195.6 µg fentanyl intraoperative, 646.7 µg fentanyl postoperative via PCA
- *Type of surgery*: laparoscopic hysterectomy

Dexamethasone (group D4)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 18
- *Received treatment (n)*: 18
- *Analysed (n)*: 18
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 58.3 ± 7.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 149.4
- *Use of perioperative opioids (if yes, which?)*: 173.9 µg fentanyl intraoperative, 655.6 µg fentanyl postoperative via PCA
- *Type of surgery*: laparoscopic hysterectomy

Dexamethasone (group D8)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 19
- *Received treatment (n)*: 19
- *Analysed (n)*: 19
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 10.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 153.7
- *Use of perioperative opioids (if yes, which?)*: 176.3 µg fentanyl intraoperative, 547.4 µg fentanyl postoperative via PCA
- *Type of surgery*: laparoscopic hysterectomy

Included criteria: ASA I and II, 18 to 60 years of age, scheduled for elective laparoscopic hysterectomy under general anaesthesia

Excluded criteria: diabetes mellitus/impaired glucose tolerance, peptic ulcer disease, endocrine disorder, morbid obesity (BMI > 30), history of motion sickness or postoperative nausea and vomiting

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Thangaswamy 2010 *(Continued)*

	(PONV) after general anaesthesia, receiving hormonal therapy, receiving long-term steroids or non-steroidal anti- inflammatory drugs (NSAIDs) **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes
Interventions	**Intervention characteristics** Placebo (group P) • *Dose*: saline • *Time point of administration*: 2 hours before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.1 mg/kg ondansetron IV Dexamethasone (group D4) • *Dose*: 4 mg • *Time point of administration*: 2 hours before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.1 mg/kg ondansetron IV Dexamethasone (group D8) • *Dose*: 8 mg • *Time point of administration*: 2 hours before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.1 mg/kg ondansetron IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (0 to 7 days)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 7 days' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this work was supported by institutional sources only **Country:** India **Setting:** inpatient, single-centre **Author's name:** V. Rewari **Institution:** Department of Anaesthesiology and Intensive Care, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India **Email:** vimirewari@gmail.com **Address:** K-25, Jangpura Extn, New Delhi 110014, India **Duration of study:** NA **Language:** English **Study's primary outcome:** total fentanyl consumption at 2, 4, 8, 12, and 24 hours postoperatively

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Thangaswamy 2010 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the patients were randomized to one of the three groups based on a computer generated random number list"
Allocation concealment (selection bias)	Unclear risk	Quote: "the study solution to be given to the patient was concealed in a sealed envelope bearing the patient's number which was handed over by the second author to the ward nurse who was not involved in the study. The study solution was prepared by the ward nurse and administered to the patient intravenously 2 h before the start of the surgery" Judgement comment: not stated; "sequentially numbered, opaque, sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...ward nurse who was not involved in the study. The study solution was prepared by the ward nurse" Quote: "all patients were blinded to the nature of the drug administered"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "in the PACU, a blinded investigator (first author) recorded the pain scores at rest and on movement (patient was asked to log roll to one side) and PONV at 0 min, 30 min, 1, 2, 4, 8, 12, and 24 h postoperatively"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "sixty seven consecutive patients were considered for inclusion in the study. Fifty-five patients were included and randomly assigned to their treatment group (Fig. 1)" Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "all groups were comparable with regard to patient characteristics and intraoperative details (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes

Thimmasettaiah 2012

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, different times of administration
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: -

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Thimmasettaiah 2012 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: all patients with same standard anaesthetic technique
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 4 patients with tramadol
- *Type of surgery*: tonsillectomy

Dexamethasone (intra-group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: all patients with same standard anaesthetic technique
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0 patients with tramadol
- *Type of surgery*: tonsillectomy

Dexamethasone (pre-group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: all patients with same standard anaesthetic technique
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0 patients with tramadol
- *Type of surgery*: tonsillectomy

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Thimmasettaiah 2012 *(Continued)*

Dexamethasone (post-group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: all patients with same standard anaesthetic technique
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 0 patients with tramadol
- *Type of surgery*: tonsillectomy

Included criteria: over 15 years of age, undergoing tonsillectomy

Excluded criteria: coagulopathy disorders, diabetes, gastritis, peptic ulcer, hypertension, and cardiovascular and renal disease; on therapy with corticosteroids, antiemetics, antihistamines, or aspirin; undergoing additional procedure at the same time as tonsillectomy (e.g. adenoidectomy, uvula-palatopharyngoplastic procedure)

Pretreatment: baseline characteristics (age): no; (ASA, weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

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Interventions

Intervention characteristics

Control

- *Dose*: saline
- *Time point of administration*: NA
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 0.1 mg/kg IV

Dexamethasone (intra-group)

- *Dose*: 0.5 mg/kg
- *Time point of administration*: after induction and before commencement of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 0.1 mg/kg IV

Dexamethasone (pre-group)

- *Dose*: 0.5 mg/kg
- *Time point of administration*: immediately after IV access was established
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron 0.1 mg/kg IV

Dexamethasone (post-group)

- *Dose*: 0.5 mg/kg
- *Time point of administration*: just after shifting patient to the postoperative recovery unit
- *Route of administration*: IV

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Thimmasettaiah 2012 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: ondansetron 0.1 mg/kg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Nagaraj Bangalore Thimmasettaiah **Institution:** Department of ENT, MVJ Medical College and Research Hospital, Hoskote, Bangalore, Karnataka, India **Email:** drnag_79@yahoo.co.in **Address:** # 84, Satyanarayana Layout 2nd Stage, J C Nagar, Mahalakshmipuram, Bangalore – 560 086, Karnataka, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Three out of 4 groups relevant (administration postoperative)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated according to a computer generated random table into control or dexamethasone group"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "in this randomized double-blind study, 100 patients who underwent tonsillectomy were enrolled and were randomly allocated into control or dexamethasone group (pre operative, intra operative and post operative groups)" Judgement comment: no blinding of anaesthesiologist
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding of outcome assessors ("double-blind")
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Thimmasettaiah 2012 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no statistically significant differences seen between the groups for age, sex and tonsillar size" Judgement comment: baseline characteristics (age): no; (ASA, weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Thomas 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: 60 • *Analysed (n)*: 60 • *Age (mean ± SD, median (IQR), median (range))*: 34.9 (mean) (20 to 50) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.1 ± 4.2 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 67 • *History of PONV/motion sickness (%)*: 58 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 30.5 • *Use of perioperative opioids (if yes, which?)*: 3/60 fentanyl (n/N), 47/60 tramadol (n/N), laparoscopic surgery, additionally tramadol intraoperative; postoperative codeine, dextropropoxyphen • *Type of surgery*: outpatient gynaecological surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 59 • *Received treatment (n)*: 59 • *Analysed (n)*: 59 • *Age (mean ± SD, median (IQR), median (range))*: 36.2 (mean) (21 to 53) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 23.8 ± 3.5 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Thomas 2001 *(Continued)*

- *Non-smoker (%)*: 69
- *History of PONV/motion sickness (%)*: 58
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 29.7
- *Use of perioperative opioids (if yes, which?)*: 4/59 fentanyl (n/N), 43/59 tramadol (n/N), laparoscopic surgery, additionally tramadol intraoperative; postoperative codeine, dextropropoxyphen
- *Type of surgery*: outpatient gynaecological surgery

Dexamethasone + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 58
- *Received treatment (n)*: 58
- *Analysed (n)*: 58
- *Age (mean ± SD, median (IQR), median (range))*: 36.0 (mean) (19 to 53)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24.1 ± 3.3
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 55
- *History of PONV/motion sickness (%)*: 57
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 30.2
- *Use of perioperative opioids (if yes, which?)*: 6/58 fentanyl (n/N), 46/58 tramadol (n/N), laparoscopic surgery, additionally tramadol intraoperative; postoperative codeine, dextropropoxyphen
- *Type of surgery*: outpatient gynaecological surgery

Included criteria: ASA I or II, premenopausal female, 19 to 53 years of age, undergoing day-case gynaecological surgery

Excluded criteria: gastrointestinal, liver, or renal disease; had received any antiemetic medication within 24 hours before surgery or complained of preoperative nausea or vomiting; pregnant or lactating; body mass index > 35

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: immediately after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: cyclizine 50 mg

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: immediately after induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: cyclizine 50 mg

Dexamethasone + ondansetron

- *Dose*: dexamethasone 8 mg, ondansetron 4 mg
- *Time point of administration*: immediately after induction

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Thomas 2001 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: cyclizine 50 mg

Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 12 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** outpatient, single-centre **Author;s name:** R. Thomas **Institution:** Shackleton Department of Anaesthetics, Southampton General Hospital, United Kingdom **Email:** NA **Address:** Shackleton Department of Anaesthetics, Southampton General Hospital, Tremona Road, Southampton, Hampshire SO16 6YD, UK **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** difference in response rates (PONV)
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a randomization list was prepared using a mechanical randomization device"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "personnel not involved in the study prepared identical syringes containing the study drug(s). The drug(s) were diluted with normal saline to achieve a volume of 5 ml"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were interviewed on discharge from the day surgical unit (3 h post-surgery) by blinded nursing staff and by phone at 24 h post-surgery by one of the two blinded investigators"

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Thomas 2001 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Thomas 2007

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: NA • *Analysed (n)*: 55 • *Age (mean ± SD, median (IQR), median (range))*: 43.33 ± 12.24 • *Weight (mean ± SD, median (IQR), median (range))*: 64.26 ± 6.27 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 52.73 • *Non-smoker (%)*: 76.37 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) + epidural catheter • *Duration of anaesthesia or surgery (in min; as mean or median)*: 135.20 • *Use of perioperative opioids (if yes, which?)*: morphine • *Type of surgery*: abdominal and lower limb surgery Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 60 • *Received treatment (n)*: NA • *Analysed (n)*: 55 • *Age (mean ± SD, median (IQR), median (range))*: 42.83 ± 11.82 • *Weight (mean ± SD, median (IQR), median (range))*: 65.30 ± 5.94 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 49.09 • *Non-smoker (%)*: 72.73

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Thomas 2007 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) + epidural catheter
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 129.80
- *Use of perioperative opioids (if yes, which?)*: morphine
- *Type of surgery*: abdominal and lower limb surgery

Included criteria: ASA I and II, 20 to 60 years of age, weighing 40 to 75 kg, requiring general anaesthesia with endotracheal intubation for abdominal and lower limb surgery, estimated to last 1 to 3 hours

Excluded criteria: history of recent respiratory tract infection; risk factors for postoperative aspiration; cardiac, respiratory, hepatic, or major renal disease; obesity; diabetes mellitus; pregnancy; prior treatment with analgesics; use of corticosteroids and calcium channel blockers; neuromuscular disease

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 6 mg • *Time point of administration*: saline before anaesthesia, ondansetron at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dexamethasone + ondansetron • *Dose*: dexamethasone 8 mg, ondansetron 6 mg • *Time point of administration*: dexamethasone before anaesthesia, ondansetron at end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** NA, single-centre **Author's name:** Siji Thomas **Institution:** Department of Anesthesiology, Amala Institute of Medical Sciences, Thrissur, Kerala, India **Email:** sijithomas2k@yahoo.com **Address:** Valiamiyalil, Kainady Layout, Florican Road, Malaparamba, Calicut 673009 Kerala **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of postoperative sore throat **Trial registry number:** NA

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Thomas 2007 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated codes"
Allocation concealment (selection bias)	Unclear risk	Quote: "only the pharmacist and the statistician knew the identity of the study medication" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "only the pharmacist and the statistician knew the identity of the study medication"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...assessed by a second trained observer who, along with the patient, was blinded to study group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 120 patients studied, ten (five patients in each group) were excluded from the data analysis. Of these patients, six patients required intravenous rescue analgesia apart from the usual epidural rescue analgesia, and four required more than two attempts at intubation"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...than two attempts at intubation. Patient characteristics in the remaining 110 subjects were comparable with respect to age, weight, smoking habits and intubation time (Table I). The number of patients requiring..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Tigerstedt 1988

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Transdermal scopolamine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 32 • *Received treatment (n)*: NA • *Analysed (n)*: 32

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Tigerstedt 1988 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 2
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 75 ± 5
- *Use of perioperative opioids (if yes, which?)*: oxycodone (0.13 mg/kg IM + 4 mg when needed), 0.13 ± 0.01 mg fentanyl
- *Type of surgery*: superficial short-stay surgery (7 breast, 17 varicose veins, 1 anal, 2 thyroid, 5 other)

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: NA
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 40 ± 2
- *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79 ± 6
- *Use of perioperative opioids (if yes, which?)*: oxycodone (0.13 mg/kg IM + 4 mg when needed), 0.15 ± 0.02 mg fentanyl
- *Type of surgery*: superficial short-stay surgery (7 breast, 18 varicose veins, 1 anal, 2 thyroid, 4 other)

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 32
- *Received treatment (n)*: NA
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 2
- *Weight (mean ± SD, median (IQR), median (range))*: 68 ± 2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 74 ± 5
- *Use of perioperative opioids (if yes, which?)*: oxycodone (0.13 mg/kg IM + 4 mg when needed), 0.15 ± 0.01 mg fentanyl
- *Type of surgery*: superficial short-stay surgery (10 breast, 18 varicose veins, 1 anal, 0 thyroid, 3 other)

Included criteria: female, superficial short-stay surgery, ASA I or II, 18 to 65 years of age

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Tigerstedt 1988 *(Continued)*

Excluded criteria: allergy to scopolamine or droperidol, glaucoma, pyloric stenosis, obstruction of the urinary bladder neck, anticholinergic medication, pregnancy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Transdermal scopolamine • *Dose*: transdermal scopolamine 140 µg initially and 5 µg/h thereafter, placebo 0.5 mL • *Time point of administration*: transdermal scopolamine morning of operation, placebo 5 minutes before end of surgery • *Route of administration*: scopolamine transdermal, placebo IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg (9) Droperidol • *Dose*: 1.25 mg • *Time point of administration*: transdermal placebo morning of operation, droperidol 5 minutes before end of surgery • *Route of administration*: placebo transdermal, droperidol IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg (4) Placebo • *Dose*: placebo 0.5 mL • *Time point of administration*: transdermal placebo morning of operation, placebo 5 minutes before end of surgery • *Route of administration*: transdermal, IV • *Rescue antiemetics (if yes, which?)*: droperidol 1.25 mg (2)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (end of recovery room period, still asleep)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** inpatient, single-centre **Author's name:** I. Tigerstedt

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Tigerstedt 1988 *(Continued)*

Institution: Department of Anaesthesia, Helsinki University Central Hospital, Finland

Email: NA

Address: Department of AnaesthesiaHelsinki University Central HospitalHaartmaninkatuSF-00290 Helsinki, Finland

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the test drugs were given in a double-blind, double-dummy randomised manner. The patients were randomly allocated to three groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Tolksdorf 1986

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis

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Tolksdorf 1986 *(Continued)*

Participants	**Baseline characteristics** Scopolamine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 31 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 65 (50 to 80) • *Weight (mean ± SD, median (IQR), median (range))*: 72 (43 to 88) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 174 • *Use of perioperative opioids (if yes, which?)*: 0.15 mg fentanyl, 16/30 other opioids (n/N) • *Type of surgery*: general surgery, gynaecological surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 29 • *Age (mean ± SD, median (IQR), median (range))*: 63 (50 to 79) • *Weight (mean ± SD, median (IQR), median (range))*: 74 (50 to 100) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 66 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (enflurane, isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 168 • *Use of perioperative opioids (if yes, which?)*: 0.15 mg fentanyl, 9/29 other opioids (n/N) • *Type of surgery*: general surgery, gynaecological surgery **Included criteria:** male and female, older than 50 years of age, surgical or gynaecological interventions in general anaesthesia **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics** Scopolamine • *Dose*: NA • *Time point of administration*: evening before surgery (continuous application until day after surgery) • *Route of administration*: transdermal

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Tolksdorf 1986 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: yes (not specified) Placebo • *Dose*: NA • *Time point of administration*: evening before surgery (continuous application until day after surgery) • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: yes (not specified)
Outcomes	*Vomiting (overall, until day after surgery)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Werner Tolksdorf **Institution:** Institut für Anästhesiologie und Reanimation an der Fakultät für klinische Medizin Mannheim der Universität Heidelberg **Email:** NA **Address:** Institut für Anästhesiologie und Reanimation am Klinikum der Stadt Mannheim, Theodor-Kutzer-Ufer, 6800 Mannheim 1 **Language:** German (2 German reviewers) **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomisiert" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")

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Tolksdorf 1986 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "von 61 Patienten konnten 59 ausgewertet werden. Bei einem Patienten der 'ITS-S-Gruppe wurde präoperativ das Pflaster wegen starker Mundtrockenheit entfernt, ein Patient der TTS-P-Gruppe wurde nicht operiert"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Tolver 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 58 (20 to 77) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25 (19 to 31) • *ASA I/II/III/IV (n)*: 37/3/0/0 • *Gender (female in %)*: 0 • *Non-smoker (%)*: 55 • *History of PONV/motion sickness (%)*: 15.63/22.5 • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 52 • *Use of perioperative opioids (if yes, which?)*: 2.1 mg remifentanil intraoperative, 0.2 mg fentanyl • *Type of surgery*: transabdominal preperitoneal (TAPP) inguinal hernia repair Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 59 (22 to 79) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25 (18 to 34) • *ASA I/II/III/IV (n)*: 32/8/0/0 • *Gender (female in %)*: 0

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Tolver 2012 *(Continued)*

- *Non-smoker (%)*: 65
- *History of PONV/motion sickness (%)*: 6.25/12.5
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 52
- *Use of perioperative opioids (if yes, which?)*: 2.1 mg remifentanil intraoperative, 0.2 mg fentanyl
- *Type of surgery*: transabdominal preperitoneal (TAPP) inguinal hernia repair

Included criteria: men with unilateral inguinal or femoral hernia (primary and recurrent hernia) scheduled for TAPP repair, 18 to 85 years of age, able to speak Danish, ASA I or II

Excluded criteria: presumed poor compliance, allergy to dexamethasone, daily intake of opioids or anxiolytics during the week before surgery, systemic use of steroids or other immunosuppressant drugs, history of manic episodes, narrow-angle or open-angle glaucoma, weekly alcohol consumption of more than 21 drinks (1 drink equals 12 g pure alcohol), fever or signs of bacterial infection within the last 10 days before the operation, vaccination within the last 14 days before surgery, treatment with thiazide or loop diuretics, endocrine disease of any kind, acute or subacute hernia operation, concomitant ventral hernia repair with a mesh during the same procedure, operation for bilateral hernia, lack of written informed consent for participation in the study

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 30 to 60 minutes before operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron IV Placebo • *Dose*: saline • *Time point of administration*: 30 to 60 minutes before operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron IV
Outcomes	*Vomiting (0 to 24 hours, postoperative day 0 to 1)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours, postoperative day 0 to 1, moderate to severe nausea)* • Outcome type: dichotomous outcome *Postoperative wound infection (time point unknown)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, observation period unknown)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this trial was funded by Region Zealand's Health Research Fund (RESUS) and the Department of Surgery, Køge Hospital, Køge, Denmark **Country:** Denmark **Setting:** outpatient, single-centre **Author's name:** M. A. Tolver

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Tolver 2012 *(Continued)*

Institution: Departments of Surgery and Anaesthesiology, Køge Hospital, University of Copenhagen, Køge

Email: mette.astrup@gmail.com

Address: Department of Surgery, Køge Hospital, Lykkebækvej 1, 4600 Køge, Denmark

Duration of study: August 2010 to August 2011

Language: English

Study's primary outcome: pain during coughing on postoperative day 1

Trial registry number: NCT01170780

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed by a doctor not participating in the study and by a block-randomized computer-generated method"
Allocation concealment (selection bias)	Low risk	Quote: "from the randomization list, 80 sealed non-transparent envelopes were created and numbered 1–80"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "thus, the patient, surgeon, anaesthetist, nurses in the operating room and the PACU, as well as the investigators, were unaware of the nature of the injected solution" Quote: "a randomization code 1–80 was used in the patient records. A nurse not participating in the study or care of the patient opened a sealed envelope in a closed medicine room 30–60 min before operation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "thus, the patient, surgeon, anaesthetist, nurses in the operating room and the PACU, as well as the investigators, were unaware of the nature of the injected solution"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: 80 participants were randomized; 73 were analysed. Reason for missing outcome data: did not return questionnaire (6), not operated (1)
Selective reporting (reporting bias)	Low risk	Judgement comment: NCT01170780 (prospective registration). The prospectively registered primary outcome (pain) was reported in the pre-specified way in the final study report. The primary outcome was not PONV-related
Other bias	Low risk	Quote: "the two groups were comparable for reported variables, including type of hernia (Table 1)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Tomar 2017

Study characteristics

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Tomar 2017 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 27 • *Received treatment (n)*: 27 • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 44.6 ± 9.6 • *Weight (mean ± SD, median (IQR), median (range))*: 68.3 ± 9.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 51.85 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 88.62 • *Use of perioperative opioids (if yes, which?)*: 102.36 µg fentanyl intraoperative, 147.6 µg fentanyl postoperative • *Type of surgery*: unilateral nephrectomy Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 28 • *Received treatment (n)*: 28 • *Analysed (n)*: 28 • *Age (mean ± SD, median (IQR), median (range))*: 43.6 ± 10.8 • *Weight (mean ± SD, median (IQR), median (range))*: 70.4 ± 10.48 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 42.86 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 90.8 • *Use of perioperative opioids (if yes, which?)*: 98.62 µg fentanyl intraoperative, 98.6 µg fentanyl postoperative • *Type of surgery*: unilateral nephrectomy **Included criteria:** ASA I or II, either sex, 18 to 65 years of age, undergoing elective unilateral nephrectomy **Excluded criteria:** history of anaphylaxis to local anaesthetics, diabetes, hypertension, cyanotic heart disease, pregnancy, neurological and respiratory disease, coagulopathy, acid peptic disease **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

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Tomar 2017 *(Continued)*

Interventions	**Intervention characteristics** Placebo (group B) • *Dose*: saline • *Time point of administration*: after induction • *Route of administration*: perineural • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone (group D) • *Dose*: 8 mg • *Time point of administration*: after induction • *Route of administration*: perineural • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Gaurav Singh Tomar **Institution:** Department of Anaesthesiology and Critical Care, St. Stephen's Hospital, Delhi, India **Email:** spunkygst@gmail.com **Address:** Flat-5C, Vidhata Apartment, Vasundhara enclave, Delhi-96, India **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated using a computer-generated randomization list into 2 groups (n 5 30)"
Allocation concealment (selection bias)	Unclear risk	Quote: "sealed envelops containing one syringe with bupivacaine and saline or bupivacaine and dexamethasone were prepared by an anesthesiology resident not involved in this study" Judgement comment: not stated; "sequentially numbered, opaque" envelopes (SNOSE)

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Tomar 2017 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the enrolled patient, concerned anesthesiologist, and surgeon were unaware of the nature of the drug in each syringe" Quote: "sealed envelops containing one syringe with bupivacaine and saline or bupivacaine and dexamethasone were prepared by an anesthesiology resident not involved in this study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all patients were observed postoperatively by anesthesiology resident who was unaware of the study group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "among 60 patients, 6.67% (2 patients) in group D and 10% (3 patients) in group B were declared as failure to perceive desired effect with medications given. These 5 patients were excluded from the study (Figure 1). Hence, 57 patients were available for data analysis"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "demographic variables in terms of age, gender, body weight, and height were found to be comparable along with duration of surgery in both groups (P. 0.05) (Table 1). The groups were also comparable regarding fentanyl and propofol consumption during intraoperative period (P. 0.05) (Table 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker): unclear; (perioperative opioids): yes

Triem 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dolasetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 54.6 ± 17.4 • *Weight (mean ± SD, median (IQR), median (range))*: 67.2 ± 9.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 7/8/5/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 110.3

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Triem 1999 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 3 µg/kg fentanyl at induction, 16.3 mg piritramide postoperative
- *Type of surgery*: hysterectomy

DHB (droperidol)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 52.4 ± 13.3
- *Weight (mean ± SD, median (IQR), median (range))*: 71.7 ± 12.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 5/12/3/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 129.8
- *Use of perioperative opioids (if yes, which?)*: 3 µg/kg fentanyl at induction, 14.8 mg piritramide postoperative
- *Type of surgery*: hysterectomy

Dolasetron + DHB (droperidol)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 51.8 ± 15.0
- *Weight (mean ± SD, median (IQR), median (range))*: 67.7 ± 11.2
- *BMI (mean +/- SD, median (IQR), median [range])*: NA
- *ASA I/II/III/IV (n)*: 8/9/3/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 107.4
- *Use of perioperative opioids (if yes, which?)*: 3 µg/kg fentanyl at induction, 14.2 mg piritramide postoperative
- *Type of surgery*: hysterectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 50.6 ± 16.7
- *Weight (mean ± SD, median (IQR), median (range))*: 67.1 ± 11.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 8/10/2/0

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Triem 1999 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 111.2
- *Use of perioperative opioids (if yes, which?)*: 3 µg/kg fentanyl at induction, 15.1 mg piritramide postoperative
- *Type of surgery*: hysterectomy

Included criteria: female, ASA I to III, scheduled for elective hysterectomy

Excluded criteria: liver disease (glutamate-oxaloacetate-transaminase > 40 U/L, glutamate-pyruvate-transaminase > 40 U/L), severe renal disease (kreatinine > 2.0 mg/dL), known bowel motility disturbance, history of chemotherapy, fever (> 38°C), known allergy to 5-HT3-receptor antagonists or dehydrobenzperidole, extreme obesity (> 110 kg), had taken antiemetics or vomited in the past 24 hours before administration of study drug, history of psychiatric disease (including addictions) and psychosomatic disorder, NPO 6 hours

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions	**Intervention characteristics** Dolasetron • *Dose*: 50 mg • *Time point of administration*: 45 to 60 minutes before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV DHB (droperidol) • *Dose*: 2.5 mg DHB + placebo • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV (DHB), PO (placebo) • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Dolasetron + DHB (droperidol) • *Dose*: dolasetron 50 mg, DHB 2.5 mg • *Time point of administration*: dolasetron 45 to 60 minutes before induction of anaesthesia, DHB at induction of anaesthesia • *Route of administration*: IV (DHB), PO (placebo) • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo • *Dose*: placebo • *Time point of administration*: 45 to 60 minutes before induction of anaesthesia • *Route of administration*: PO • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 4 hours' observation)* • Outcome type: general notes on side effects

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Triem 1999 *(Continued)*

Identification	**Sponsorship source:** Hoechst Marion Roussel Deutschland provided their product Anemet (Dolasetron); no other financial support **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Swen Piper **Institution:** Klinik für Anästhesiologie und Operative Intensivmedizin, Klinik für Gynäkologie und Geburtshilfe, Klinikum der Stadt Ludwigshafen **Email:** NA **Address:** Klinik für Anästhesiologie und Operative Intensivmedizin Klinikum der Stadt Ludwigshafen, Bremserstraße 79, D-67063 Ludwigshafen a. Rh. **Duration of study:** NA **Language:** German (2 German reviewers) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "um eine randomisierte, prospektive einfach" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: single-blinded study design. Blinding of anaesthesiologists not possible due to study design
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "Zwischen den vier Gruppen bestanden bezüglich demographischer und perioperativer Daten keine signifikanten Unterschiede (Tab. 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

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Tseng 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 70 • *Received treatment (n)*: 70 • *Analysed (n)*: 70 • *Age (mean ± SD, median (IQR), median (range))*: 38 ± 8.342 • *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 10.028 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 13 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 155 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl, 43% of patients received morphine via PCA, 57% of patients received pethidine IM • *Type of surgery*: major gynaecological laparoscopic surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 70 • *Received treatment (n)*: 70 • *Analysed (n)*: 70 • *Age (mean ± SD, median (IQR), median (range))*: 38 ± 8.164 • *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 8.164 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 14 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 135 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl, 38% of patients received morphine via PCA, 62% received pethidine IM • *Type of surgery*: major gynaecological laparoscopic surgery **Included criteria:** women with preoperative diagnosis of benign gynaecological disease, scheduled to undergo inpatient laparoscopic treatment procedures, ASA I or II, 19 to 64 years of age, weighing 31 to 93 kg **Excluded criteria:** abnormal renal or hepatic function test results, had received an antiemetic or medication with antiemetic properties within 24 hours before entering the operating room, had experi-

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Tseng 2006 *(Continued)*

	enced moderate to severe nausea and vomiting the day before surgery, had taken the experimental drug within 3 months of the study, current history of smoking or habitual alcohol consumption, known to have an allergy to 5-HT3-receptor antagonists **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear
Interventions	**Intervention characteristics** Granisetron • *Dose*: 1 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (prochlorperazine 5 mg IM) Placebo • *Dose*: saline • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 67% (prochlorperazine 5 mg IM)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Suh-Yam Wong **Institution:** Chang Gung Memorial Hospital and Chang Gung University **Email:** dw0909@cgmh.org.tw **Address:** Chang Gung Memorial Hospital and Chang Gung University, College of Medicine, 5 Fu-Hsing Street, Gueishan, Taoyuan, Taiwan 333, Republic of China **Language:** English **Duration of study:** July to September 2005 **Trial registry number:** NA **Study's primary outcome:** incidence of PONV

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Tseng 2006 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "after enrolment, patients were randomly allocated (by use of sealed opaque envelopes), via permuted block method with a block of four, into two groups. 'Blocks' having equal numbers of As and Bs (A = granisetron and B = saline solution) are used, with the order of treatmends within the block being randomly permuted. A random number sequence was used to choose a particular block, which sets the allocation order to the first four subjects. Similarly, the treatment group is allocated to the next four patients in the order specified by the next randomly selected block. The process is then repeated"
Allocation concealment (selection bias)	Low risk	Judgement comment: quote: "after enrolement, patients were randomly allocated (by use of sealed opaque envelopes), via permuted block method with a block of four, into two groups"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote" "all of the study drugs were prepared and given in equal amount of 5 mL so that investigators were blinded to the drug and dose given"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the nurses, without knowing the patient allocation, started continuous observation of the patients in the recovery room"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV, perioperative opioids): no; (history of motion sickness): unclear

Tsui 1999

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA

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Tsui 1999 *(Continued)*

- *Analysed (n)*: 39
- *Age (mean ± SD, median (IQR), median (range))*: 46.5 ± 10.0
- *Weight (mean ± SD, median (IQR), median (range))*: 55.9 ± 11.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 15/22/2/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, intraoperative and postoperative morphine via PCA
- *Type of surgery*: gynaecological laparotomy

Tropisetron (group T)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 37
- *Age (mean ± SD, median (IQR), median (range))*: 49.8 ± 11.5
- *Weight (mean ± SD, median (IQR), median (range))*: 59.5 ± 10.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 14/23/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 89
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, intraoperative and postoperative morphine via PCA
- *Type of surgery*: gynaecological laparotomy

Control (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 45
- *Age (mean ± SD, median (IQR), median (range))*: 49.6 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 55.6 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 23/18/4/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 87
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, intraoperative and postoperative morphine via PCA
- *Type of surgery*: gynaecological laparotomy

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Tsui 1999 *(Continued)*

Included criteria: scheduled for gynaecological laparotomy

Excluded criteria: over 65 years of age, ASA III or more, significant medical disease, known allergy to tropisetron or ondansetron, received antiemetic within 24 hours of the operation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Tropisetron (group T) • *Dose*: 5 mg • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Control (group C) • *Dose*: saline • *Time point of administration*: before induction of general anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** S.L. Tsui **Institution:** Division of Pain Management, Department of Anaesthesiology, Queen Mary Hospital, Hong Kong **Email:** NA **Address:** Division of Pain Management, Department of Anaesthesiology, Queen Mary Hospital, 102 Pokfulam Road, Pokfulam, Hong Kong **Duration of study:** NA **Language:** English

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Tsui 1999 *(Continued)*

	Study's primary outcome: incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly allocated into one of the following groups". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "all interviews concerning nausea or vomit scores were conducted by a single team of nurses blinded to the drug used"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no information on numbers of enrolled and randomized participants.
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Tsutsumi 2014

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Fosaprepitant (NK1 group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 34 • *Received treatment (n)*: 34 • *Analysed (n)*: 32 • *Age (mean ± SD, median (IQR), median (range))*: 62 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 59 ± 11 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Tsutsumi 2014 *(Continued)*

- *ASA I/II/III/IV (n)*: 2/30/0/0
- *Gender (female in %)*: 53.13
- *Non-smoker (%)*: 93.75
- *History of PONV/motion sickness (%)*: 6.25
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 460
- *Use of perioperative opioids (if yes, which?)*: 6.8 mg remifentanil intraoperative, 1 patient received 15 mg pentazocine IV postoperative
- *Type of surgery*: craniotomy

Ondansetron (ONS group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 34
- *Received treatment (n)*: 34
- *Analysed (n)*: 32
- *Age (mean ± SD, median (IQR), median (range))*: 58 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 1/31/0/0
- *Gender (female in %)*: 65.63
- *Non-smoker (%)*: 87.5
- *History of PONV/motion sickness (%)*: 6.25
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 513
- *Use of perioperative opioids (if yes, which?)*: 8.0 mg remifentanil intraoperative, 1 patient received 15 mg pentazocine IV postoperative
- *Type of surgery*: craniotomy

Included criteria: 20 to 80 years of age, ASA I or II, undergoing elective craniotomy under general anaesthesia

Excluded criteria: ASA III or IV, neuronal disease, abnormal liver and/or renal function, receiving another antiemetic

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioid): no

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Interventions

Intervention characteristics

Fosaprepitant (NK1 group)

- *Dose*: 150 mg
- *Time point of administration*: before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 10 mg metoclopramide

Ondansetron (ONS group)

- *Dose*: 4 mg
- *Time point of administration*: before anaesthesia induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 10 mg metoclopramide

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Outcomes

Vomiting (0 to 24 hours)

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Tsutsumi 2014 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (0 to 2 hours)

- Outcome type: dichotomous outcome

PONV (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 48 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this work was supported by JSPS KAKENHI Grants nos. 24791598 and 25861378 **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Yasuo M. Tsutsumi **Institution:** Department of Anesthesiology, The University of Tokushima, Japan **Email:** tsutsumi@tokushima-u.ac.jp **Address:** Department of Anesthesiology, The University of Tokushima, 3-18-15 Kuramoto, Tokushima 770-8503, Japan **Duration of study:** 1 October 2012 to 5 February 2014 **Language:** English **Study's primary outcome:** incidence of vomiting (power analysis) **Trial registry number:** JPRN-UMIN000008621
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the patients received allocations in a randomized, double-blinded manner using a computer-generated distribution (QuickCalcs, GraphPad Inc., La Jolla, CA, USA)"
Allocation concealment (selection bias)	Unclear risk	Quote: "on the day of surgery, patients were randomized to 1 of 2 groups" Quote: "to ensure blinding among the investigators, the randomization schedule was generated by a statistician who was not involved in the clinical study" Judgement comment: insufficient information on allocation concealment (was the randomization code kept in sequentially numbered, opaque, and sealed envelopes?)
Blinding of participants and personnel (performance bias)	Low risk	Quote: "to ensure blinding among the investigators"

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Tsutsumi 2014 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an anesthesiologist unaware of the patients' randomization collected the data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "70 randomized patients, 68 received study medications and 64 completed the trial: 32 in the NK1 group and 32 in the ONS group (Figure 1)" Judgement comment: reasons for missing outcome data were reported: prolonged postoperative ventilation, loss to follow-up, abnormal liver function. Exclusions are balanced among groups
Selective reporting (reporting bias)	Unclear risk	Judgement comment: JPRN-UMIN000008621 (prospective registration). The final study report did not identify the primary outcome
Other bias	Low risk	Quote: "there was no difference in patient demographics, risk factors for PONV, duration of surgery and anesthesia, intraoperative opioid usage, or postoperative analgesic consumption between the 2 groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioid): no

Turhanoglu 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: 25 • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 41.9 ± 11.7 • *Weight (mean ± SD, median (IQR), median (range))*: 69.9 ± 15.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 131.2 • *Use of perioperative opioids (if yes, which?)*: 5 µg/kg fentanyl, 225 ± 64.3 mg pethidine • *Type of surgery*: major elective gynaecological surgery Ondansetron + dimenhydrinate • *Assessed for eligibility (n)*: -

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Turhanoglu 1999 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 44.3 ± 11.6
- *Weight (mean ± SD, median (IQR), median (range))*: 71.6 ± 10.9
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 128
- *Use of perioperative opioids (if yes, which?)*: 5 µg/kg fentanyl, 235 ± 57.9 mg pethidine
- *Type of surgery*: major elective gynaecological surgery

Dimenhydrinate

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 44.5 ± 10.8
- *Weight (mean ± SD, median (IQR), median (range))*: 71.4 ± 15.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 130.8
- *Use of perioperative opioids (if yes, which?)*: 5 µg/kg fentanyl, 232 ± 58.2 mg pethidine
- *Type of surgery*: major elective gynaecological surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 25
- *Received treatment (n)*: 25
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 43.7 ± 9.4
- *Weight (mean ± SD, median (IQR), median (range))*: 68.3 ± 12.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 131.2
- *Use of perioperative opioids (if yes, which?)*: 5 µg/kg fentanyl, 220 ± 67.5 mg pethidine
- *Type of surgery*: major elective gynaecological surgery

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Turhanoglu 1999 *(Continued)*

Included criteria: ASA I or II, women, 30 to 56 years of age, weighing 54 to 83 kg, undergoing major elective gynaecological surgery

Excluded criteria: morbidly obese, history of motion sickness, liver disease, allergy to any of the study drugs, history of PONV during previous surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg, saline • *Time point of administration*: ondansetron just before anaesthesia induction, saline 30 minutes before surgery • *Route of administration*: ondansetron IV, saline IM • *Rescue antiemetics (if yes, which?)*: 32% (metoclopramide 10 mg) Ondansetron + dimenhydrinate • *Dose*: ondansetron 4 mg, dimenhydrinate 50 mg • *Time point of administration*: ondansetron just before anaesthesia induction dimenhydrinate 30 minutes before surgery • *Route of administration*: ondansetron IV, dimenhydrinate IM • *Rescue antiemetics (if yes, which?)*: 4% (metoclopramide 10 mg) Dimenhydrinate • *Dose*: 50 mg • *Time point of administration*: dimenhydrinate 30 minutes before surgery, saline just before anaesthesia induction • *Route of administration*: dimenhydrinate IM, saline IV • *Rescue antiemetics (if yes, which?)*: 24% (metoclopramide 10 mg) Placebo • *Dose*: saline 0.9% • *Time point of administration*: first dose 30 minutes before surgery and second dose just before anaesthesia induction • *Route of administration*: saline first dose IM and second dose IV • *Rescue antiemetics (if yes, which?)*: 60% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome

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Turhanoglu 1999 *(Continued)*

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, singe-centre **Author's name:** S. Turhanoglu **Institution:** Departement of Anaesthesiology, Faculty of Medicine, University of Dicle, Diyarbakir, Turkey **Email:** NA **Address:** Dicle Üniversitesi Rektörlüğü, 21280 Sur/Diyarbakır **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "patients were randomly allocated to receive one of four medications according to a double-blind protocol" No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the drugs were prepared by the same anaesthesiologist who was not included in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "a trained nurse, blinded to the study drugs, assessed nausea (...) and vomiting (...) during each interval and recorded at the end of each interval"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

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Turner 2004

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 46 • *Age (mean ± SD, median (IQR), median (range))*: 33 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 3 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 71.74/32.61 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 40 • *Use of perioperative opioids (if yes, which?)*: 126 µg fentanyl intraoperative • *Type of surgery*: gynaecological laparoscopic surgery Dimenhydrinate • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 48 • *Age (mean ± SD, median (IQR), median (range))*: 34 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24 ± 3 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 68.75/77.08 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 40 • *Use of perioperative opioids (if yes, which?)*: 130 µg fentanyl intraoperative • *Type of surgery*: gynaecological laparoscopic surgery Droperidol + dimenhydrinate • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 47 • *Age (mean ± SD, median (IQR), median (range))*: 34 ± 6

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Turner 2004 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 26 ± 5
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 61.70/42.55
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 44
- *Use of perioperative opioids (if yes, which?)*: 143 µg fentanyl intraoperative
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: women scheduled for elective outpatient gynaecological laparoscopic surgery

Excluded criteria: pregnant; intolerant or allergic to any of the drugs used in the study protocol; underlying gastrointestinal disease requiring active treatment; known history of vomiting or use of antiemetic drugs in the last 24 hours; body mass index > 35; concurrent use of antihistamines, phenothiazines, or drugs with known antiemetic effect; inability to ingest oral medication with a sip (approximately 30 mL) of water

Pretreatment: baseline characteristics (age): no; (ASA): unclear; (BMI): yes. Potential effect modifiers (gender, history of PONV, duration of anaesthesia, perioperative opioids): no; (non-smoker): unclear; (history of motion sickness): yes

Interventions

Intervention characteristics

Droperidol

- *Dose*: 0.625 mg
- *Time point of administration*: before induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: ondansetron

Dimenhydrinate

- *Dose*: 75 mg (25 mg immediate + 50 mg sustained release drug)
- *Time point of administration*: one hour before anticipated procedure time
- *Route of administration*: PO
- *Rescue antiemetics (if yes, which?)*: ondansetron

Droperidol + dimenhydrinate

- *Dose*: dimenhydrinate LA 75 mg (25 mg immediate + 50 mg sustained release drug), droperidol 0.625 mg
- *Time point of administration*: dimenhydrinate LA 1 hour before anticipated procedure time, droperidol before induction
- *Route of administration*: PO, IV
- *Rescue antiemetics (if yes, which?)*: ondansetron

Outcomes

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification

Sponsorship source: NA

Country: Canada

Setting: outpatient, single-centre

Author's name: Kim E. Turner

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Turner 2004 *(Continued)*

Institution: Department of Anesthesiology, Kingston General Hospital, Kingston, Ontario, Canada

Email: ket1@post.queensu.ca

Address: Department of Anesthesiology, Kingston General Hospital, 76 Stuart St., Kingston, Ontario, Canada, K7L 2S6

Duration of study: NA

Language: English

Study's primary outcome: complete treatment failure (CTF) defined as administration of rescue medication in PACU or nausea, vomiting, or retching at any time point during the study

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomized using a computer- generated randomization table, in a stratified manner"
Allocation concealment (selection bias)	Unclear risk	Quote: "all study drug packages were prepared in pharmacy to contain active GLA capsules or an identical placebo and a preloaded syringe containing IV droperidol 0.625 mg or an identical syringe of saline" Judgement comment: no statement on allocation concealment and randomization details
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, study and hospital personnel were blinded to the medication received"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "trained study personnel collected all information recorded in the patient diaries via telephone interview" Quote: "patients, study and hospital personnel were blinded to the medication received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there were no significant differences among the three groups with respect to demographics, type of surgery, or anesthetic medications (Table 1), except that body mass index was significantly greater in the combination group (P 0.05)" Judgement comment: baseline characteristics (age): no; (ASA): unclear; (BMI): yes. Potential effect modifiers (gender, history of PONV, duration of anaesthesia, perioperative opioids): no; (non-smoker): unclear; (history of motion sickness): yes

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Tzeng 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 32 ± 5 • *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 42/NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 7.8 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl intraoperative • *Type of surgery*: dilatation and curettage to terminate pregnancy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 36 • *Age (mean ± SD, median (IQR), median (range))*: 33 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 50/NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 7.2 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl intraoperative • *Type of surgery*: dilatation and curettage to terminate pregnancy Droperidol + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 37

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Tzeng 2000 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 41/NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 5.9
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl intraoperative
- *Type of surgery*: dilatation and curettage to terminate pregnancy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 32 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 55 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 40/NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 7.5
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl intraoperative
- *Type of surgery*: dilatation and curettage to terminate pregnancy

Included criteria: ASA I or II, women undergoing outpatient dilatation and curettage under intravenous general anaesthesia, 20 to 45 years of age, 6 to 10 weeks pregnant

Excluded criteria: clinical laboratory evidence of severe renal, haematologic, or hepatic abnormalities or history of drug abuse; any antiemetic therapy within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV): no; (history of motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: 1 minute before initiation of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 29% (metoclopramide 10 mg)

Droperidol

- *Dose*: 1.25 mg
- *Time point of administration*: 1 minute before initiation of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 14% (metoclopramide 10 mg)

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Tzeng 2000 *(Continued)*

	Droperidol + dexamethasone • *Dose*: droperidol 1.25 mg, dexamethasone 8 mg • *Time point of administration*: 1 minute before initiation of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 14% (metoclopramide 10 mg) Placebo • *Dose*: saline • *Time point of administration*: 1 minute before initiation of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 38% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** outpatient, single-centre **Author's name:** Dr. Jann-Inn Tzeng **Institution:** Department of Anesthesiology, Municipal Women's and Children's General Hospital, Kaohsiung, Taiwan **Email:** NA **Address:** Department of Anesthesiology, Municipal Women's and Children's General Hospital, Kaohsiung, Taiwan **Language:** English **Duration of study:** NA **Trial registry number:** NA

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Tzeng 2000 *(Continued)*

	Study's primary outcome: incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "before the study, a randomization table was made for assignment of patients to four groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: insufficient information on allocation concealment ("the randomized process was concealed...")
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "the randomized process and the identity of the study drugs were concealed to the patients, the anaesthesiologists who were involved in the anaesthesia, ..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "the randomized process and the identity of the study drugs were concealed to the patients, the anaesthesiologists who were involved in the anaesthesia, and the investigators who collected the postoperative data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: quote: "of the 160 patients who were enrolled in this study, 9 were excluded due to loss of contact by telephone after discharge (7 patients) or intraoperative bleeding of more than 500 ml (2 patients)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, history of PONV): no; (history of motion sickness, non-smoker): unclear

Ulusoy 1996

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 28.0 ± 14.2 • *Weight (mean ± SD, median (IQR), median (range))*: 70.5 ± 14.4 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0

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Ulusoy 1996 *(Continued)*

- *Gender (female in %)*: 40
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 96.0
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: emergency major abdominal operation

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 29.8 ± 13.5
- *Weight (mean ± SD, median (IQR), median (range))*: 69.9 ± 4.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 35
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, isoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 78.0
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: emergency major abdominal operation

Included criteria: ASA I or II, both sexes, 18 to 65 years of age, undergoing emergency major abdominal operation under general anaesthesia

Excluded criteria: body weight < 45 kg or > 90 kg; pregnant and nursing; major renal, hepatic, or cardiovascular disorder, as shown in laboratory and clinic examination; had taken antiemetic agent during 24 hours before induction; nausea and vomiting; were planned for a liver or peritoneal intragastric tube during operation; received a postoperative nasogastric tube

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron • *Dose*: 4 mg • *Time point of administration*: before induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome

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Ulusoy 1996 *(Continued)*

	Nausea (0 to 24 hours) • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** H. Ulusoy **Institution:** Department of Anaesthesiology, Karadeniz Technical University, Farabi Hospital, Trabzon, Turkey **Email:** NA **Address:** Department of Anaesthesiology, Karadeniz Technical University, Farabi Hospital, 61080, Trabzon, Turkey **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two publications with identical content but different year/volume: secondary publications

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: hospital pharmacist prepared study drugs and labelled both as ondansetron. Blinding assumed
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")

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Ulusoy 1996 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Unal 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 43.9 ± 12.2 • *Weight (mean ± SD, median (IQR), median (range))*: 66.9 ± 13.1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 14/6/0/0 • *Gender (female in %)*: 70 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 166.9 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil infusion at a dose of 0.2 µg/kg • *Type of surgery*: middle ear operation Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20

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Unal 2009 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 46.1 ± 13.1
- *Weight (mean ± SD, median (IQR), median (range))*: 67.4 ± 12.6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 16/2/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 164.3
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil infusion at a dose of 0.2 µg/kg
- *Type of surgery*: middle ear operation

Included criteria: adult, 25 to 55 years of age, 39 female and 21 male, scheduled for middle ear operation, ASA I or II

Excluded criteria: history of hepatic, renal, cardiovascular disease; chronic obstructive pulmonary disease; haematological and/or gastrointestinal disorder; hypersensitivity to propofol or any other drugs; history of vertigo and motion sickness; pregnant or menstruating; had taken antiemetics 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Metoclopramide • *Dose*: 0.2 mg/kg • *Time point of administration*: at time of skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 35% (10 mg metoclopramide) Placebo • *Dose*: serum physiological solution (0.9%) (bolus) • *Time point of administration*: at time of skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 65% (10 mg metoclopramide)
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 12 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** Mustafa Arslan **Institution:** Department of Anesthesiology and Reanimation, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

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Unal 2009 *(Continued)*

	Email: mustarslan@gmail.com **Address:** Department of Anesthesiology and Reanimation, Faculty of Medicine, Gazi University, Özel Yaşam Tıp Merkezi Zafer Cad. 7 **Duration of study:** December 2004 to October 2005 **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were assigned to one of the 3 study groups using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "all syringes with propofol, metoclopramide, or placebo were prepared by the same investigator. Administration of anesthesia and drugs used in the study and intraoperative data collection were made by the other investigators blinded to the study drugs" Judgement comment: no statement on blinding of participants
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there was no significant difference among the study groups in terms of age, body weight, length, ASA group, gender, duration of operation, and anesthesia" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Uppington 1986

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis

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Uppington 1986 *(Continued)*

Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 21 • *Received treatment (n)*: NA • *Analysed (n)*: 19 • *Age (mean ± SD, median (IQR), median (range))*: 39.3 ± 6.3 • *Weight (mean ± SD, median (IQR), median (range))*: 64.6 ± 10.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperative • *Type of surgery*: major gynaecological surgery Transdermal hyoscine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 21 • *Received treatment (n)*: NA • *Analysed (n)*: 19 • *Age (mean ± SD, median (IQR), median (range))*: 39.9 ± 7.1 • *Weight (mean ± SD, median (IQR), median (range))*: 65.9 ± 6.9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, enflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: fentanyl intraoperative • *Type of surgery*: major gynaecological surgery **Included criteria:** adult women, ASA I and II, between 18 and 65 years of age, undergoing major gynaecological surgery (vaginal or abdominal hysterectomy, oophorectomy, or tubal surgery) **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo • *Dose*: placebo patch • *Time point of administration*: on the evening before surgery • *Route of administration*: transdermal

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Uppington 1986 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM, prochlorperazine 12.5 mg IM, if more than 3 or 4 doses needed

Transdermal hyoscine

- *Dose*: 1.5 mg (0.5 mg over 3 days)
- *Time point of administration*: on the evening before surgery
- *Route of administration*: transdermal
- *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IM, prochlorperazine 12.5 mg IM, if more than 3 or 4 doses needed

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 24 hours, 24 to 48 hours, 48 to 72 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** UK **Setting:** inpatient, single-centre **Author's name:** J. Uppington **Institution:** Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford **Email:** NA **Address:** Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford, OX2 OHE **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated to receive either a transdermal hyoscine patch (Transderm Scop, ALZA Corp.) or placebo"

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Uppington 1986 *(Continued)*

		Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the placebo was a Band-aid patch (Johnson and Johnson) and each hyoscine patch was covered by a similar Band-aid for protection and so that its identity could not be distinguished from placebo by patient or assessor" Judgement comment: no information on blinding of anaesthesiologists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients were visited 24, 48 and 72 hours postoperatively by an author who had not seen them pre-operatively and who had not been told which medication they had been given"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 42 patients who started the trial, four were withdrawn. Three of these received non-standard anaesthetics (extradural or spinal block), two in the hyoscine group and one in the placebo group. The other patient who was withdrawn was in the placebo group, and had been given metoclopramide prior to induction. Thus, data on 38 patients were completed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the mean values (SD) for age were 39.9 (7.1) and 39.3 (6.3) years in the hyoscine and placebo groups respectively. The respective weights were 65.9 (6.9) and 64.6 (10.7) kg. These differences were not statistically significant" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Valanne 1985

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 27 ± 5.6 • *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 14 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 38.78 • *Non-smoker (%)*: NA

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Valanne 1985 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 58
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: restorative dentistry, oral surgery

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 28 ± 5.6
- *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 26
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (enflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 62
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: restorative dentistry, oral surgery

Included criteria: un-premedicated, ASA I or II, undergoing restorative dentistry or oral surgery under general anaesthesia

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Droperidol • *Dose*: 0.014 mg/kg • *Time point of administration*: 5 minutes after intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: saline • *Time point of administration*: 5 minutes after intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 12 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)*

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Valanne 1985 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 2 days' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Finland **Setting:** outpatient, single-centre **Author's name:** Jukka Valanne **Institution:** Department of Anaesthesia, Lappi Central Hospital, Rovaniemi **Email:** NA **Address:** Department of Anaesthesia, Lappi Central Hospital, SF-96100 Rovaniemi 10, Finland **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "random fashion". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one patient in the droperidol group was excluded because he did not wake up within 1 h, and thus the tests were not performed on schedule. He was discharged from the clinic 3 h 20 min after anaesthesia"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Vale 2011

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 22 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 53 ± 17 • *Weight (mean ± SD, median (IQR), median (range))*: 70 ± 16 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 6/12/2/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 85 • *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia, tramadol in PCA • *Type of surgery*: non-laparoscopic hernioplasty (inguinal (15), crural (1), umbilical (4), incisional (1), thyroidectomy (19)) Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 22 • *Received treatment (n)*: 20 • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 59 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 73 ± 13 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 2/16/2/0 • *Gender (female in %)*: 50 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 97 • *Use of perioperative opioids (if yes, which?)*: fentanyl for anaesthesia, tramadol in PCA • *Type of surgery*: non-laparoscopic hernioplasty (inguinal (15), crural (1), umbilical (4), incisional (1), thyroidectomy (19)) **Included criteria:** 18 to 75 years of age, ASA I to III, undergoing elective non-laparoscopic hernioplasty under general balanced anaesthesia and postoperative analgesia by PCA for 24 hours **Excluded criteria:** allergy to tramadol, ondansetron, or another antagonist at 5-HT3 receptors; pregnant and lactating women; inability to use or understand PCA; history of epilepsy; history of severe renal or hepatic impairment; history of alcohol or drug abuse; use of analgesic, antidepressant, antipsychotic, antiepileptic, rifampicin, or antiemetic medications; history of PONV or motion sickness

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Vale 2011 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes
Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: at beginning of wound closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 4 mg IV, propofol 20 mg IV Placebo • *Dose*: saline 0.9% • *Time point of administration*: at beginning of wound closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: dexamethasone 4 mg IV, propofol 20 mg IV
Outcomes	*Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** this work had no financial support or sponsorship **Country:** Portugal **Setting:** inpatient, single-centre **Author's name:** Frederico C. Pereira **Institution:** Laboratory of Pharmacology and Experimental Therapeutics/Biomedical Institute for Research on Light and Image, Faculty of Medicine, University of Coimbra **Email:** fredcp@ci.uc.pt **Address:** Laboratory of Pharmacology and Experimental Therapeutics/Biomedical Institute for Research on Light and Image, Faculty of Medicine, University of Coimbra PT–3000-354 Coimbra (Portugal) **Duration of study:** NA **Language:** English **Study's primary outcome:** tramadol consumption **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "they were allocated into two groups using a computer-generated randomization list"
Allocation concealment (selection bias)	Unclear risk	Quote: "both solutions were prepared in a 2-ml syringe, according to the randomization plan, by a nurse not involved in patient care" Judgement comment: no further statement provided

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Vale 2011 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "staff members involved in patient care as well as investigators and patients were blinded to patient assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "staff members involved in patient care as well as investigators and patients were blinded to patient assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: 2 participants in each group were excluded due to use of rescue medication for pain and emesis
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "during the 2nd hour of PCA, tramadol consumption (mg x kg^{-1} x h^{-1}) was 41% greater in group O than in group C (fig. 2). This increment in tramadol consumption in group O decreased by 57% during the 2- to 4-hour period and disappeared during the last 20-hour period" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes

Vallejo 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Aprepitant + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 75 • *Received treatment (n)*: 75 • *Analysed (n)*: 75 • *Age (mean ± SD, median (IQR), median (range))*: 43.7 ± 14.3 • *Weight (mean ± SD, median (IQR), median (range))*: 73.8 ± 17.7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 93.3 • *Non-smoker (%)*: 89.3 • *History of PONV/motion sickness (%)*: 33.3/29.3 • *Type of general anaesthesia*: inhalational anesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 164.3 • *Use of perioperative opioids (if yes, which?)*: 97.3% received postoperative opioids • *Type of surgery*: plastic surgery Ondansetron

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Vallejo 2012 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 75
- *Received treatment (n)*: 75
- *Analysed (n)*: 75
- *Age (mean ± SD, median (IQR), median (range))*: 45.3 ± 16.3
- *Weight (mean ± SD, median (IQR), median (range))*: 76.5 ± 18.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 93.3
- *Non-smoker (%)*: 88.0
- *History of PONV/motion sickness (%)*: 34.7 / 26.7
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 153.2
- *Use of perioperative opioids (if yes, which?)*: 98.7% received postoperative opioids
- *Type of surgery*: plastic surgery

Included criteria: men and women; 18 to 65 years of age; ASA I to III; considered at high risk for postoperative nausea and vomiting; undergoing ambulatory plastic surgery under general anaesthesia of at least 1 hour duration were eligible for this prospective, randomized, double-blind trial. Subjects were recruited on the day of surgery during the preoperative evaluation by study investigators (M.C.V. and R.C.R.), who were anaesthesiologists already involved in patient care. Major postoperative nausea and vomiting patient-related risk factors for inclusion in this study were (1) female gender, (2) history of postoperative complication or history of motion sickness, (3) non-smoking status, (4) postoperative use of opioids. Patients with 2 or more risk factors were eligible for the study. All patients who were scheduled for either outpatient or 23-hour observation were included in the study, as,depending on the time of day, the 2 groups of patients were interchangeable

Excluded criteria: patient refusal to participate in the study, had received other antiemetics before their procedure, history of allergy or sensitivity to study drugs, pregnancy, history of long-term opioid use (chronic pain syndrome). Women of reproductive age were routinely screened for pregnancy; patients who were pregnant were informed and excluded from the study

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions

Intervention characteristics

Aprepitant + ondansetron

- *Dose*: aprepitant 40 mg, ondansetron 4 mg
- *Time point of administration*: aprepitant 2 hours before scheduled operation, ondansetron after endotracheal intubation
- *Route of administration*: oral aprepitant, IV ondansetron
- *Rescue antiemetics (if yes, which?)*: NA (4 mg ondansetron, 4 mg dexamethasone, 10 mg metoclopramide, 6.25 mg promethazine, 1 mg granisetron, 10 mg prochlorperazine, transdermal scopolamine patch, 0.625 mg droperidol, 12.5 mg dolasetron)

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: placebo 2 hours before scheduled operation, ondansetron after endotracheal intubation
- *Route of administration*: oral placebo, IV ondansetron
- *Rescue antiemetics (if yes, which?)*: NA (4 mg ondansetron, 4 mg dexamethasone, 10 mg metoclopramide, 6.25 mg promethazine, 1 mg granisetron, 10 mg prochlorperazine, a transdermal scopolamine patch, 0.625 mg droperidol, 12.5 mg dolasetron)

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Vallejo 2012 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** grant support, including study drug and placebo, was provided by Merck Healthcare, Whitehouse Station, NJ, USA, and the Department of Anesthesiology, Magee-Womens Hospital, Pittsburgh, PA, USA. Study authors have no other disclosures to report in relation to the content of this article **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Manuel C. Vallejo **Institution:** Department of Anesthesiology, Magee-Womens Hospital of the University of Pittsburgh, Medical Center, USA **Email:** vallejomc@anes.upmc.edu **Address:** Medical Center 300 Halket Street Pittsburgh, PA 15213, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of vomiting at any time within the first 48 hours after surgery **Trial registry number:** PRO07070325
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...one of the study investigators. Patients were randomized by a computer-generated number table(http://www.graphpad.com/ quickcalcs/randomize1.cfm), which the pharmacy department used to assign patients to one of two groups (group A: 40 mg of oral aprepitant plus 4 mg of intravenous ondansetron; or group B: oral placebo plus intravenous 4 mg of ondansetron intravenously). The oral aprepitant or placebo..."
Allocation concealment (selection bias)	Low risk	Judgement comment: central allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the placebo and study drug were identical in appearance; hence, both the investigators and the patients were blinded to the patient's study group, eliminating any potential bias"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a study investigator blinded to the treatment group recorded the occurrence of nausea and vomiting in the preoperative period, on admission to the postanesthesia care unit, and at hourly intervals until the patient was discharged from the hospital. While at home, patients rated their nausea according to the same scale, indicated whether they retched or vomited, and recorded in a structured diary which analgesics they consumed. Patients made diary entries every 4 hours while awake for up to 24 hours after the first day of

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Vallejo 2012 *(Continued)*

		surgery, and every 8 hours while awake during the second day after surgery (48 hours). The information from the patient diary was obtained through a follow-up telephone interview by the principal investigator"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 150 patients were enrolled, and only one patient was lost during follow-up (did not answer follow-up telephone calls or return daily log). Data for this subject were included in the results until hospital discharge. All other patients completed their daily log"
Selective reporting (reporting bias)	High risk	Judgement comment: PRO07070325 (prospective registration). The prospectively registered primary outcome (number of participants having postoperative emesis and nausea) was changed in the final study report (incidence of vomiting only) and "nausea" moved to secondary endpoints in the final study article
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Veneziani 2006

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo (group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 47.7 ± 14.1 • *Weight (mean ± SD, median (IQR), median (range))*: 63.4 ± 11.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (N_2O, sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 78.89 • *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 1.5 µg/kg + 50 µg/h, morphine PCA • *Type of surgery*: major gynaecological surgery by laparotomy Dehydrobenzperidol (group DBP) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 25

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Veneziani 2006 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 55.4 ± 16.7
- *Weight (mean ± SD, median (IQR), median (range))*: 64.6 ± 8.95
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 72.78
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 1.5 µg/kg + 50 µg/h, morphine PCA
- *Type of surgery*: major gynaecological surgery by laparotomy

Dolasetron (group A)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 52.5 ± 13.7
- *Weight (mean ± SD, median (IQR), median (range))*: 61.5 ± 9.25
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 77.94
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 1.5 µg/kg + 50 µg/h, morphine PCA
- *Type of surgery*: major gynaecological surgery by laparotomy

Dexamethasone + dolasetron (group AD)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 25
- *Age (mean ± SD, median (IQR), median (range))*: 47.9 ± 14.1
- *Weight (mean ± SD, median (IQR), median (range))*: 64.8 ± 14.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 75.00
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 1.5 µg/kg + 50 µg/h, morphine PCA
- *Type of surgery*: major gynaecological surgery by laparotomy

Included criteria: women, ASA classes I and II, 25 to 80 years of age, about to undergo major gynaecological surgery by laparotomy

Excluded criteria: ASA III; renal and hepatic insufficiency; pregnancy; current menstruation; body weight > 50% of ideal weight; vomiting or nausea in the 24 hours before surgery; psychoactive or

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Veneziani 2006 *(Continued)*

	antiemetic medication in the preceding 24 hours; positive history for cardiovascular, respiratory, metabolic, endocrine, or neurological disease; drug or alcohol abuse **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear
Interventions	**Intervention characteristics** Placebo (group P) • *Dose*: saline • *Time point of administration*: after surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dehydrobenzperidol (group DBP) • *Dose*: 1.25 to 2.5 mg or 10 to 20 µg/kg on the basis of age and clinical condition • *Time point of administration*: at beginning of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dolasetron (group A) • *Dose*: 12.5 mg • *Time point of administration*: at time of suturing wounds • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone + dolasetron (group AD) • *Dose*: dexamethasone 8 mg, dolasetron 12.5 mg • *Time point of administration*: dexamethasone at entry into the operating theatre, dolasetron at beginning of suturing • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, single-centre **Author's name:** Andrea Veneziani **Institution:** Anestesia e Rianimazione, Nuovo Ospedale San Giovanni di Dio, Azienda Ospedaliera, Firenze **Email:** andyven@ciao.cc

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Veneziani 2006 *(Continued)*

Address: Via delle Campora, 19-50124 Firenze

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "participants were randomly assigned to four groups based on the type of intravenous antiemetic therapy received" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "group A were given a bolus with dolasetron 12.5 mg at time of suturing wounds; Group AD received dexamethasone 8 mg at entry in the operating theatre plus dolasetron 12.5 mg in a bolus at the beginning of suturing. The various timings of administration were compatible with the pharmacokinetic/pharmacodynamic differences of the drugs used" Judgement comment: no blinding of anaesthetists due to different time points of administration
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the study observation period was 24 hours post-surgery during which an investigator (blind as to the type of treatment received) recorded the onset of episodes of nausea associated or not to vomiting, the number of such episodes and whether isolated, prolonged and/or repeated"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the sample demographic characteristics and the length of treatments, expressed as mean and standard deviation are shown on table 2. Groups were matched for age, body weight, SPAIAS score and duration of surgery" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Verhasselt 1988

Study characteristics

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Verhasselt 1988 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different time points of administration
Participants	**Baseline characteristics** Control (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 55 • *Age (mean ± SD, median (IQR), median (range))*: 42.4 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: curettage or laparoscopy Droperidol (group 2: IM) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 66 • *Age (mean ± SD, median (IQR), median (range))*: 37.9 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: curettage or laparoscopy Droperidol (group 3: IV) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 71 • *Age (mean ± SD, median (IQR), median (range))*: 37.7 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0

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Verhasselt 1988 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: curettage or laparoscopy

Included criteria: female, 19 to 82 years of age, undergoing curettage or laparoscopy and without history of vomiting with previous anaesthesia, ASA I or II

Excluded criteria: NA

Pretreatment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control (group 1) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: NA Droperidol (group 2: IM) • *Dose*: 0.050 mg/kg • *Time point of administration*: during premedication • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: NA Droperidol (group 3: IV) • *Dose*: 0.050 mg/kg • *Time point of administration*: during induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Belgium **Setting:** inpatient, single-centre **Author's name:** L. Verhasselt **Institution:** St. Lucaskliniek, Laar 140, 2070 Ekeren, Belgium **Email:** NA **Address:** U. Z. Gasthuisberg, Herestraat 49, 3000 Leuven

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Verhasselt 1988 *(Continued)*

	Duration of study: NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Three out of 4 groups relevant (treatment)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomized". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: blinding not possible due to different interventions at different time points and no placebo intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: quote: "the patients were closely observed by recovery nurses". No further information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Voigt 2011-1

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, combination prophylaxis
Participants	**Baseline characteristics** Control (VP group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 81 • *Received treatment (n)*: NA

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Voigt 2011-1 *(Continued)*

- *Analysed (n)*: 81
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 88.9
- *History of PONV/motion sickness (%)*: 22.2/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane or desflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or remifentanil, 66.7% of patients received postoperative opioids
- *Type of surgery*: elective breast surgery

Haloperidol + tropisetron (VHT group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 81.3
- *History of PONV/motion sickness (%)*: 26.3/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane or desflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or remifentanil, 48.8% of patients received postoperative opioids
- *Type of surgery*: elective breast surgery

Dimenhydrinate + dexamethasone (VDD group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 79
- *Received treatment (n)*: NA
- *Analysed (n)*: 79
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 87.3
- *History of PONV/motion sickness (%)*: 26.6/NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane or desflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or remifentanil, 57% of patients received postoperative opioids
- *Type of surgery*: elective breast surgery

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Voigt 2011-1 *(Continued)*

Included criteria: scheduled for different types of elective breast surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV): no; (history of motion sickness, duration of anaesthesia, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control (VP group) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: patients experiencing an episode of nausea and/or vomiting in the recovery room received an antiemetic drug that was not included in their perioperative antiemetic prophylaxis Haloperidol + tropisetron (VHT group) • *Dose*: haloperidol 1.25 mg, tropisetron 2 mg • *Time point of administration*: shortly after endotracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: patients experiencing an episode of nausea and/or vomiting in the recovery room received an antiemetic drug that was not included in their perioperative antiemetic prophylaxis Dimenhydrinate + dexamethasone (VDD group) • *Dose*: dimenhydrinate 31 mg, dexamethasone 4 mg • *Time point of administration*: shortly after endotracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: patients experiencing an episode of nausea and/or vomiting in the recovery room received an antiemetic drug that was not included in their perioperative antiemetic prophylaxis
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Matthias Voigt **Institution:** Evangelian Deaconry Hospital, Freiburg, Germany **Email:** voigt-m-fr@t-online.de **Address:** Praxis für Plastische Chirurgie Freiburg, Bismarckallee 17, D-79098 Freiburg, Germany **Duration of study:** NA **Language:** English

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Voigt 2011-1 *(Continued)*

	Study's primary outcome: primary outcome in this study was the incidence of nausea, emesis, or both, in the early (0 to 2 hours) and late (2 to 24 hours) postoperative periods **Trial registry number:** NA
Notes	Two sub-studies (inhalational, TIVA) with 3 groups each

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "...to 6 subgroups of 80 patients each by sealed envelope assignment" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the nurses in the recovery room and ward were unblinded as to the prophylactic combination administered preoperatively"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blinded" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "outcome data were complete for all 480 patients"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV): no; (history of motion sickness, duration of anaesthesia, perioperative opioids): unclear

Voigt 2011-2

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, combination prophylaxis
Participants	**Baseline characteristics** Control (TP group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 80 • *Received treatment (n)*: NA

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Voigt 2011-2 *(Continued)*

- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 97.5
- *Non-smoker (%)*: 81.3
- *History of PONV/motion sickness (%)*: 20/NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or remifentanil, 68.8% of patients received postoperative opioids
- *Type of surgery*: elective breast surgery

Haloperidol + tropisetron (THT group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 98.8
- *Non-smoker (%)*: 76.3
- *History of PONV/motion sickness (%)*: 30/NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or remifentanil, 65% of patients received postoperative opioids
- *Type of surgery*: elective breast surgery

Dimenhydrinate + dexamethasone (TDD group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 80
- *Received treatment (n)*: NA
- *Analysed (n)*: 80
- *Age (mean ± SD, median (IQR), median (range))*: NA
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 77.5
- *History of PONV/motion sickness (%)*: 33.8/NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl or remifentanil, 78.8% of patients received postoperative opioids
- *Type of surgery*: elective breast surgery

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Voigt 2011-2 *(Continued)*

Included criteria: scheduled for different types of elective breast surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV): no; (history of motion sickness, duration of anaesthesia, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control (TP group) • *Dose*: no treatment • *Time point of administration*: - • *Route of administration*: - • *Rescue antiemetics (if yes, which?)*: patients experiencing an episode of nausea and/or vomiting in the recovery room received an antiemetic drug that was not included in their perioperative antiemetic prophylaxis Haloperidol + tropisetron (THT group) • *Dose*: haloperidol 1.25 mg, tropisetron 2 mg • *Time point of administration*: shortly after endotracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: patients experiencing an episode of nausea and/or vomiting in the recovery room received an antiemetic drug that was not included in their perioperative antiemetic prophylaxis Dimenhydrinate + dexamethasone (TDD group) • *Dose*: dimenhydrinate 31 mg, dexamethasone 4 mg • *Time point of administration*: shortly after endotracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: patients experiencing an episode of nausea and/or vomiting in the recovery room received an antiemetic drug that was not included in their perioperative antiemetic prophylaxis
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Germany **Setting:** inpatient, single-centre **Author's name:** Matthias Voigt **Institution:** Evangelian Deaconry Hospital, Freiburg, Germany **Email:** voigt-m-fr@t-online.de **Address:** Praxis für Plastische Chirurgie Freiburg, Bismarckallee 17, D-79098 Freiburg, Germany **Duration of study:** NA **Language:** English

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Voigt 2011-2 *(Continued)*

	Study's primary outcome: primary outcome in this study was the incidence of nausea, emesis, or both, in the early (0 to 2 hours) and late (2 to 24 hours) postoperative periods **Trial registry number:** NA
Notes	Two sub-studies (inhalational, TIVA) with 3 groups each

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "to 6 subgroups of 80 patients each by sealed envelope assignment" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the nurses in the recovery room and ward were unblinded as to the prophylactic combination administered preoperatively"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blinded" Judgement comment: insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "outcome data were complete for all 480 patients"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): unclear. Potential effect modifiers (gender, non-smoker, history of PONV): no; (history of motion sickness, duration of anaesthesia, perioperative opioids): unclear

Volpe 1994

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA

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Volpe 1994 *(Continued)*

- *Analysed (n)*: 464
- *Age (mean ± SD, median (IQR), median (range))*: 53.6 ± 13.4
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 56.90
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, enflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 2 µg/kg to 4 µg/kg, postoperative morphine
- *Type of surgery*: ophthalmic, gynaecological, abdominal, and urological procedures

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 464
- *Age (mean ± SD, median (IQR), median (range))*: 52.3 ± 11.2
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 56.90
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (N_2O, enflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 130
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 2 µg/kg to 4 µg/kg, postoperative morphine
- *Type of surgery*: ophthalmic, gynaecological, abdominal, and urological procedures

Included criteria: ASA I or II; scheduled to undergo elective ophthalmic, gynaecological, abdominal, or urological procedure under general anaesthesia

Excluded criteria: liver, renal,and cardiac failure; had received antiemetic medication 24 hours before the surgical procedure

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Placebo

- *Dose*: saline
- *Time point of administration*: before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 79.96% (ondansetron 4 mg IV, metoclopramide 10 mg IV)

Ondansetron

- *Dose*: 4 mg
- *Time point of administration*: before induction of anaesthesia

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Volpe 1994 *(Continued)*

	• *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20.04% (ondansetron 4 mg IV, metoclopramide 10 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Italy **Setting:** inpatient, multi-centre **Author's name:** Nicola Volpe **Institution:** Department of Anaesthesia, Ospedale S. Cerardo, Monza, Milan, Italy **Email:** NA **Address:** Servizio de Anestesia, Ospedale S. Cerardo, Via Donizetti 106, 20052 Monua, Italy **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomised". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("single-blind")

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Volpe 1994 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "independent anaesthetic personnel, blinded to the study drugs, monitored the patients"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: no missing data for efficacy outcomes. Adverse events are provided for only a small number of participants (16%) without any explanation from study authors
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Wadaskar 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Granisetron (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 30.35 ± 6.53 • *Weight (mean ± SD, median (IQR), median (range))*: 47.37 ± 4.67 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 55.57 • *Use of perioperative opioids (if yes, which?)*: fentanyl • *Type of surgery*: diagnostic laparoscopy, laparoscopic tubal ligation Ondansetron (group B) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 28.72 ± 4.21 • *Weight (mean ± SD, median (IQR), median (range))*: 46.77 ± 3.95 • *BMI (mean ± SD, median (IQR), median (range))*: NA

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Wadaskar 2008 *(Continued)*

- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 53.52
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: diagnostic laparoscopy, laparoscopic tubal ligation

Placebo (group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 29.00 ± 5.17
- *Weight (mean ± SD, median (IQR), median (range))*: 46.32 ± 3.54
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 53.95
- *Use of perioperative opioids (if yes, which?)*: fentanyl
- *Type of surgery*: diagnostic laparoscopy, laparoscopic tubal ligation

Included criteria: female, ASA I or II, 20 to 40 years of age, undergoing diagnostic laparoscopic tubal ligation

Excluded criteria: history of allergy to drug(s), pregnancy lactation, menstruation, vomiting or retching within 24 hours before the operation, administration of antiemetic or psychoactive medication within 24 hours before surgery, active alcohol or drug abuse

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Granisetron (group A)

- *Dose*: 40 µg/kg
- *Time point of administration*: 2 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg IV; 20%

Ondansetron (group B)

- *Dose*: 80 µg/kg
- *Time point of administration*: 2 minutes before induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg IV; 45%

Placebo (group C)

- *Dose*: 0.9% saline
- *Time point of administration*: 2 minutes before induction of anaesthesia

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Wadaskar 2008 *(Continued)*

- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: metoclopramide 0.2 mg/kg IV; 77.5%

Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (7 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** India **Setting:** inpatient, single-centre **Author's name:** Abhishek Wadaskar **Institution:** Department of Anesthesiology and Intensive care, Datta Meghe Institute of Medical Sciences **Email:** drabhi1118@gmail.com **Address:** M5GD-4, Meghdoot Apartments, JNMC campus, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha-442001, MH, India **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly allocated in to three groups of 40 each" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...vomiting episodes), requiring rescue antiemetic. The study was kept double blind by one anesthetist preparing the drug(s) and putting code on the syringes while drug(s) were administered by anesthetist who was not part of the study team. Data and proformas were collected..."

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Wadaskar 2008 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...part of the study team. Data and proformas were collected by resident anesthetist blinded to the study and handed over to the investigator. Decoding of the patients was done"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...three groups of 40 each. In this study, the treatment groups were similar with regards to age, weight and type of surgical procedures. The duration of anesthesia was also comparable in all the three groups (p>0.05) (Table 1). Figure 1 Table 1: demographics..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Wadood 2014

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Ondansetron (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: middle ear surgery Ondansetron + dexamethasone (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA

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Wadood 2014 *(Continued)*

- *Analysed (n)*: 20
- *Age (mean +/- SD, median (IQR), median [range])*: NA
- *Weight (mean +/- SD, median (IQR), median [range])*: NA
- *BMI (mean +/- SD, median (IQR), median [range])*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: NA
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: middle ear surgery

Included criteria: ASA I or II, either sex, 20 to 40 years of age, undergoing middle ear surgery

Excluded criteria: received antiemetics within 24 hours before surgery, allergy to any anaesthetic drug, allergy to dexamethasone or ondansetron, pregnant, having any medical illness

Pretreatment: data on baseline details and potential effect modifiers not shown. Baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group 1) • *Dose*: 4 mg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV; 15% Ondansetron + dexamethasone (group 2) • *Dose*: ondansetron 4 mg, dexamethasone 8 mg • *Time point of administration*: just before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV; 0%
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (in postoperative ward)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, observation in postoperative ward)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Pakistan **Setting:** NA, single-centre **Author's name:** Fazal Wadood

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Wadood 2014 *(Continued)*

Institution: Department of Anaesthesia, Ayub Medical Complex Abbottabad, Pakistan

Email: wadood_bjr@yahoo.com

Address: NA

Language: English

Duration of study: January to June 2012

Trial registry number: NA

Study's primary outcome: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned to one of the two study groups (20 in each group) through blocked randomization" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the drugs were administered intravenously (IV) slowly just before induction of anaesthesia by the anaesthetist who was blinded to the nature of the drug in the syringe"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...each. General characteristics of patients in relation to age, weight and sex, type of surgery, duration of surgery and anaesthesia, total amount of opioid used, intra-operative and postoperative haemodynamics which may modify PONV were comparable in the two groups" Judgement comment: data on baseline details and potential effect modifiers not shown. Baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): unclear

Wagley 1999

Study characteristics

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Wagley 1999 *(Continued)*

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 23.0 ± 3.8 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 48 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: balanced anaesthesia (methohexital, fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 57.8 • *Use of perioperative opioids (if yes, which?)*: 107.0 µg fentanyl • *Type of surgery*: dentoalveolar surgery Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 25 • *Received treatment (n)*: NA • *Analysed (n)*: 25 • *Age (mean ± SD, median (IQR), median (range))*: 23.1 ± 4.3 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 52 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: balanced anaesthesia (methohexital, fentanyl, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 61.7 • *Use of perioperative opioids (if yes, which?)*: 126.0 µg fentanyl • *Type of surgery*: dentoalveolar surgery **Included criteria:** requiring routine dentoalveolar surgery (removal of multiple impacted or erupted teeth) that required general anaesthesia, ASA I or II, adult (18 or older) with anticipated surgical procedure requiring 30 to 60 minutes of anaesthesia time, without a history of nausea or vomiting subsequent to prior anaesthesia or surgery **Excluded criteria:** NA **Pretreatment:** baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics**

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Wagley 1999 *(Continued)*

	Placebo • *Dose*: 2 ml saline • *Time point of administration*: not less than 30 seconds immediately before induction of general anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: within 30 minutes postoperatively: 2 mL saline; continuing after 10 minutes: prochlorperazine 5 mg IV; after discharge/at home: prochlorperazine 5 mg oral Ondansetron • *Dose*: 4 mg • *Time point of administration*: not less than 30 seconds immediately before induction of general anaesthesia. • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: within 30 minutes postoperatively: 4 mg ondansetron; continuing after 10 minutes: prochlorperazine 5 mg IV; after discharge/ at home: prochlorperazine 5 mg oral
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** supported by Clinical Applications Research, Glaxo Wellcome, Inc, Research Triangle Park, NC S3A-R54, USA **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Craig Wagley **Institution:** Division of Oral and Maxillofacial Surgery, Metro-Health Medical Center, Cleveland, OH, USA **Email:** NA **Address:** 5437 Mahoning Ave, Youngstown, OH 44515, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...and were then randomly assigned (by coin toss) to either the placebo or ondansetron group by 1 investigator"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Wagley 1999 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "this investigator then provided a 2.0-n test vial containing either 4.0 mg ondansetron or saline to the anesthesiologist, who was blinded as to the contents"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the recording of PONV data was done by a recovery room nurse who was unaware of the medication received by the patient"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no references to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: ".05 was considered significant. No statistically significant differences (P < .05) existed between the placebo and ondansetron groups for gender distribution, age, number of impactions, number of erupted teeth, duration of anesthesia, midolazolam dosage, fentanyl dosage, or methohexital dosage (Table 1). For those who developed PONV..." Judgement comment: baseline characteristics (age, ASA): no; (weight, BMI): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (history of motion sickness, non-smoker): unclear

Wagner 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 34.2 ± 8.6 • *Weight (mean ± SD, median (IQR), median (range))*: 68.7 ± 14.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 39/11/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 26/28 • *Type of general anaesthesia*: inhalational anaesthesia (en-/isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 119.4 • *Use of perioperative opioids (if yes, which?)*: 149.0 µg fentanyl intraoperative, 5.8 mg morphine postoperative

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Wagner 1996 *(Continued)*

- *Type of surgery*: closed laparoscopic gynaecological surgery, cholecystectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 59
- *Age (mean ± SD, median (IQR), median (range))*: 35.5 ± 7.6
- *Weight (mean ± SD, median (IQR), median (range))*: 67.3 ± 14.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 43/16/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 30.5/44.1
- *Type of general anaesthesia*: inhalational anaesthesia (en-/isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 120.3
- *Use of perioperative opioids (if yes, which?)*: 143.5 µg fentanyl intraoperative, 6.3 mg morphine post-operative
- *Type of surgery*: closed laparoscopic gynaecological surgery, cholecystectomy

Included criteria: female, 18 years of age or older, ASA I or II, scheduled for elective closed laparoscopic gynaecological surgery or cholecystectomy

Excluded criteria: pregnant or nursing; required antiemetic therapy within 14 days before surgery; allergic to substituted benzamides, anaesthetics, or narcotics; history of significant gastrointestinal disease; required medications that could cause extrapyramidal side effects; had received emetogenic chemotherapy within 30 days before surgery; history of epistaxis or nasal passage abnormalities; history of chronic exposure to alcohol, barbiturates, or tranquilizers; had taken part in an investigational drug study within 30 days before surgery; suffering from rhinitis or nasal tissue inflammation

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 2 × 0.05 mL vehicle solution • *Time point of administration*: approximately 15 minutes before expected emergence from anaesthesia • *Route of administration*: intranasal, 1 spray in each nostril • *Rescue antiemetics (if yes, which?)*: droperidol in PACU, prochlorperazine and trimethobenzamide in ward Metoclopramide • *Dose*: 20 mg (200 mg/mL in a buffered aqueous solution; 0.05 mL (10 mg) of solution with each spray) • *Time point of administration*: approximately 15 minutes before expected emergence from anaesthesia • *Route of administration*: intranasal, 1 spray in each nostril • *Rescue antiemetics (if yes, which?)*: droperidol in PACU, prochlorperazine and trimethobenzamide in ward
Outcomes	*Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)*

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Wagner 1996 *(Continued)*

- Outcome type: dichotomous outcome

Sedation/drowsiness (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** supported in part by Naska Pharmacal, Lincolnton, North Carolina, USA **Country:** USA **Setting:** NA, single-centre **Author's name:** Bertil K.J. Wagner **Institution:** College of Pharmacy, Rutgers University and the Department Anesthesiology, University of Medicine and Dentistry of New Jersey, Piscataway, New Jersey, USA **Email:** NA **Address:** Rutgers University, College of Pharmacy, Busch Campus, Piscataway, NJ 08855, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized to receive either metoclopramide 20 mg or placebo according to a randomized, block design" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 119 patients were enrolled with 109 patients considered eligible for efficacy analysis. Ten patients were excluded from the statistical analysis due to protocol violations. Of these, six patients underwent other surgical procedures, two patients received unauthorized medications, and two patients did not receive the study drug (one in each group). The two patient groups (elective closed laparoscopic gynecological surgery and elective closed laparoscopic cholecystectomy) were combined since the laparoscopic procedure itself is a primary inciting event for the development of PONV"

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Wagner 1996 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...are shown in parentheses. I demographics (Table 1) revealed no significant differences between the treatment groups. The frequency of a history..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Waldmann 1985

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 24.6 ± 6.61 • *Weight (mean ± SD, median (IQR), median (range))*: 58.5 ± 7.93 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 12.1 • *Use of perioperative opioids (if yes, which?)*: 0.05 mg fentanyl, pethidine • *Type of surgery*: day-care termination Domperidone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 21.7 ± 4.4 • *Weight (mean ± SD, median (IQR), median (range))*: 56.6 ± 8.73 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA

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Waldmann 1985 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 16
- *Use of perioperative opioids (if yes, which?)*: 0.05 mg fentanyl, pethidine
- *Type of surgery*: day-care termination

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 23.2 ± 5.96
- *Weight (mean ± SD, median (IQR), median (range))*: 60 ± 6.93
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, halothane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 14.2
- *Use of perioperative opioids (if yes, which?)*: 0.05 mg fentanyl, pethidine
- *Type of surgery*: day-care termination

Included criteria: un-premedicated women requiring day-care terminations

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Domperidone • *Dose*: 10 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Metoclopramide • *Dose*: 10 mg • *Time point of administration*: at induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*PONV (0 to 24 hours)*

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Waldmann 1985 *(Continued)*

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** NA **Country:** UK **Setting:** outpatient, single-centre **Author's name:** C.S. Waldmann **Institution:** Anaesthetics Unit, London Hospital Medical College, Whitechapel, London, UK **Email:** NA **Address:** Anaesthetics Unit, London Hospital Medical College, Whitechapel, London El 1BB, UK **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "a randomised double-blind investigation was undertaken to assess the value of domperidone and metoclopramide as prophylactic anti-emetics in unpremedicated patients undergoing general anaesthesia for therapeutic abortion on a day care basis" Quote: "sixty randomly numbered ampoules" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "sixty randomly numbered ampoules containing 2 ml normal saline, 2 ml (10 mg) metoclopramide, or 2 ml (10 mg) domperidone were disguised in the pharmacy and issued as the 'anti-emetic' solution" Judgement comment: no statement on identical appearance of the ampoules provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "a randomised double-blind investigation was undertaken to assess the value of domperidone and metoclopramide as prophylactic anti-emetics in unpremedicated patients undergoing general anaesthesia for therapeutic abortion on a day care basis" Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the incidence of nausea and vomiting in the recovery room was assessed by the recovery staff. On full recovery the patients received a questionnaire to take home, complete and return the following day" Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Waldmann 1985 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients in each of the three drug groups had similar weight, age, length of pregnancy and duration of anaesthetic" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Wang 1995

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 47.5 ± 10.4 • *Weight (mean ± SD, median (IQR), median (range))*: 57.4 ± 10.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 44 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: abdominal surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 46.4 ± 13.8 • *Weight (mean ± SD, median (IQR), median (range))*: 59.3 ± 11.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 52 • *Non-smoker (%)*: NA

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Wang 1995 *(Continued)*

- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: abdominal surgery

Included criteria: scheduled for selective abdominal surgery

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo • *Dose*: 0.9% NaCl • *Time point of administration*: 10 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Xiangrui Wang **Institution:** Renji Hospital, Shanghai Second Medical University, Shanghai **Email:** NA **Address:** Renji Hospital, Shanghai Second Medical University, Shanghai 200001 **Duration of study:** NA **Language:** Chinese (translated by Jiechu Chen) **Study's primary outcome:** NA **Trial registry number:** NA

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Wang 1995 *(Continued)*

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "...were randomly and double-blindly allocated to receiving ....". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blind")
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Wang 1999a

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 41.3 (34 to 54) • *Weight (mean ± SD, median (IQR), median (range))*: 74.1 ± 7.6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 60 • *Non-smoker (%)*: NA

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Wang 1999a *(Continued)*

- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 96.2
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction, postoperative morphine via PCA in 1 hour (3 mg), 2 hours (2 mg), 3 hours (2 mg), 4 hours (1 mg)
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 43.2 (30 to 55)
- *Weight (mean ± SD, median (IQR), median (range))*: 71.3 ± 8.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 68
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 94.1
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction, postoperative morphine via PCA in 1 hour (4 mg), 2 hours (3 mg), 3 hours (2 mg), 4 hours (2 mg)
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, 30 to 55 years of age, undergoing general anaesthesia for elective laparoscopic cholecystectomy

Excluded criteria: history of motion sickness, had received antiemetics within 48 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Placebo • *Dose*: saline 2 mL • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)*

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Wang 1999a *(Continued)*

- Outcome type: dichotomous outcome

Identification	**Sponsorship source:** this work was supported by Grant DOII 88-11R-402 from the National Health Research Institutes, Taiwan **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** J.J. Wang **Institution:** Department of Anaesthesiology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan **Email:** NA **Address:** No. 280, Section 4, Ren'ai Road, Da'an District, Taipei City, Taiwan 106 **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Judgement comment: quote: "study medications were prepared by a single nurse anaesthetist in identical 2-ml syringes to ensure blinding of the anaesthetists"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote" "...patients and investigators who collected the postoperative data were blind to the randomization..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: 90 participants were enrolled, 78 completed the study. Twelve participants who required open cholecystectomy were excluded
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or a trial registry number reported
Other bias	Unclear risk	Quote: "...the interpretation of the excluded. Patient characteristics were similar between groups (Table 1). study data, we controlled these..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

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Wang 1999b

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group 1) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 41 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 145 • *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl perioperative • *Type of surgery*: thyroidectomy Droperidol (group 2) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 38 ± 9 • *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 9 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 156 • *Use of perioperative opioids (if yes, which?)*: 250 µg fentanyl perioperative • *Type of surgery*: thyroidectomy Placebo (group 3) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 38

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Wang 1999b *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 148
- *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl perioperative
- *Type of surgery*: thyroidectomy

Included criteria: adult female patients undergoing elective partial or total thyroidectomy; all patients were in a physiologically euthyroid state

Excluded criteria: had an intrathoracic goiter, gastrointestinal disorder, or history of motion sickness; had received an antiemetic within 48 hours before surgery; had suffered from a difficult endotracheal intubation (more than 2 attempts at tracheal intubation) at induction of anaesthesia

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone (group 1) • *Dose*: 10 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: IV ondansetron 4 mg Droperidol (group 2) • *Dose*: 1.25 mg • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: IV ondansetron 4 mg Placebo (group 3) • *Dose*: 2 ml saline • *Time point of administration*: 1 minute before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: IV ondansetron 4 mg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA

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Wang 1999b *(Continued)*

Country: Taiwan

Setting: inpatient, single-centre

Author's name: Jhi-Joung Wang

Institution: Department of Anesthesiology, Tri-Service GeneralHospital/National Defense Medical Center, No. 8, Sec. 3, Ting-ChowRd., Taipei, Taiwan

Email: painlab@tpts5.seed.net.tw

Address: Department of Anesthesiology, Tri-Service General Hospital/National Defense Medical Center, No.8, Sec.3, Ting-Chow Rd., Taipei, Taiwan

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: incidence of need for rescue antiemetics

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a randomization table was used to assign patients into one of three groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "identity of the study drugs were blinded from the patients, the anesthetists during surgery"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "and the investigators who collected the postoperative data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 120 patients enrolled in the study, 4 patients had suffered from difficult intubations and were eliminated. The data obtained from the remaining 116 patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients' characteristics (e.g., age, weight, and height), duration of anesthesia and surgery, and the total doses of perioperative fentanyl were similar among the three groups (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

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Wang 2000a

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different time points of administration
Participants	**Baseline characteristics** Dexamethasone (group 1: pre induction) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 42 (36 to 44) • *Weight (mean ± SD, median (IQR), median (range))*: 54 (42 to 71) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 136 • *Use of perioperative opioids (if yes, which?)*: 250 µg fentanyl perioperative, morphine 1 hour (12 mg) and 2 hours (2 mg) in PACU and in ward (15 mg) • *Type of surgery*: abdominal total hysterectomy Dexamethasone (group 2: end of anaesthesia) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 41 (35 to 45) • *Weight (mean ± SD, median (IQR), median (range))*: 56 (46 to 75) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA/0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 142 • *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl perioperative, morphine 1 hour (10 mg) and 2 hours (3 mg) in PACU and in ward (14 mg) • *Type of surgery*: abdominal total hysterectomy Placebo (group 3) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40

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Wang 2000a *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 39 (35 to 43)
- *Weight (mean ± SD, median (IQR), median (range))*: 54 (41 to 69)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 145
- *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl perioperative, morphine 1 hour (14 mg) and 2 hours (3 mg) in PACU and in ward (17 mg)
- *Type of surgery*: abdominal total hysterectomy

Included criteria: adult female, ASA I and II, 35 to 45 years of age, scheduled for abdominal total hysterectomy under general anaesthesia

Excluded criteria: history of motion sickness or gastrointestinal disorder, had received antiemetics within 48 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone (group 1: pre-induction) • *Dose*: 10 mg • *Time point of administration*: dexamethasone 1 minute before induction of anaesthesia, saline at end of administration of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 1.25 mg IV droperidol; 0 to 2 hours: 8%, 2 to 24 hours: 13% Dexamethasone (group 2: end of anaesthesia) • *Dose*: 10 mg • *Time point of administration*: saline 1 minute before induction of anaesthesia, dexamethasone at end of administration of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 1.25 mg IV droperidol; 0 to 2 hours: 30%, 2 to 24 hours: 15% Placebo (group 3) • *Dose*: saline • *Time point of administration*: saline 1 minute before induction of anaesthesia, saline at end of administration of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 1.25 mg IV droperidol; 0 to 2 hours: 35%, 2 to 24 hours: 38%
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Taiwan

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Wang 2000a *(Continued)*

Setting: inpatient, NA

Author's name: Jhi-Joung Wang

Institution: Department of Anesthesiology, Tri-Service General Hospital/National Defense Medical Center, Taiwan

Email: painlab@tpts5.seed.net.tw

Address: No 8, Sec. 3, Ting-ChowRd., Taipei, Taiwan

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: proportion of participants requiring rescue IV droperidol

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "in the preoperative holding area, patients were allocated randomly to one of three groups (n 40 each) by using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the randomized process and the identity of the study drug were blinded from the patients, the anesthesiologists"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...during surgery, and the investigators who collected the postoperative data" Quote: "the randomized process and the identity of the study drug were blinded from the patients, the anesthesiologists"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all 120 patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no significant differences among the three groups with respect to age, weight, height, last menstrual period, types of surgery, duration of anesthesia and surgery, and the total of perioperative fentanyl doses (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness, perioperative opioids): no; (history of PONV, non-smoker): unclear

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Wang 2000b

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA • *Analysed (n)*: 41 • *Age (mean ± SD, median (IQR), median (range))*: 32 (28 to 36) • *Weight (mean ± SD, median (IQR), median (range))*: 54 (42 to 73) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 68 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction • *Type of surgery*: laparoscopic tubal ligation Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 34 (31 to 35) • *Weight (mean ± SD, median (IQR), median (range))*: 56 (46 to 75) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 65 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl for induction • *Type of surgery*: laparoscopic tubal ligation **Included criteria:** women, ASA I or II, scheduled for outpatient laparoscopic tubal ligation **Excluded criteria:** breastfeeding, weighing > 90 kg, taking any medication other than an oral contraceptive pill **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear
Interventions	**Intervention characteristics**

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Wang 2000b *(Continued)*

	Dexamethasone • *Dose*: 10 mg • *Time point of administration*: at time of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (7%) ondansetron 4 mg IV Placebo • *Dose*: 2 ml saline • *Time point of administration*: at time of induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (28%) ondansetron 4 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** this work was supported in part by grant NSC89-2314-B-016-060 from the National Council of Science, Taiwan **Country:** Taiwan **Setting:** outpatient, single-centre **Author's name:** J.J. Wang **Institution:** Department of Anesthesiology Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan **Email:** NA **Address:** Department of Anesthesiology, Tri-Service General Hospital/National Defense Medical Center, No. 8, Sec. 3, Ting-Chow Road, Taipei, Taiwan **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of PONV
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Wang 2000b *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "both patient and investigator were blinded" Quote: "medications (2 ml) were prepared by one of the investigators" Judgement comment: no statement on blinding of anaesthesiologists (investigators = anaesthesiologists?)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "both patient and investigator were blinded" Judgement comment: no information on who is doing the outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "patients enrolled in this study, six patients who did not complete the surgical procedure (laparoscopic tubal Discussion ligation) because of intra-abdominal adhesions and three patients who could not be contacted by telephone after. Although the use of..."
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patient characteristics, interval since the the last menstrual period and the durations of anaesthesia and surgery were reported. In our study, we found that the total incidence of PONV was 73% within 24 h postoperatively in patients similar in the two groups (Table 1). There were no significant differences" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Wang 2000c

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Dexamethasone (10 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: NA • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 53 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA

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Wang 2000c *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138
- *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl perioperative
- *Type of surgery*: thyroidectomy

Dexamethasone (5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: NA
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 9
- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 135
- *Use of perioperative opioids (if yes, which?)*: 250 µg fentanyl perioperative
- *Type of surgery*: thyroidectomy

Dexamethasone (2.5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: NA
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 5
- *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 140
- *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl perioperative
- *Type of surgery*: thyroidectomy

Dexamethasone (1.25 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: NA
- *Analysed (n)*: 44
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 7

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Wang 2000c *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 53 ± 6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142
- *Use of perioperative opioids (if yes, which?)*: 350 µg fentanyl perioperative
- *Type of surgery*: thyroidectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 45
- *Received treatment (n)*: NA
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 41 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 54 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 146
- *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl perioperative
- *Type of surgery*: thyroidectomy

Included criteria: adult female patients undergoing elective partial or total thyroidectomy; all patients were in a physiologically euthyroid state

Excluded criteria: history of PONV, motion sickness, gastrointestinal disorder; receipt of antiemetic within 24 hours before surgery; intrathoracic goiter or difficult endotracheal intubation (more than 2 attempts at tracheal intubation) at induction of anaesthesia

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (peri-operative opioids): yes

Interventions	**Intervention characteristics** Dexamethasone (10 mg group) • *Dose*: 10 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; 11% Dexamethasone (5 mg group) • *Dose*: 5 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; 12%

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Wang 2000c *(Continued)*

	Dexamethasone (2.5 mg group) • *Dose*: 2.5 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; 19% Dexamethasone (1.25 mg group) • *Dose*: 1.25 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; 23% Placebo • *Dose*: 2 mL saline • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV; 35%
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Postoperative wound infection (during hospital stay)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, observation during hospital stay)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** inpatient, NA **Author's name:** Jhi-Joung Wang **Institution:** Departments of Anesthesiology Tri-Service General Hospital, National Defense Medical Center, Taipei,Taiwan **Email:** painlab@tpts5.seed.net.tw **Address:** Department of Anesthesiology, Chi-Mei Medical Center, No. 901, Chung-Hwa Road, Yung-Kang City, Tainan Hsien, Taiwan **Language:** English **Duration of study:** NA **Trial registry number:** NA

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Wang 2000c *(Continued)*

	Study's primary outcome: incidence of PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "before the study, a randomization table was used to assign patients to one of five groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the randomized process and the identity of the study drugs were blinded from the patients, the anesthetists during surgery"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the randomized process and the identity of the study drugs were blinded from the patients, the anesthetists during surgery, and the investigators who collected the postoperative data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 225 patients enrolled in the study, 8 suffered from difficult intubations and were eliminated from the study. The data obtained from the remaining 217 patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "patient characteristics, such as age, weight, and height, as well as last menstrual cycle, duration of operation and anesthesia, the total doses of perioperative fentanyl, and duration of hospital stay were similar among the five groups (Table 1)" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes

Wang 2002a

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 39

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Wang 2002a *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 5
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 56.41
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane or desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 178
- *Use of perioperative opioids (if yes, which?)*: 300 µg fentanyl intraoperative
- *Type of surgery*: tympanomastoidectomy

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 52.63
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane or desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 169
- *Use of perioperative opioids (if yes, which?)*: 350 µg fentanyl intraoperative
- *Type of surgery*: tympanomastoidectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 39
- *Age (mean ± SD, median (IQR), median (range))*: 39 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 58.97
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane or desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 170
- *Use of perioperative opioids (if yes, which?)*: 350 µg fentanyl intraoperative
- *Type of surgery*: tympanomastoidectomy

Included criteria: 35 to 55 years of age, ASA I or II, approved to receive general anaesthesia for tympanomastoid surgery

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Wang 2002a *(Continued)*

	Excluded criteria: history of PONV, motion sickness, gastrointestinal disorder; major systemic disease (e.g. hypertension, diabetes mellitus, morbid obesity), had received an antiemetic within 48 hours before surgery **Pretreatment:** baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear
Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 5 mg • *Time point of administration*: after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide hydrochloride 10 mg IV Tropisetron • *Dose*: 2 mg • *Time point of administration*: after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide hydrochloride 10 mg IV Placebo • *Dose*: 1 mL saline • *Time point of administration*: after tracheal intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide hydrochloride 10 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** NA **Author's name:** Jhi-Joung Wang **Institution:** Departments of Anesthesiology and Oto-laryngology, Cathay General Hospital, Taipei, Taiwan **Email:** NA **Address:** Departments of Anesthesiology and Oto-laryngology, Cathay General Hospital, Taipei, Taiwan **Language:** English **Duration of study:** NA **Trial registry number:** NA

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Wang 2002a *(Continued)*

	Study's primary outcome: incidence of nausea and vomiting
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "before the study, a randomization table was used to assign patients into one of the three groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...were not routinely emptied (suctioned). The randomization process and the identities of the study drugs were blinded from the patients, the surgeon, the anesthetists during surgery, and the investigators who collected the postoperative data. Patients were observed postoperatively"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...were not routinely emptied (suctioned). The randomization process and the identities of the study drugs were blinded from the patients, the surgeon, the anesthetists during surgery, and the investigators who collected the postoperative data. Patients were observed postoperatively"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "excluded because of missing data" Judgement comment: 4 of 120 patients were excluded due to missing data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patients' characteristics (eg, age, weight, and gender), duration of anesthesia and surgery, and perioperative fentanyl administration were similar among groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Wang 2002b

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 5

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Wang 2002b *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 56 ± 4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60.53
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 80
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction of anaesthesia, no further opioids
- *Type of surgery*: laparoscopic cholecystectomy

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 38
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 5
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 6
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 63.16
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 86
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction of anaesthesia, no further opioids
- *Type of surgery*: laparoscopic cholecystectomy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 39
- *Age (mean ± SD, median (IQR), median (range))*: 42 ± 4
- *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 64.10
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 82
- *Use of perioperative opioids (if yes, which?)*: fentanyl 2 µg/kg for induction of anaesthesia, no further opioids
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: ASA I or II, undergoing general anaesthesia for elective laparoscopic cholecystectomy

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Wang 2002b *(Continued)*

Excluded criteria: history of PONV, motion sickness, or major systemic disease (e.g., hypertension, diabetes mellitus, morbid obesity); had received an antiemetic within 48 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 5 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 13% (metoclopramide 10 mg IV) Tropisetron • *Dose*: 2 mg • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16% (metoclopramide 10 mg IV) Placebo • *Dose*: saline • *Time point of administration*: immediately after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 41% (metoclopramide 10 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported in part by Tri-Service General Hospital Grant DOD-90-75 **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Jhi-Joung Wang **Institution:** Department of Anesthesiology, Chi-Mei Medical Center, Tainan, Taiwan **Email:** 400002@mail.chimei.org.tw **Address:** Department of Anesthesiology, Chi-Mei Medical Center, Tainan, Taiwan **Duration of study:** NA **Language:** English

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Wang 2002b *(Continued)*

	Study's primary outcome: complete response was defined as no nausea, no vomiting, and no antiemetic medication during a 24-hour postoperative period; this was also the primary efficacy end-point of the study **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "in the preoperative holding area, patients were allocated randomly to one of the three groups (n 40 each) by use of a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications were prepared by a nurse anesthetist in identical 2-mL syringes to ensure blinding of the anesthesiologists"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients and the investigators who collected the data were blinded to the patient's group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 120 patients enrolled in this study, 115 completed it. Five patients who required open cholecystectomy were excluded. The data obtained from the remaining 115 patients were analyzed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Wang 2008

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Haloperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 50 • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 33.5 ± 5.2

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Wang 2008 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 55.4 ± 9.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 11/22
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 48.2
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: gynaecological laparoscopic surgery (tubal ligation, ovarian cystectomy, myomectomy)

Droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 44
- *Age (mean ± SD, median (IQR), median (range))*: 34.2 ± 6.1
- *Weight (mean ± SD, median (IQR), median (range))*: 57.2 ± 9.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 14/25
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 52.1
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: gynaecological laparoscopic surgery (tubal ligation, ovarian cystectomy, myomectomy)

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: NA
- *Analysed (n)*: 47
- *Age (mean ± SD, median (IQR), median (range))*: 32.3 ± 5.6
- *Weight (mean ± SD, median (IQR), median (range))*: 56.5 ± 9.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 11/17
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 50.6
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction
- *Type of surgery*: gynaecological laparoscopic surgery (tubal ligation, ovarian cystectomy, myomectomy)

Included criteria: women, ASA I or II, scheduled for gynaecological laparoscopic surgery in an ambulatory setting

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Wang 2008 *(Continued)*

Excluded criteria: breastfeeding, weighed over 90 kg, taking any medication other than an oral contraceptive pill, had received an antiemetic within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Haloperidol • *Dose*: 1 mg • *Time point of administration*: 15 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 13% (ondansetron 4 mg IV) Droperidol • *Dose*: 0.625 mg • *Time point of administration*: 15 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16% (ondansetron 4 mg IV) Placebo • *Dose*: saline • *Time point of administration*: 15 minutes after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 38% (ondansetron 4 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *QT prolongation (during anaesthesia)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan

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Wang 2008 *(Continued)*

Setting: outpatient, single-centre

Author's name: Jhi-Joung Wang

Institution: Department of Anaesthesiology, Chi-Mei Medical Centre, Yung-Kang City, Tainan Hsien, Taiwan

Email: 400002@mail.chimei.org.tw

Address: Department of Anaesthesiology, Chi-Mei Medical Centre, No. 901, Chung-Hwa Rd, Yung-Kang City, Tainan Hsien, Taiwan

Duration of study: NA

Language: English

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study medications in identical 2 ml syringes were prepared by a nurse anaesthetist to ensure that the anaesthesiologists were blinded to their contents. The patients and the investigators who collected the post-operative data were blinded to the randomization"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients and the investigators who collected the post-operative data were blinded to the randomization"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 150 patients enrolled in this study, 14 patients were withdrawn due to surgical reasons (n 5 6) or incomplete data collection after they had been discharged from the hospital (n 5 8). The data from the remaining 136 patients were analysed"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "no differences were found between the three groups in patient characteristics and anaesthesia (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker, perioperative opioids): unclear

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Wang 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 44 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 11 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 20/45 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 144 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, 22 mg/24 hours morphine via PCA • *Type of surgery*: gynaecological, abdominal, orthopaedic surgery Dexamethasone + haloperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 43 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 58 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 23/41 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 147 • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, 20 mg/24 hours morphine via PCA • *Type of surgery*: gynaecological, abdominal, orthopaedic surgery Dexamethasone + ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 45 • *Received treatment (n)*: 45 • *Analysed (n)*: 43

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Wang 2012 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 44 ± 12
- *Weight (mean ± SD, median (IQR), median (range))*: 57 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 21/51
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 148
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg fentanyl at induction, 23 mg/24 hours morphine via PCA
- *Type of surgery*: gynaecological, abdominal, orthopaedic surgery

Included criteria: female, ASA I or II, 18 to 65 years of age, scheduled for elective gynaecological (modified radical hysterectomy, total hysterectomy), abdominal (colorectal), or orthopaedic (hip or knee arthroplasty) surgery, with postoperative analgesia with morphine PCA

Excluded criteria: had received any antiemetic medication in the 24 hours before surgery, complained of preoperative nausea or vomiting, history of cardiac arrhythmia, extrapyramidal syndrome, significant gastric reflux, liver/renal disease, those for whom intubation during induction of anaesthesia was difficult

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Dexamethasone • *Dose*: 5 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 1 mg IV if symptoms do not improve Dexamethasone + haloperidol • *Dose*: dexamethasone 5 mg, haloperidol 2 mg • *Time point of administration*: dexamethasone after induction of anaesthesia, haloperidol 30 minutes before end of surgery • *Route of administration*: dexamethasone IV, haloperidol IM • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 1 mg IV if symptoms do not improve Dexamethasone + ondansetron • *Dose*: dexamethasone 5 mg, ondansetron 4 mg • *Time point of administration*: dexamethasone after induction of anaesthesia, ondansetron 30 minutes before end of surgery • *Route of administration*: both IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, ondansetron 1 mg IV if symptoms do not improve
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)*

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Wang 2012 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (2 to 24 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Arrhythmia (in recovery room)

- Outcome type: dichotomous outcome

QT prolongation (in recovery room)

- Outcome type: dichotomous outcome

Extrapyramidal symptoms (0 to 24 hours)

- Outcome type: dichotomous outcome

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** this study was funded by the departmental resources **Country:** Taiwan **Setting:** inpatient, single-centre **Author's name:** Po-Kai Wang **Institution:** Department of Anesthesiology, Buddhist Tzu-Chi General, Taiwan **Email:** pk8511034@yahoo.com.tw **Address:** Department of Anesthesiology, Buddhist Tzu-Chi General Hospital, 707, Section 3, Chung-Yang Road, 970, Hualien, Taiwan, R.O.C **Duration of study:** NA **Language:** English **Study's primary outcome:** complete response, defined as no PONV and no administration of rescue antiemetic medication during the first 24-hour postoperative period **Trial registry number:** NA
Notes	None

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Wang 2012 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "according to a computer-generated random sequence, patients were allocated to one of three groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "...before the end of surgery. The anesthesiologist was not blind to the group assignment. Postoperative evaluations were performed"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the presence or absence of nausea and vomiting experienced by the patients were recorded by trained nurse anesthetists without knowledge of which treatment the patients had received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "data collection was incomplete" Quote: "of the 135 patients enrolled in the study, five were later withdrawn"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "patient characteristics, surgical types, duration of surgery and anesthesia, and consumption of morphine in the 24 h observation period were not different among the three groups" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Warrick 1999

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 27 • *Age (mean ± SD, median (IQR), median (range))*: 32.7 ± 6.4 • *Weight (mean ± SD, median (IQR), median (range))*: 61 ± 10 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/3/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 37/52 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane or isoflurane)

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Warrick 1999 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 73
- *Use of perioperative opioids (if yes, which?)*: fentanyl, alfentanil, sufentanil for anaesthesia (26 patients), morphine, codeine, fentanyl for postoperative pain (14 patients)
- *Type of surgery*: gynaecological laparoscopy

Ondansetron + droperidol

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 26
- *Age (mean ± SD, median (IQR), median (range))*: 33.2 ± 7.2
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 20/6/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 35/35
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, enflurane or isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 79
- *Use of perioperative opioids (if yes, which?)*: fentanyl, alfentanil, sufentanil for anaesthesia (25 patients), morphine, codeine, fentanyl for postoperative pain (10 patients)
- *Type of surgery*: gynaecological laparoscopy

Included criteria: female, ASA I or II, outpatient undergoing gynaecological laparoscopy

Excluded criteria: had experienced nausea or vomiting or taken antiemetic medication in the last 24 hours, were breastfeeding

Pretreatment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Droperidol • *Dose*: 1.25 mg • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 11% NA Ondansetron + droperidol • *Dose*: ondansetron 4 mg, droperidol 1.25 mg • *Time point of administration*: at induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 7.1% NA
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)*

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Warrick 1999 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** supported by St. Michael's Hospital Health Science Research Centre, Toronto, and Glaxo, Inc. of Canada, Mississauga, Ontario, Canada **Country:** Canada **Setting:** outpatients, single-centre **Author's name:** Susan E. Belo **Institution:** Department of Anaesthesia, St. Michael's Hospital, Toronto, Ontario, Canada **Email:** NA **Address:** Department of Anaesthesia, St. Michael's Hospital, 30 Bond St., Toronto, Ontario, Canada M5B 1W8 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two out of 4 groups relevant (repetitive doses of antiemetics after 4 hours in 2 groups)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a computer-generated scheme was used to randomize 30 patients to each of four treatment groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding provided ("double-blind")
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the same blinded observer (PDW) performed all the interviews prior to discharge, as well as the telephone follow-up 24 hours after the laparoscopy"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 106 patients were included in the statistical analysis. Fourteen patients were eliminated from the analysis because the anesthesiologist found it necessary to use a treatment not consistent with our study protocol; these included other drugs (n 12) and nasogastric tube"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no differences among the groups with regard to the type or duration of surgery. Predisposing factors to PONV, such as day of menstrual cycle, history of PONV, history of motion sickness, and presence of an abnormal cycle, did not vary among the treatment groups. The use of all inhaled anesthetics, neuromuscular blocking agents, opioids, analgesics, and neuromus-

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Warrick 1999 *(Continued)*

	cular blocker antagonists was evenly distributed among the four treatment groups..." Judgement comment: baseline characteristics (age, ASA, weight): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Warriner 1997

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 5 groups, dose-finding study, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 75 • *Received treatment (n)*: NA • *Analysed (n)*: 75 • *Age (mean ± SD, median (IQR), median (range))*: 42.5 ± 7.7 • *Weight (mean ± SD, median (IQR), median (range))*: 67.9 ± 14.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 50/25/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 53.3/22.7 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 90 • *Use of perioperative opioids (if yes, which?)*: 291 ± 3 µg fentanyl • *Type of surgery*: total abdominal hysterectomy (TAH) Dolasetron (25 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 76 • *Received treatment (n)*: NA • *Analysed (n)*: 76 • *Age (mean ± SD, median (IQR), median (range))*: 43.5 ± 6.9 • *Weight (mean ± SD, median (IQR), median (range))*: 69.5 ± 14.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 48/28/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 42.1/28.9 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 90 • *Use of perioperative opioids (if yes, which?)*: 294 ± 115 µg fentanyl • *Type of surgery*: total abdominal hysterectomy (TAH)

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Warriner 1997 *(Continued)*

Dolasetron (50 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 74
- *Received treatment (n)*: NA
- *Analysed (n)*: 74
- *Age (mean ± SD, median (IQR), median (range))*: 44.3 ± 8.3
- *Weight (mean ± SD, median (IQR), median (range))*: 71.0 ± 14.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 50/24/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 51.4/33.8
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 293 ± 93 µg fentanyl
- *Type of surgery*: total abdominal hysterectomy (TAH)

Dolasetron (100 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 74
- *Received treatment (n)*: NA
- *Analysed (n)*: 74
- *Age (mean ± SD, median (IQR), median (range))*: 43.7 ± 7.8
- *Weight (mean ± SD, median (IQR), median (range))*: 71.8 ± 14.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 51/23/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 43.2/24.0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90
- *Use of perioperative opioids (if yes, which?)*: 286 ± 115 µg fentanyl
- *Type of surgery*: total abdominal hysterectomy (TAH)

Dolasetron (200 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 75
- *Received treatment (n)*: NA
- *Analysed (n)*: 75
- *Age (mean ± SD, median (IQR), median (range))*: 42.8 ± 8.3
- *Weight (mean ± SD, median (IQR), median (range))*: 71.2 ± 17.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 42/33/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 44.0/28.0
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90

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Warriner 1997 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: 274 ± 6 µg fentanyl
- *Type of surgery*: total abdominal hysterectomy (TAH)

Included criteria: non-pregnant, ASA I or II, women between 18 and 70 years of age, booked for total abdominal hysterectomy (TAH) under general anaesthesia

Excluded criteria: previous or current history of serious cardiovascular, respiratory, metabolic, hepatic, or renal dysfunction; had used medication known to have potential antiemetic efficacy within 24 hours before study drug administration

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: NA • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: 60% (NA) Dolasetron (25 mg group) • *Dose*: 25 mg • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: 42.7% (NA) Dolasetron (50 mg group) • *Dose*: 50 mg • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: 54.1% (NA) Dolasetron (100 mg group) • *Dose*: 100 mg • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: 39.2% (NA) Dolasetron (200 mg group) • *Dose*: 200 mg • *Time point of administration*: 1 to 2 hours before induction of anaesthesia • *Route of administration*: oral • *Rescue antiemetics (if yes, which?)*: 40.0% (NA)
Outcomes	*Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Subjects with any SAE (0 to 24 hours)* • Outcome type: dichotomous outcome *Mortality (0 to 24 hours)* • Outcome type: dichotomous outcome

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Warriner 1997 *(Continued)*

	Headache (0 to 24 hours) • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by Hoechst Marion Roussel Canada Research Inc., Laval, Qué **Country:** Canada **Setting:** multi-centre (13) **Author's name:** C. Brian Warriner **Institution:** Department of Anaesthesia, St. Paul's Hospital, Vancouver **Email:** NA **Address:** Department of Anaesthesia, St. Paul's Hospital, 1081 Burrard St., Vancouver, B.C., V6Z 1Y6 **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** complete response
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: no information about the randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "total of 374 women were enrolled at 13 investigative sites. One genotypically female patient was undergoing abdominal hysterectomy as the final step in file process to become male and was legally male (but hormonally female) at the time of the study. This patient was included in the primary analysis of efficacy. Of the 374 study patients, one was excluded from the intent- to-treat efficacy analysis because surgery was cancelled after drug administration"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Warriner 1997 *(Continued)*

Other bias	Unclear risk	Quote: "demographic information is summarized in Table I. There were no differences between groups. There were no differences between treatment groups in the doses of medications used for premedication, induction, maintenance, reversal of muscle relaxation, or postoperative analgesia (Table II)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Watts 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 59 • *Age (mean ± SD, median (IQR), median (range))*: 30.5 ± 5.68 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 27/25 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 20 to 30 • *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl at induction, 9.4 mg morphine postoperative • *Type of surgery*: laparoscopic procedure Metoclopramide • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 55 • *Age (mean ± SD, median (IQR), median (range))*: 30.9 ± 2.89 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 20/20 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)

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Watts 1996 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 20 to 30
- *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl at induction, 8.7 mg morphine postoperative
- *Type of surgery*: laparoscopic procedure

Cyclizine

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 53
- *Age (mean ± SD, median (IQR), median (range))*: 30.3 ± 7.06
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 23/28
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 20 to 30
- *Use of perioperative opioids (if yes, which?)*: 1.5 µg/kg fentanyl at induction, 8.4 mg morphine postoperative
- *Type of surgery*: laparoscopic procedure

Included criteria: women presenting for elective laparoscopic procedure on a day-stay basis

Excluded criteria: pregnant, had taken any opiate or antiemetic in the preceding 24 hours, history of hypersensitivity to any of the trial agents, on assessment were deemed to be better served by an anaesthetic different from the standard technique (obesity, reflux, difficult airway)

Pretreatment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: immediately following cannula insertion • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Metoclopramide • *Dose*: 10 mg • *Time point of administration*: immediately following cannula insertion • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM Cyclizine • *Dose*: 50 mg • *Time point of administration*: immediately following cannula insertion • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: prochlorperazine 12.5 mg IM

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Watts 1996 *(Continued)*

Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Extrapyramidal symptoms (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** New Zealand **Setting:** outpatient, single-centre **Author's name:** S.A. Watts **Institution:** Palmerston North Hospital, Palmerston North, New Zealand **Email:** NA **Address:** Department of Anaesthesia, Waikato Hospital, Hamilton, New Zealand **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	Two studies (1 non-randomized pilot study, 1 RCT)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the second phase was a randomized, double-blind comparison of the efficacy of the three study antiemetics" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "all test agents were supplied to the administering anaesthetist in capped and coded syringes containing 2 ml of colourless liquid" Judgement comment: insufficient information on allocation concealment and time point of randomization
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all test agents were supplied to the administering anaesthetist in capped and coded syringes containing 2 ml of colourless liquid"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...hours postoperatively and at time of discharge from the day-stay unit (usually four to six hours post operation), by the attending nursing staff. Scores at 24 hours were attained by phone or standard questionnaire via return mail by the investigator"

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Watts 1996 *(Continued)*

		Judgement comment: no information on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...166 making up the comparative trial population. Of the patients in the comparative trial, 54 were given metoclopramide (Group M), 59 received ondansetron (Group O) and 53 cyclizine (Group C)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "...similar in the three groups for mean patient age, day of menstrual cycle and type of operation. Distribution of patients with a past history of motion sickness or previous PONV was comparable between groups and likewise there was no difference of significance in the distribution of operative procedures" Judgement comment: baseline characteristics (age): no; (weight, BMI, ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness, perioperative opioids): no; (duration of anaesthesia, non-smoker): unclear

Wattwil 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 55 (31 to 78) • *Weight (mean ± SD, median (IQR), median (range))*: 70 (48 to 109) • *BMI (mean ± SD, median (IQR), median (range))*: 26 (18 to 43) • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 71.05 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 53 • *Use of perioperative opioids (if yes, which?)*: fentanyl at induction, 5 mg postoperative morphine equivalent consumption • *Type of surgery*: breast surgery for carcinoma Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA

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Wattwil 2003 *(Continued)*

- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 58 (18 to 75)
- *Weight (mean ± SD, median (IQR), median (range))*: 71 (50 to 90)
- *BMI (mean ± SD, median (IQR), median (range))*: 26 (19 to 34)
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 80
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 51
- *Use of perioperative opioids (if yes, which?)*: fentanyl at induction, 3 mg postoperative morphine equivalent consumption
- *Type of surgery*: breast surgery for carcinoma

Included criteria: ASA I to III, 19 to 80 years of age, undergoing breast surgery for carcinoma

Excluded criteria: receiving preoperative steroid medication

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, non-smoker): no; (history of PONV/motion sickness): unclear

Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 4 mg • *Time point of administration*: immediately after induction of anaesthesia but before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2.5% (NA) Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: immediately after induction of anaesthesia but before the start of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0% (NA)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 8 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects

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Wattwil 2003 *(Continued)*

Identification	**Sponsorship source:** NA **Country:** Sweden **Setting:** in- and outpatient, single-centre **Author's name:** M. Wattwil **Institution:** Department of Anesthesiology and Intensive Care, University Hospital, Örebro, Sweden **Email:** magnus.wattwil@orebroll.se **Address:** Department of Anesthesiology and Intensive Care, University Hospital, SE-701 85 Örebro, Sweden **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using computer-generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Quote: "using computer- generated random numbers inserted into sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "patients were blinded since they received the study drug after induction of anesthesia" Judgement comment: no information on blinding of anaesthesiologist
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "nurses recording episodes of retching or vomiting were not blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "eighty patients were scheduled for the study but two patients in Group D were excluded due to violation of the study protocol (one incorrect premedication and one intubation anesthesia)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic data and duration of operation are presented in Table 1. No differences were seen between the groups" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, non-smoker): no; (history of PONV/motion sickness): unclear

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Weren 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 38 • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 45.03 ± 16.07 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 28.05 ± 10.50 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 86.85 • *History of PONV/motion sickness (%)*: 10.53/NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 112.5 • *Use of perioperative opioids (if yes, which?)*: 26.51 µg sufentanil, 10 mg piritramide • *Type of surgery*: gynaecological, laparoscopic, abdominal Methylprednisolone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 45.35 ± 15.23 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 25.20 ± 20 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 67.5 • *History of PONV/motion sickness (%)*: 7.50/NA • *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 127.5 • *Use of perioperative opioids (if yes, which?)*: 27.94 µg sufentanil, 10 mg piritramide • *Type of surgery*: gynaecological, laparoscopic, abdominal Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40

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Weren 2008 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 47.28 ± 16.58
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 25.80 ± 7.45
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 87.5
- *History of PONV/motion sickness (%)*: 10.00/NA
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 105.0
- *Use of perioperative opioids (if yes, which?)*: 23.94 µg sufentanil, 10 mg piritramide
- *Type of surgery*: gynaecological, laparoscopic, abdominal

Included criteria: female adult, elective abdominal or gynaecological surgery, informed consent

Excluded criteria: pregnancy, lactation, intake of antiemetic drugs within 24 hours preceding surgery and emergency procedure

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness): unclear; (perioperative opioids, non-smoker, duration of anaesthesia): yes

Interventions

Intervention characteristics

Dexamethasone

- *Dose*: 8 mg
- *Time point of administration*: at induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: alizapride 50 mg or ondansetron 4 mg

Methylprednisolone

- *Dose*: 40 mg
- *Time point of administration*: at induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: alizapride 50 mg or ondansetron 4 mg

Placebo

- *Dose*: normal saline
- *Time point of administration*: at induction of anaesthesia
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: alizapride 50 mg or ondansetron 4 mg

Outcomes

Vomiting (0 to 2 hours)

- Outcome type: dichotomous outcome

Vomiting (2 to 24 hours)

- Outcome type: dichotomous outcome

PONV (0 to 24 hours)

- Outcome type: dichotomous outcome

Identification

Sponsorship source: NA

Country: Belgium

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Weren 2008 *(Continued)*

Setting: inpatient, single-centre

Author's name: Matijn Weren

Institution: Kliniek St. Jan, Brussels, Kruidtuinlaan 32, 1000 Brussel

Email: matijnweren@yahoo.co.uk

Address: UZ Gasthuisberg, Department of Anesthesia, Herestraat 49, 3000 Leuven

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: primary endpoint is to compare dexamethasone and methylprednisolone to placebo for prevention of PONV

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: "patients were randomized in three groups by a computer generated list"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: "prophylactic anti-emetic drugs were given according to the randomization in a double-blind matter. all patients were given a 10 ml intravenous solution at the induction of anaesthesia". Insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: quote: "there were no significant differences between our 3 groups with regard to age, type of surgery, body mass index (BMI), history of PONV, smoking status, use of N_2O or use of clonidine. Duration of anaesthesia was significantly longer in the methylprednisolone group in comparison with placebo. Significantly more sufentanil was used in the methylprednisolon group in comparison with placebo.Neither the use of sufentanil nor the duration of anaesthesia was significantly different between the two steroid groups" Baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness): unclear; (perioperative opioids, non-smoker, duration of anaesthesia): yes

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White 2005-1

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, dose-finding study, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 47 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 82 ± 22 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 6/13/1/0 • *Gender (female in %)*: 65 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 156 • *Use of perioperative opioids (if yes, which?)*: 1.318 µg remifentanil • *Type of surgery*: ENT surgery (tympanoplasty, sinusotomy, septoplasty, other) Droperidol (0.625 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 16 • *Weight (mean ± SD, median (IQR), median (range))*: 81 ± 1 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 6/12/2/0 • *Gender (female in %)*: 45 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 123 • *Use of perioperative opioids (if yes, which?)*: 1.217 µg remifentanil • *Type of surgery*: ENT surgery (tympanoplasty, sinusotomy, septoplasty, other) Droperidol (1.25 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20 • *Received treatment (n)*: NA • *Analysed (n)*: 20 • *Age (mean ± SD, median (IQR), median (range))*: 45 ± 15

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White 2005-1 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 77 ± 21
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 6/14/0/0
- *Gender (female in %)*: 50
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (desflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 164
- *Use of perioperative opioids (if yes, which?)*: 1.217 µg remifentanil
- *Type of surgery*: ENT surgery (tympanoplasty, sinusotomy, septoplasty, other)

Included criteria: outpatient, ASA I to III, scheduled to undergo otolaryngologic surgical procedures

Excluded criteria: clinically significant cardiac disease, atrioventricular conduction delay or bundle branch block, history of alcohol or drug abuse within the past 3 months, morbid obesity (body mass index > 40 kg/m^2), had taken any antiemetic medication within 24 hours before surgery, were pregnant or experiencing menstrual symptoms

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia for study 1): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: approximately 15 minutes before surgical incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (0.625 mg group) • *Dose*: 0.625 mg • *Time point of administration*: approximately 15 minutes before surgical incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol (1.25 mg group) • *Dose*: 1.25 mg • *Time point of administration*: approximately 15 minutes before surgical incision • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Arrhythmia (until discharge)* • Outcome type: dichotomous outcome *QT prolongation (0 to 10% at 10 minutes, 10% to 25% at 10 minutes)* • Outcome type: dichotomous outcome

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White 2005-1 *(Continued)*

Headache (0 to 24 hours)

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** supported in part by the Margaret Milam McDermott Distinguished Chair in Anesthesiology and the White Mountain Institute, a private not-for-profit foundation in Los Altos, California (Dr. Paul F. White, President) **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Paul F. White **Institution:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Texas, USA **Email:** paul.white@utsouthwestern.edu **Address:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, CS 2. 282, Dallas, Texas, USA 75390-9068 **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Two studies. First as dose-finding study, and second with higher dose only (follow-up study)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "based on a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study medication consisted of either saline (control) or 0.625 or 1.25 mg droperidol, prepared in identical-appearing 2-ml syringes by an individual not involved in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the electrocardiographic measurements were independently performed by two investigators who were unaware of which of the three treatment groups the patient had been assigned to. Heart rate was calculated..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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White 2005-1 *(Continued)*

Other bias	High risk	Quote: "the three study groups were similar with respect to their demographic characteristics, durations of anesthesia, and total dosages of anesthetic and analgesic drugs, as well as intravenous fluid administration during the operation" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia for study 1): yes

White 2005-2

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 47 ± 12 • *Weight (mean ± SD, median (IQR), median (range))*: 81 ± 18 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (desflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 122 • *Use of perioperative opioids (if yes, which?)*: remifentanil (NA) • *Type of surgery*: ENT surgery (tympanoplasty, sinusotomy, septoplasty, other) Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 46 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 88 ± 24 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (desflurane, remifentanil)

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White 2005-2 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 129
- *Use of perioperative opioids (if yes, which?)*: remifentanil (NA)
- *Type of surgery*: ENT surgery (tympanoplasty, sinusotomy, septoplasty, other)

Included criteria: outpatient, ASA I to III, scheduled to undergo otolaryngologic surgical procedures

Excluded criteria: clinically significant cardiac disease, atrioventricular conduction delay, bundle branch block, history of alcohol or drug abuse within the past 3 months, morbid obesity (body mass index > 40 kg/m^2), had taken any antiemetic medication within 24 hours before surgery, were pregnant or were experiencing menstrual symptoms

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia for study 1): yes

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Droperidol • *Dose*: 1.25 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Arrhythmia (until discharge)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported in part by the Margaret Milam McDermott Distinguished Chair in Anesthesiology and the White Mountain Institute, a private not-for-profit foundation in Los Altos, California, USA (Dr. Paul F. White, President) **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Paul F. White **Institution:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Texas, USA **Email:** paul.white@utsouthwestern.edu **Address:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, CS 2. 282, Dallas, Texas 75390-9068, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** NA

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White 2005-2 *(Continued)*

	Trial registry number: NA
Notes	Two studies. First as dose-finding study, second with higher dose only (follow-up study)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "based on a computer-generated random number table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the study medication consisted of either saline (control) or 0.625 or 1.25 mg droperidol, prepared in identical-appearing 2-ml syringes by an individual not involved in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the electrocardiographic measurements were independently performed by two investigators who were unaware of which of the three treatment groups the patient had been assigned to. Heart rate was calculated..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "the three study groups were similar with respect to their demographic characteristics, durations of anesthesia, and total dosages of anesthetic and analgesic drugs, as well as intravenous fluid administration during the operation" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear; (duration of anaesthesia for study 1): yes

White 2006

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 110 • *Received treatment (n)*: NA • *Analysed (n)*: 101 • *Age (mean ± SD, median (IQR), median (range))*: 39 ± 14

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White 2006 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 100 ± 36
- *BMI (mean ± SD, median (IQR), median (range))*: 37 ± 10
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 89.11
- *Non-smoker (%)*: 89
- *History of PONV/motion sickness (%)*: 15/12
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 116
- *Use of perioperative opioids (if yes, which?)*: 236 µg fentanyl intraoperative, 76 µg fentanyl PACU, 1.7 mg hydromorphone PACU, 3 mg hydromorphone after PACU
- *Type of surgery*: cholecystectomy, laparoscopic tubal ligation, gastric bypass

Granisetron + dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 110
- *Received treatment (n)*: NA
- *Analysed (n)*: 104
- *Age (mean ± SD, median (IQR), median (range))*: 38 ± 13
- *Weight (mean ± SD, median (IQR), median (range))*: 104 ± 34
- *BMI (mean ± SD, median (IQR), median (range))*: 38 ± 11
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 87.5
- *Non-smoker (%)*: 85
- *History of PONV/motion sickness (%)*: 18/11
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 122
- *Use of perioperative opioids (if yes, which?)*: 239 µg fentanyl intraoperative, 81 µg fentanyl PACU, 1.6 mg hydromorphone PACU, 4 mg hydromorphone after PACU
- *Type of surgery*: cholecystectomy, laparoscopic tubal ligation, gastric bypass

Included criteria: undergoing surgery procedure (e.g. cholecystectomy, laparoscopic tubal ligation, gastric bypass)

Excluded criteria: history of allergy to any of the potential study medications; pregnancy; breastfeeding; active menstruation; vomiting or retching within 24 hours before the operation; administration of antiemetic or psychoactive medication within 24 hours before surgery; history of severe (or unstable) cardiovascular, respiratory, metabolic, endocrine, or neurologic disease; active alcohol or drug abuse; impaired renal or hepatic function

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ondansetron + dexamethasone • *Dose*:ondansetron 4 mg, dexamethasone 4 mg • *Time point of administration*: oral placebo 1 hour before surgery, dexamethasone after tracheal intubation, ondansetron at end of surgery • *Route of administration*: ondansetron IV, dexamethasone IV, placebo PO • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Granisetron + dexamethasone

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White 2006 *(Continued)*

	• *Dose*: granisetron 1 mg, dexamethasone 4 mg • *Time point of administration*: oral granisetron 1 hour before surgery, dexamethasone after tracheal intubation, placebo at end of surgery • *Route of administration*: granisetron PO, dexamethasone IV, placebo IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** supported, in part, by the White Mountain Institute, a non-for-profit private educational and research foundation dedicated to art and medicine. Endowment funds from the Margaret Milam McDermott Distinguished Chair in Anesthesiology are used to support Dr. White's academic activities **Country:** USA **Setting:** inpatients and outpatients, multi-centre **Author's name:** Paul F. White **Institution:** Department of Anesthesiology and Pain Management, UT Southwestern Medical Center, Dallas, Texas, USA **Email:** paul.white@utsouthwestern.edu **Address:** Department of Anesthesiology and Pain Management, UT Southwestern Medical Center, 5323 Harry Hines Boulevard, F2.208A; Dallas, Texas 75390-906, USA **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "assigned to one of two prophylactic treatment groups according to a computer-generated random numbers table"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the patients, the investigators collecting data, and the nurses involved in the post- operative care of the patients were blinded as to the content of the study medication, which were prepared by a research pharmacist at each hospital. The active and placebo pills were identical in appearance"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patients, the investigators collecting data, and the nurses involved in the post- operative care of the patients were blinded as to the content of the

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White 2006 *(Continued)*

		study medication, which were prepared by a research pharmacist at each hospital"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 220 patients were enrolled in the study. However, 15 patients (9 patients in the ondansetron group and 6 patients in the granisetron group) were excluded from the final data analysis because of protocol violations and/or incomplete data"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "demographic characteristics, including age, body weight, body mass index, smoking status, and history of PONV or motion sickness were comparable in both antiemetic treatment groups (Table 1). In addition, there were no differences in the durations of anesthesia and surgery or in the doses of preoperative medication, induction and maintenance anesthetics, muscle relaxant reversal drugs, and use of intraoperative (Table 1) and postoperative (Table 2) opioid analgesic medications in the ondansetron and granisetron groups" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

White 2007-1

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Scopolamine + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 32 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 14 • *Weight (mean ± SD, median (IQR), median (range))*: 95 ± 41 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 7/18/7/0 • *Gender (female in %)*: 91 • *Non-smoker (%)*: 75 • *History of PONV/motion sickness (%)*: 31/22 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 174 • *Use of perioperative opioids (if yes, which?)*: 43 µg sufentanil • *Type of surgery*: plastic surgery Droperidol + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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White 2007-1 *(Continued)*

- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 34
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 11
- *Weight (mean ± SD, median (IQR), median (range))*: 91 ± 36
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 7/21/6/0
- *Gender (female in %)*: 79
- *Non-smoker (%)*: 76
- *History of PONV/motion sickness (%)*: 26/18
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 172
- *Use of perioperative opioids (if yes, which?)*: 51 µg sufentanil
- *Type of surgery*: plastic surgery

Included criteria: 18 to 65 years of age, scheduled to undergo major laparoscopic (e.g. bariatric) (n = 80) or plastic (e.g. abdominoplasty, reduction mammoplasty) (n = 70) surgery procedure

Excluded criteria: had received an antiemetic drug within the preceding 24 hours, history of alcohol or drug abuse within the past 3 months, allergic to any of the study medications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Scopolamine + dexamethasone • *Dose*: scopolamine 1.5 mg, dexamethasone 4 mg • *Time point of administration*: scopolamine 60 minutes before entering the operating room, dexamethasone after induction of anaesthesia • *Route of administration*: scopolamine TD, dexamethasone IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV in the recovery room and promethazine 12.5 mg to 25 mg IM on the postsurgical ward, prochlorperazine 25 mg at time of discharge Droperidol + dexamethasone • *Dose*: dexamethasone 4mg, droperidol 1.25 mg • *Time point of administration*: dexamethasone after induction of anaesthesia, droperidol at the start of skin closure • *Route of administration*: both IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV in the recovery room and promethazine 12.5 mg to 25 mg IM on the postsurgical ward, prochlorperazine 25 mg at time of discharge
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 72 hours)* • Outcome type: dichotomous outcome *Visual disturbances (e.g. blurred vision) (0 to 72 hours)* • Outcome type: dichotomous outcome

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White 2007-1 *(Continued)*

	Adverse events (general notes in the publication, 72 hours' observation) • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by Baxter Healthcare and Margaret Milam McDermott Distinguished Chair in Anesthesiology, as well as the White Mountain Institute, a private foundation **Country:** USA **Setting:** inpatient, multi-centre (2) **Author's name:** Paul F. White **Institution:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA **Email:** paul.white@utsouthwestern.edu **Address:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5161 Harry Hines Boulevard, CS 2. 282, Dallas, TX 75390-9068, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** incidence of emetic symptoms
Notes	Two parallel, randomized, double-blind sham and placebo-controlled studies with 2 groups each (2 types of surgery × 2 antiemetics)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the patients undergoing plastic surgery were randomized to receive either TDS or droperidol, while the laparoscopic patients received either TDS or ondansetron according to computer generated randomization schemes"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all investigational medications were prepared by a pharmacist who was not involved in the study to maintain the double-blind study design"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...by a blinded observer who directly questioned each patient about these side effects"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 150 patients were enrolled in these two studies. However, five patients were excluded due to failure to follow the protocol (i.e., an additional anti- emetic was given during the intraoperative period) and two patients refused to complete the postoperative assessments" Judgement comment: missing outcome data described and unrelated to outcomes of interest

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White 2007-1 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to study protocol or trial registry number reported
Other bias	Low risk	Quote: "the treatment groups at both study sites were comparable with respect to demographic data, duration of anesthesia, the amounts of anesthetic and analgesic medications, and IV fluid administered during the intraoperative period (Tables 1 and 2)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

White 2007-2

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, combination prophylaxis
Participants	**Baseline characteristics** Scopolamine + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 43 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 124 ± 19 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 0/0/38/0 • *Gender (female in %)*: 79 • *Non-smoker (%)*: 87 • *History of PONV/motion sickness (%)*: 16/21 • *Type of general anaesthesia*: inhalational anaesthesia (desflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 115 • *Use of perioperative opioids (if yes, which?)*: 183 µg fentanyl, hydromorphone 1.6 mg (in PACU) and 4 mg (after PACU) • *Type of surgery*: laparoscopic surgery Ondansetron + dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 39 • *Age (mean ± SD, median (IQR), median (range))*: 42 ± 10 • *Weight (mean ± SD, median (IQR), median (range))*: 135 ± 25 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 0/0/40/0 • *Gender (female in %)*: 82

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White 2007-2 *(Continued)*

- *Non-smoker (%)*: 87
- *History of PONV/motion sickness (%)*: 18/15
- *Type of general anaesthesia*: inhalational anaesthesia (desflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 115
- *Use of perioperative opioids (if yes, which?)*: 205 µg fentanyl, hydromorphone 1.6 mg (in PACU) and 3 mg (after PACU)
- *Type of surgery*: laparoscopic surgery

Included criteria: 18 to 65 years of age, scheduled to undergo major laparoscopic (e.g. bariatric) (n = 80) or plastic (e.g. abdominoplasty, reduction mammoplasty) (n = 70) surgery procedure

Excluded criteria: had received an antiemetic drug within preceding 24 hours, history of alcohol or drug abuse within past 3 months, allergic to any of the study medications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Scopolamine + dexamethasone • *Dose*: scopolamine 1.5 mg, dexamethasone 4mg • *Time point of administration*: scopolamine 60 minutes before entering the operating room, dexamethasone after induction of anaesthesia • *Route of administration*: scopolamine TD, dexamethasone IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV in recovery room, promethazine 12.5 mg to 25 mg IM on postsurgical ward, prochlorperazine 25 mg at time of discharge Ondansetron + dexamethasone • *Dose*: dexamethasone 4 mg, ondansetron 4 mg • *Time point of administration*: dexamethasone after induction of anaesthesia, ondansetron upon withdrawal of laparoscope • *Route of administration*: both IV • *Rescue antiemetics (if yes, which?)*: metoclopramide10 mg IV in recovery room, promethazine 12.5 mg to 25 mg IM on postsurgical ward, prochlorperazine 25 mg at time of discharge
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 72 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 72 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by Baxter Healthcare and Margaret Milam McDermott Distinguished Chair in Anesthesiology, as well as the White Mountain Institute, a private foundation **Country:** USA

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White 2007-2 *(Continued)*

Setting: inpatient, multi-centre (2)

Author's name: Paul F. White

Institution: Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA

Email: paul.white@utsouthwestern.edu

Address: Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5161 Harry Hines Boulevard, CS 2. 282, Dallas, TX 75390-9068, USA

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: incidence of emetic symptoms

Notes	Two parallel, randomized, double-blind sham and placebo-controlled studies with 2 groups each (2 types of surgery × 2 antiemetics)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the patients undergoing plastic surgery were randomized to receive either TDS or droperidol, while the laparoscopic patients received either TDS or ondansetron according to computer generated randomization schemes"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all investigational medications were prepared by a pharmacist who was not involved in the study to maintain the double-blind study design"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...by a blinded observer who directly questioned each patient about these side effects"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 150 patients were enrolled in these two studies. However, five patients were excluded due to failure to follow the protocol (i.e., an additional anti- emetic was given during the intraoperative period) and two patients refused to complete the postoperative assessments" Judgement comment: missing outcome data described and unrelated to outcomes of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to study protocol or trial registry number reported
Other bias	Low risk	Quote: "the treatment groups at both study sites were comparable with respect to demographic data, duration of anesthesia, the amounts of anesthetic and analgesic medications, and IV fluid administered during the intraoperative period (Tables 1 and 2)"

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White 2007-2 *(Continued)*

	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Wilkinson 1989

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 95 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 23.16/18.95 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: no significant difference in opioid analgesic usage between the 2 groups • *Type of surgery*: plastic surgical or orthopaedic procedure Hyoscine • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 95 • *Age (mean ± SD, median (IQR), median (range))*: NA • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: NA • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 25.26/34.74 • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: no significant difference in opioid analgesic usage between the 2 groups • *Type of surgery*: plastic surgical or orthopaedic procedure

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Wilkinson 1989 *(Continued)*

	Included criteria: ASA I or II, elective plastic surgical or orthopaedic procedure of less than 2 hours' duration, 16 to 65 years of age, weighing between 40 and 100 kilograms, no history of gastro-oesophageal reflux or regular antiemetic or anticholinergic medication **Excluded criteria:** NA **Pretreatment:** baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (history of PONV): no; (gender, duration of anaesthesia, non-smoker, perioperative opioids): unclear; (history of motion sickness): yes
Interventions	**Intervention characteristics** Placebo • *Dose*: placebo patch • *Time point of administration*: 7 to 12 hours before undergoing minor orthopaedic or plastic surgery • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: metoclopramide, prochlorperazine Hyoscine • *Dose*: NA • *Time point of administration*: 7 to 12 hours before undergoing minor orthopaedic or plastic surgery • *Route of administration*: transdermal • *Rescue antiemetics (if yes, which?)*: metoclopramide, prochlorperazine
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** a grant from Ciba-Geigy (New Zealand) Ltd. **Country:** New Zealand **Setting:** inpatient and outpatient, single-centre **Author's name:** F.M. Davis **Institution:** Departments of Anaesthesia and Commmunity Health, Christchurch School of Medicine, Christchurch, New Zealand **Email:** NA **Address:** Depanment of Anaesthesia, Christchurch School of Medicine, P.O. Box 4345, Christchurch, New Zealand **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of vomiting **Trial registry number:** NA
Notes	None

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Wilkinson 1989 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "supplied by Ciba-Geigy (NZ) Ltd. Random number lists were used to assign patients to one of two treatment groups, and a sealed enveloped containing..."
Allocation concealment (selection bias)	Unclear risk	Quote: "a sealed enveloped containing the trial medication, either Scopoderm or a placebo patch, was allocated for each patient" Judgement comment: not stated; sequentially numbered, opaque, and sealed envelope (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "identical, unlabelled patches containing either hyoscine or placebo were supplied by Ciba-Geigy (NZ) Ltd. Random number lists were used" Quote: "using a double-blind technique" Judgement comment: insufficient information on who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "patients were carefully interviewed either personally or by telephone by a trained independent observer"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 221 patients entering the trial, 31 were subsequently excluded for the reasons outlined in Table 1"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there were no demographic differences between the two treatment groups, each of 95 subjects, excepting that the hyoscine group contained more individuals with a past history of motion sickness (P < 0.05)" Judgement comment: baseline characteristics (ASA): no; (age, weight): unclear. Potential effect modifiers (history of PONV): no; (gender, duration of anaesthesia, non-smoker, perioperative opioids): unclear; (history of motion sickness): yes

Wilson 1996

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, dose-finding study, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 133 • *Received treatment (n)*: 133

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Wilson 1996 *(Continued)*

- *Analysed (n)*: 133
- *Age (mean ± SD, median (IQR), median (range))*: 48.5 (25 to 83)
- *Weight (mean ± SD, median (IQR), median (range))*: 65.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 95
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 32.3/15.8
- *Type of general anaesthesia*: inhalational anaesthesia (volatile agent, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 102
- *Use of perioperative opioids (if yes, which?)*: 85.7% of patients received opioid analgesics
- *Type of surgery*: gynaecological/gastrointestinal

Granisetron (0.1 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 132
- *Received treatment (n)*: 132
- *Analysed (n)*: 132
- *Age (mean ± SD, median (IQR), median (range))*: 46.8 (24 to 77)
- *Weight (mean ± SD, median (IQR), median (range))*: 66.0
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 96
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 26.5/12.1
- *Type of general anaesthesia*: inhalational anaesthesia (volatile agent, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95.4
- *Use of perioperative opioids (if yes, which?)*: 84.8% of patients received opioid analgesics
- *Type of surgery*: gynaecological/gastrointestinal

Granisetron (1.0 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 134
- *Received treatment (n)*: 134
- *Analysed (n)*: 134
- *Age (mean ± SD, median (IQR), median (range))*: 48.0 (18 to 88)
- *Weight (mean ± SD, median (IQR), median (range))*: 62.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 98
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 17.2/9.7
- *Type of general anaesthesia*: inhalational anaesthesia (volatile agent, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 108
- *Use of perioperative opioids (if yes, which?)*: 81.3% of patients received opioid analgesics
- *Type of surgery*: gynaecological/gastrointestinal

Granisetron (3.0 mg group)

- *Assessed for eligibility (n)*: -

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Wilson 1996 *(Continued)*

- *Enrolled (n)*: -
- *Randomized (n)*: 128
- *Received treatment (n)*: 128
- *Analysed (n)*: 128
- *Age (mean ± SD, median (IQR), median (range))*: 46.1 (21 to 79)
- *Weight (mean ± SD, median (IQR), median (range))*: 65.1
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 96
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 30.5/18.0
- *Type of general anaesthesia*: inhalational anaesthesia (volatile agent, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100.2
- *Use of perioperative opioids (if yes, which?)*: 82.0% of patients received opioid analgesics
- *Type of surgery*: gynaecological/gastrointestinal

Included criteria: both sexes; over the legal age of consent; undergoing elective open cholecystectomy, open gynaecological procedure, or vaginal hysterectomy during general anaesthesia.

Excluded criteria: ASA IV or V, body weight ≥ 25% above ideal, breastfeeding or pregnancy, known sensitivity to 5-HT3 antagonists, already experiencing vomiting or moderate to severe nausea, had taken antiemetic drugs in the 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: NA • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 39.8% (prochlorperazine, metoclopramide) Granisetron (0.1 mg group) • *Dose*: 0.1 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA (prochlorperazine, metoclopramide) Granisetron (1.0 mg group) • *Dose*: 1.0 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 24.6% (prochlorperazine, metoclopramide) Granisetron (3.0 mg group) • *Dose*: 3.0 mg • *Time point of administration*: 5 minutes before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 22.7% (prochlorperazine, metoclopramide)
Outcomes	*Vomiting (0 to 24 hours)*

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Wilson 1996 *(Continued)*

- Outcome type: dichotomous outcome

Vomiting (0 to 6 hours)

- Outcome type: dichotomous outcome

Nausea (0 to 24 hours)

- Outcome type: dichotomous outcome

Complete response (no PONV) in 24 hours

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Denmark, Finland, France, Italy, The Netherlands, South Africa, Switzerland, UK **Setting:** NA, multi-centre (35) **Author's name:** K.L. Kong **Institution:** City Hospital, Dudley Road, Birmingham, UK **Email:** NA **Address:** City Hospital, Dudley Road, Birmingham, UK **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** no vomiting
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated randomization schedule"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "on the randomization code" Quote: "the study was blinded by each syringe being preloaded with the same amount of fluid but a different dose of granisetron (0, 0.1 mg, 1.0 mg or 3.0 mg), depending..."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias)	Low risk	Judgement comment: no missing outcome data

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Wilson 1996 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the groups were comparable in the type of surgery performed, anaesthetic agents and technique used, duration of operation and perioperative use of opioid analgesics (table 2)" Quote: "there were no significant treatment-by-factor interactions for age, weight, previous history of PONV–motion sickness, menopausal status, duration of anaesthesia or study country (table 4)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness, perioperative opioids): no; (non-smoker): unclear

Wilson 2001

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Metoclopramide (group II) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 72 • *Age (mean ± SD, median (IQR), median (range))*: 42 (18 to 72) • *Weight (mean ± SD, median (IQR), median (range))*: 81 (42 to 136) • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: I to III (distribution unclear) • *Gender (female in %)*: 79 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 5 µg/kg fentanyl intraoperative, postoperative analgesia, if required, was provided with meperidine • *Type of surgery*: laparoscopic cholecystectomy Ondansetron (group I) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 78 • *Age (mean ± SD, median (IQR), median (range))*: 43 (19 to 69)

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Wilson 2001 *(Continued)*

- *Weight (mean ± SD, median (IQR), median (range))*: 80 (45 to 132)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: I to III (distribution unclear)
- *Gender (female in %)*: 79
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 5 µg/kg fentanyl intraoperative, postoperative analgesia, if required, was provided with meperidine
- *Type of surgery*: laparoscopic cholecystectomy

Placebo (group III)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: NA
- *Received treatment (n)*: NA
- *Analysed (n)*: 82
- *Age (mean ± SD, median (IQR), median (range))*: 43 (20 to 73)
- *Weight (mean ± SD, median (IQR), median (range))*: 81 (52 to 121)
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: I to III (distribution unclear)
- *Gender (female in %)*: 78
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: 2 µg/kg to 5 µg/kg fentanyl intraoperative, postoperative analgesia, if required, was provided with meperidine
- *Type of surgery*: laparoscopic cholecystectomy

Included criteria: scheduled for laparoscopic cholecystectomy under general anaesthesia

Excluded criteria: pregnancy; breastfeeding; excessive weight ≥ 50% ideal body weight; nausea, vomiting, or use of antiemetics within 24 hours before surgery; insulin-dependent diabetes mellitus; conversion to open cholecystectomy; allergy to any protocol medication; development of intraoperative complications requiring immediate hospital admission

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Metoclopramide (group II)

- *Dose*: 10 mg
- *Time point of administration*: before surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 26% (promethazine 12.5 mg IV)

Ondansetron (group I)

- *Dose*: 4 mg
- *Time point of administration*: before surgery
- *Route of administration*: IV

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Wilson 2001 *(Continued)*

	• *Rescue antiemetics (if yes, which?)*: 38% (promethazine 12.5 mg IV) Placebo (group III) • *Dose*: saline • *Time point of administration*: before surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 39% (promethazine 12.5 mg IV)
Outcomes	*Vomiting (0 to 24 hours,* PACU or day surgery*)* • Outcome type: dichotomous outcome *Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (after PACU to "day surgery", follow-up by telephone at 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours,* PACU or day surgery*)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Erik B. Wilson **Institution:** Department of Surgery, Scott and White Clinic and Memorial Hospital **Email:** erikbwilson@yahoo.com **Address:** Health Science Center College of Medicine, 2401 South 31st Street, Temple, TX 76508, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomized" Judgement comment: no details on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement

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Wilson 2001 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the pharmacy supplied syringes in a blinded fashion with normal saline utilized as diluent such that all syringes have equal volumes. The medication was given by a blinded holding area or research nurse"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: insufficient information on missing outcome data (9% missing outcome data due to protocol violations, unclear which treatment arms, reasons not further described)
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Worni 2008

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA • *Received treatment (n)*: NA • *Analysed (n)*: 37 • *Age (mean ± SD, median (IQR), median (range))*: 52 (18 to 77) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 81 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 0/NA • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane or sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 195 • *Use of perioperative opioids (if yes, which?)*: 5 µg/kg to 10 µg/kg fentanyl intraoperative, postoperative/per patient (9.7 mg) • *Type of surgery*: thyroid surgery Placebo (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: NA

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Worni 2008 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 51.5 (22 to 80)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 66
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane or sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 172
- *Use of perioperative opioids (if yes, which?)*: 5 µg/kg to 10 µg/kg fentanyl intraoperative, postoperative/per patient (17.9 mg)
- *Type of surgery*: thyroid surgery

Included criteria: undergoing thyroid surgery

Excluded criteria: had received antiemetic therapy within 48 hours before surgery; depression, chronic pain disorder, insulin-dependent diabetes mellitus; history of severe and/or repeated PONV (prolonged vomitus (first day postoperative) after previous minor surgery that led to change from standard anaesthetic protocol); pregnancy; younger than 18 years of age, had known malignant disease; had undergone previous thyroid or neck surgery. In this per-protocol analysis, patients who received extended resection because of positive findings in the fresh frozen tissue analysis and those who did not receive standard anaesthesia were also excluded. Patients with preoperative voice disturbance or a voice visual analog scale (VVAS) = 40 were not eligible

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker): unclear; (perioperative opioids -> There is a significant difference between dexamethasone and control group in terms of opioid consumption (only at 48 hours)): yes

Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 8 mg • *Time point of administration*: infusions were given over 15 minutes, 45 minutes before initiation of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg (first line), 0.625 mg droperidol (second line) Placebo (group C) • *Dose*: 2 mL 0.9% NaCl • *Time point of administration*: infusions were given over 15 minutes, 45 minutes before initiation of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg (first line), 0.625 mg droperidol (second line)
Outcomes	*Postoperative wound infection (30 days after the intervention)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA

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Worni 2008 *(Continued)*

Country: Switzerland

Setting: inpatient, single-centre

Author's name: Stephan A. Vorburger

Institution: Department of Visceral and Transplant Surgery, University Hospital Bern

Email: stephan.vorburger@insel.ch.

Address: University Hospital Bern, Freiburgstrasse 8, CH-3010 Bern, Switzerland

Language: English

Duration of study: November 2005 to June 2007

Trial registry number: NCT00619086

Study's primary outcome: nausea

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was achieved with a computerized random number table with a repetition cycle of 25"
Allocation concealment (selection bias)	Low risk	Quote: "the randomization code was kept separate and was unknown to any of the investigators until after the study was finished"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...postoperative nausea and vomiting. The treatment and control solutions were prepared off the ward, appeared transparent, and were marked identically. The infusions were given over 15 minutes by a blinded nursing staff, 45 minutes before the initiation of anesthesia. Thus, the patient, the nurse, the anesthesiologist, the surgeon, and the data analyst were all blinded..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...before the initiation of anesthesia. Thus, the patient, the nurse, the anesthesiologist, the surgeon, and the data analyst were all blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of these, ninety patients consented to participate in the study. Exclusion criteria were: depression, chronic pain disorder, insulin-dependent diabetes mellitus (n 7), history of severe and/or repeated PONV (n 2), pregnancy, age 18 years (n 0), preoperatively known malignant disease (n 23), previous thyroid or neck surgery (n 11), and no consent (n 15 denied; n 9 not consented because of absence of investigators or reasons unknown). Eighteen patients were excluded because of intraoperative detected malignancy and additional lymphadenectomy (n 10) or because of protocol violations: n 3 did not receive timely dexamethasone, n 3 received additional steroids intraoperatively, and n 2 received postoperative analgesic/antiemetic regimens that did not follow the protocol" Judgement comment: all missing outcome (18/90 exclusions due to protocol violations = 20%) data were described. Reasons were not related to the outcome of interest
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT00619086 (retrospective registration)

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Worni 2008 *(Continued)*

Other bias	Unclear risk	Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV): no; (history of motion sickness, non-smoker): unclear; (perioperative opioids -> There is a significant difference between dexamethasone and control group in terms of opioid consumption (only at 48 hours)): yes

Wu 2000

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 33.8 ± 7.8 • *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 12.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 31.58/26.32 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane and/or enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 60 • *Use of perioperative opioids (if yes, which?)*: intraoperative opioids (100%), postoperative opioids (79%) (50 µg to 350 µg fentanyl or 1.0 mg to 1.5 mg alfentanil) • *Type of surgery*: laparoscopic gynaecological procedure Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 38 • *Age (mean ± SD, median (IQR), median (range))*: 31.6 ± 6.9 • *Weight (mean ± SD, median (IQR), median (range))*: 63.2 ± 12.8 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/NA/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 36.84/34.21 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane and/or enflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 60

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Wu 2000 *(Continued)*

- *Use of perioperative opioids (if yes, which?)*: intraoperative opioids (100%), postoperative opioids (74%) (50 µg to 350 µg fentanyl or 1.0 mg to 1.5 mg alfentanil)
- *Type of surgery*: laparoscopic gynaecological procedure

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 37
- *Age (mean ± SD, median (IQR), median (range))*: 33.1 ± 5.0
- *Weight (mean ± SD, median (IQR), median (range))*: 60.5 ± 11.8
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 35.14/37.84
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane and/or enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 59
- *Use of perioperative opioids (if yes, which?)*: intraoperative opioids (100%), postoperative opioids (81%) (50 µg to 350 µg fentanyl or 1.0 mg to 1.5 mg alfentanil)
- *Type of surgery*: laparoscopic gynaecological procedure

Droperidol + ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 39
- *Age (mean ± SD, median (IQR), median (range))*: 32.9 ± 7.1
- *Weight (mean ± SD, median (IQR), median (range))*: 62.6 ± 11.4
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/NA/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 25.64/48.72
- *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane and/or enflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 60
- *Use of perioperative opioids (if yes, which?)*: intraoperative opioids (100%), postoperative opioids (67%) (50 µg to 350 µg fentanyl or 1.0 mg to 1.5 mg alfentanil)
- *Type of surgery*: laparoscopic gynaecological procedure

Included criteria: ASA I to III, female outpatients scheduled to undergo elective laparoscopic gynaecological procedure under general anaesthesia, 16 to 65 years of age

Excluded criteria: laboratory or clinical evidence of cardiovascular, haematologic, pulmonary, renal, hepatic, neurological, or endocrine abnormalities; pregnancy; morbid obesity (those > 25% above ideal body weight); history of substance abuse; antiemetic or psychoactive medication within 24 hours before surgery; previous allergic reaction to serotonin antagonists; need for a nasogastric tube postoperatively

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (non-smoker): unclear; (history of motion sickness): yes

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Wu 2000 *(Continued)*

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: upon induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 26% (dimenhydrinate 25 mg IV, metoclopramide 5 mg to 10 mg IV, ondansetron 4 mg IV) Droperidol • *Dose*: 1.25 mg • *Time point of administration*: upon induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 16% (dimenhydrinate 25 mg IV, metoclopramide 5 mg to 10 mg IV, ondansetron 4 mg IV) Ondansetron • *Dose*: 4 mg • *Time point of administration*: upon induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 30% (dimenhydrinate 25 mg IV, metoclopramide 5 mg to 10 mg IV, ondansetron 4 mg IV) Droperidol + ondansetron • *Dose*: droperidol 1.25 mg, ondansetron 4 mg • *Time point of administration*: upon induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 3% (dimenhydrinate 25 mg IV, metoclopramide 5 mg to 10 mg IV, ondansetron 4 mg IV)
Outcomes	*PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by St. Michael's Hospital Health Science Research Center, Toronto and in part by Glaxo, Inc. of Canada, Mississauga, Ontario, Canada **Country:** Canada **Setting:** outpatients, single-centre **Author's name:** Susan Belo **Institution:** Department of Anaesthesia, St. Michael's Hospital, Toronto, Ontario, Canada **Email:** belos@smh.toronto.on.ca **Address:** Department of Anaesthesia, St. Michael's Hospital, 30 Bond Street, Toronto, Ontario, M5B 1W8 Canada **Duration of study:** NA **Language:** English

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Wu 2000 *(Continued)*

	Study's primary outcome: incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "upon consent, each patient was randomized to one of four intravenous treatment categories" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "in this way, the anesthesiologist, study investigator, patient, operating room attendants, and recovery room nurses, were all blinded to the identity of the prophylactic treatment" Quote: "each of these therapy medications was prepared by either the operating room pharmacist (not otherwise involved in the study) or by the research coordinator, and presented to the attending anesthesiologist"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "in this way, the anesthesiologist, study investigator, patient, operating room attendants, and recovery room nurses, were all blinded to the identity of the prophylactic treatment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "there were eight study patients (two from the placebo group, three from the ondansetron group, two from the droperidol group, and one from the combination group) excluded from the study because they were inadvertently given thiopentol for induction of anesthesia. Thiopentol has been known to cause post-operative nausea and vomiting. 2 0 Three study patients (one in the droperidol group, one in the ondansetron group, and one in the combination group) were admitted due to surgical complications unrelated to the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "no differences in demographic data among the four treatment groups in regards to age, height, weight, history of PONV after previous general anesthesia, duration of anesthesia, and history of motion sickness were found (Table I). There were also no differences among study groups in administration of midazolam, opioids given intraoperatively and post- operatively, all known to have anti-emetic or emetic properties. However, the combination group did receive more nitrous oxide 70% than the other groups (Table II) which may lead to increased PONV" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, history of PONV, perioperative opioids): no; (non-smoker): unclear; (history of motion sickness): yes

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Wu 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: 30 • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 42.4 ± 11.1 • *Weight (mean ± SD, median (IQR), median (range))*: 60.1 ± 7.2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 53 • *Non-smoker (%)*: 67 • *History of PONV/motion sickness (%)*: 13/13 • *Type of general anaesthesia*: sevoflurane in combination with nitrous oxide (N_2O) in spontaneously breathing patients • *Duration of anaesthesia or surgery (in min; as mean or median)*: 48.6 • *Use of perioperative opioids (if yes, which?)*: 46% of patients required ketorolac with an average of 32.1 mg meperidine • *Type of surgery*: outpatient anorectal surgery Placebo (group S) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 30 • *Received treatment (n)*: NA • *Analysed (n)*: 30 • *Age (mean ± SD, median (IQR), median (range))*: 38.5 ± 11.3 • *Weight (mean ± SD, median (IQR), median (range))*: 61.3 ± 8.5 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 47 • *Non-smoker (%)*: 70 • *History of PONV/motion sickness (%)*: 20/10 • *Type of general anaesthesia*: sevoflurane in combination with nitrous oxide (N_2O) in spontaneously breathing patients • *Duration of anaesthesia or surgery (in min; as mean or median)*: 51.1 • *Use of perioperative opioids (if yes, which?)*: 67% of patients required ketorolac with an average of 37.5 mg meperidine • *Type of surgery*: outpatient anorectal surgery **Included criteria:** ASA I and II, adult outpatients scheduled for anorectal surgery **Excluded criteria:** pregnancy; history of alcohol or drug abuse; history of allergic reactions to any of the study medications; severe cardiovascular, respiratory, metabolic, endocrine, disease; use of prophylactic antiemetic drugs within 24 hours before surgery

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Wu 2009 *(Continued)*

	Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes
Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 5 mg • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV (max. 2 doses) Placebo (group S) • *Dose*: equal volume of saline • *Time point of administration*: before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: ondansetron 4 mg IV (max. 2 doses)
Outcomes	*Vomiting (0 to discharge, in the recovery area)* • Outcome type: dichotomous outcome *Vomiting (post discharge to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported in part by National Science Council Grant NSC 95-2314-B-214-011, Taipei, Taiwan **Country:** Taiwan **Setting:** outpatient, single-centre **Author's name:** Ping Heng Tan **Institution:** Department of Anesthesiology, E-DA Hospital/I-Shou University **Email:** tanphphd@hotmail.com **Address:** Rong-Jong Rd., Kaohsiung 813, Taiwan **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** we considered PONV as the primary outcome
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using computer-generated random numbers"

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Wu 2009 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: "double-blinded manner". Insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a trained interviewer who was blinded as to study group allocation, contacted all patients by telephone at home 24 hours after discharge to inquire about postdischarge side effects" Quote: "a study-blinded observer recorded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Yamamoto 2003

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, different administration time points, monoprophylaxis
Participants	**Baseline characteristics** Droperidol (pre-incision group P) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 27 • *Received treatment (n)*: NA • *Analysed (n)*: 26 • *Age (mean ± SD, median (IQR), median (range))*: 53 ± 4 • *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 2 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 31 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) with nitrous oxide in oxygen • *Duration of anaesthesia or surgery (in min; as mean or median)*: 177 • *Use of perioperative opioids (if yes, which?)*: morphine 0.2 mg/kg IV approximately 15 minutes before skin incision; postop pain (n = 3): pentazocine 15 mg IM • *Type of surgery*: shoulder rotator cuff repair

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Yamamoto 2003 *(Continued)*

Droperdol (after-incision group A)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 30
- *Received treatment (n)*: NA
- *Analysed (n)*: 30
- *Age (mean ± SD, median (IQR), median (range))*: 49 ± 4
- *Weight (mean ± SD, median (IQR), median (range))*: 62 ± 2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 27
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) with nitrous oxide in oxygen
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 186
- *Use of perioperative opioids (if yes, which?)*: morphine 0.2 mg/kg IV approximately 15 minutes before skin incision; postop pain (n = 2): pentazocine 15 mg IM
- *Type of surgery*: shoulder rotator cuff repair

Placebo (control group C)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 27
- *Received treatment (n)*: NA
- *Analysed (n)*: 27
- *Age (mean ± SD, median (IQR), median (range))*: 47 ± 3
- *Weight (mean ± SD, median (IQR), median (range))*: 63 ± 3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 19
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) with nitrous oxide in oxygen
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 176
- *Use of perioperative opioids (if yes, which?)*: morphine 0.2 mg/kg IV approximately 15 minutes before skin incision; postop pain (n = 7): pentazocine 15 mg IM
- *Type of surgery*: shoulder rotator cuff repair

Included criteria: ASA I and II, undergoing scheduled shoulder rotator cuff repair with general anaesthesia. Written informed consent was obtained from each patient

Excluded criteria: given any opioids for any purpose within 24 hours before surgery; given any analgesics for any reason but wound pain relief

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Interventions

Intervention characteristics

Droperidol (pre-incision group P)

- *Dose*: 10 µg/kg
- *Time point of administration*: after anaesthetic induction, saline solution 15 minutes after skin incision
- *Route of administration*: IV

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Yamamoto 2003 *(Continued)*

- *Rescue antiemetics (if yes, which?)*: NA

Droperdol (after-incision group A)

- *Dose*: 10 µg/kg
- *Time point of administration*: 15 minutes after skin incision, saline after anaesthetic induction
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Placebo (control group C)

- *Dose*: saline
- *Time point of administration*: after induction and 15 minutes after skin incision
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Outcomes	*PONV (0 to 18 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Japan **Setting:** inpatient, single-centre **Author's name:** Hiroshi Yamaguchi **Institution:** Department of Anesthesia, Ryugasaki Saiseikai Hospital **Email:** hyanchi@aol.com **Address:** Nakazato 1-1, Ryugasaki, Ibaraki, 301-0854, Japan **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly assigned via a table of random numbers to three groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "each solution was administered by an attending anesthesiologist who was blinded to each patient’s allocation"

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Yamamoto 2003 *(Continued)*

		Quote: "two solutions, Solution A and Solution B, were prepared in 10-mL syringes on the morning of each surgery by the anesthesiologist responsible for patient grouping"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the attending nurses in this unit were blinded to patient group assignment or anesthetic management, and were responsible for data recording"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...relief after surgery. Statistical analysis was performed using the remaining patients' data" Quote: "of the 84 patients enrolled in this study, one patient from Group P was excluded from the study because he was given pentazocine for reasons other than wound pain"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids): no; (history of PONV/motion sickness, non-smoker): unclear

Yang 1993

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups relevant, monoprophylaxis
Participants	**Baseline characteristics** Control • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 31 ± 4 • *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 7 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 100/0/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 55 ± 12 • *Use of perioperative opioids (if yes, which?)*: fentanyl for induction • *Type of surgery*: gynaecological laparoscopy Droperidol • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40

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Yang 1993 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 30 ± 5
- *Weight (mean ± SD, median (IQR), median (range))*: 51 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 100/0/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 54
- *Use of perioperative opioids (if yes, which?)*: fentanyl for induction
- *Type of surgery*: gynaecological laparoscopy

Included criteria: female undergoing outpatient gynaecological laparoscopy, ASA I, 18 to 40 years of age

Excluded criteria: NA

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Control • *Dose*: none • *Time point of administration*: none • *Route of administration*: none • *Rescue antiemetics (if yes, which?)*: no rescue antiemetics Droperidol • *Dose*: 20 µg/kg • *Time point of administration*: after intubation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: no rescue antiemetics
Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 3 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Taiwan **Setting:** outpatient, single-centre **Author's name:** Lin-Cheng Yang **Institution:** Department of Anesthesiology, Chang Gung Memorial Hospital, Kaohsiung Hsien, Taiwan, ROC **Email:** NA

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Yang 1993 *(Continued)*

	Address: Department of Anesthesiology Chang Gung Memorial Hospital 123, Ta-Pei Rd., Niao Sung Hsiang Kaohsiung Hsien, Taiwan, ROC **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	Two out of 3 groups relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly and equally allocated to one of three groups" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no blinding of anaesthesiologist and patients possible because of different treatments
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "there were no statistically significant differences in age, weight, duration of anesthesia or amount of fluid given among the three groups of patients (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia): no; (history of PONV/motion sickness, non-smoker, perioperative opioids): unclear

Yang 2015

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics**

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Yang 2015 *(Continued)*

Dexamethasone + tropisetron (group trp)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 53
- *Received treatment (n)*: 53
- *Analysed (n)*: 53
- *Age (mean ± SD, median (IQR), median (range))*: 35 (23 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 21.7 (18.3 to 30.0)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: 15
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 109
- *Use of perioperative opioids (if yes, which?)*: 0.35 mg fentanyl intraoperative, no postoperative morphine
- *Type of surgery*: gynaecological laparoscopic surgery

Dexamethasone (group dxm)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 51
- *Received treatment (n)*: 51
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 35 (22 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 22.3 (16.4 to 33.1)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 98
- *History of PONV/motion sickness (%)*: 18
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 100
- *Use of perioperative opioids (if yes, which?)*: 0.4 mg fentanyl intraoperative, no postoperative morphine
- *Type of surgery*: gynaecological laparoscopic surgery

Included criteria: female, 18 to 60 years of age, ASA I or II, undergoing elective gynaecological laparoscopic surgery under general anaesthesia

Excluded criteria: pregnancy or breastfeeding; mental retardation; psychiatric or neurological disease; use of antiemetics, emetogenic drugs, opioids, or glucocorticoids within 3 days before surgery; known allergy to tropisetron or dexamethasone; nausea, vomiting, or both within 24 hours before surgery; implantation of a cardiac pacemaker, cardioverter, or defibrillator; rash or local infection over the acupoint stimulation skin area; any disease that could influence sensibility in wrists and hands; if patient unexpectedly developed intraoperative drug allergy, converted to open procedures; surgery-related postoperative complications

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dexamethasone + tropisetron (group trp)

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Yang 2015 *(Continued)*

	• *Dose*: dexamethasone 10 mg, tropisetron 5 mg • *Time point of administration*: dexamethasone after induction of anaesthesia, tropisetron at the start of skin closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 8% (metoclopramide 10 mg) Dexamethasone (group dxm) • *Dose*: 10 mg • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 14% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** Huashan Hospital, Fudan University; departmental sources **Country:** China **Setting:** inpatient, single-centre **Author's name:** J. Zhang **Institution:** Department of Anaesthesiology, Huashan Hospital, Fudan University, Shanghai 200040, China **Email:** snapzhang@aliyun.com **Address:** NA **Duration of study:** January 2014 to December 2014 **Language:** English **Study's primary outcome:** incidence of any nausea, vomiting, or both within the first 24 hours after surgery **Trial registry number:** NCT02096835
Notes	Two out of 3 groups relevant (acupoint stimulation)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomly allocated using a computer-generated table..."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients, the anaesthetists, and the nursing staff were unaware of the group assignments"

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Yang 2015 *(Continued)*

		Quote: "the anaesthetists who managed the patient were thus blinded to group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients, the anaesthetists, and the nursing staff were unaware of the group assignments" Quote: "an anaesthetic nurse (Y.-H.C.) who was trained for the study and blinded to the randomization did the follow-up and data collection"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "a total of 157 female patients were initially included in our study, and 153 completed the study. Four patients were excluded from the study because they refused to continue the study, had insufficient follow-up, or converted to open surgery (see Fig. 1)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: NCT02096835 (retrospective registration)
Other bias	Low risk	Quote: "the clinical characteristics are presented in Table 1. The groups were similar in terms of PONV risk factors and surgery- and anaesthesia-related profiles" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Yang 2017

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (group C) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 48 • *Received treatment (n)*: NA • *Analysed (n)*: 45 • *Age (mean ± SD, median (IQR), median (range))*: 48.2 ± 10.1 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 24.1 ± 3.0 • *ASA I/II/III/IV (n)*: 38/7/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 97.8 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 118.8 • *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 17 patients received postoperative fentanyl • *Type of surgery*: primary thyroidectomy Dexamethasone (group D)

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Yang 2017 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 48
- *Received treatment (n)*: NA
- *Analysed (n)*: 43
- *Age (mean ± SD, median (IQR), median (range))*: 46.0 ± 11.1
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: 24.6 ± 3.2
- *ASA I/II/III/IV (n)*: 34/9/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 124.9
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil, 9 patients received postoperative fentanyl
- *Type of surgery*: primary thyroidectomy

Included criteria: adult female between 20 and 65 years of age, ASA, I or II, scheduled for primary thyroidectomy under general anaesthesia with endotracheal intubation and immediate postoperative extubation

Excluded criteria: known tracheal pathology; tracheostomy; previous head and neck surgery; recent upper respiratory tract infection within 6 weeks; body mass index > 35 kg/m^2; inflammation or haemorrhage in the upper gastrointestinal tract; use of non-steroidal anti-inflammatory drug or steroid medication within 24 hours; allergy to general anaesthetic used in this study; known or suspected difficult airway; expected duration of surgery exceeding 180 minutes; underwent reoperation during the first 24 hours postoperatively

Pretreatment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo (group C) • *Dose*: 2 × saline • *Time point of administration*: injections at 5 minutes before induction of anaesthesia and 10 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Dexamethasone (group D) • *Dose*: 10 mg dexamethasone • *Time point of administration*: at 5 minutes before induction of anaesthesia, saline 10 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)*

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Yang 2017 *(Continued)*

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Sung Mee Jung **Institution:** Yeungnam University School of Medicine, Daegu, Korea **Email:** applejsm@gmail.com **Address:** Department of Anesthesiology and Pain Medicine, Yeungnam University School of Medicine, 170, Hyeonchung-ro, Nam-gu, Daegu 42415, Korea **Duration of study:** October 2013 to October 2015 **Language:** English **Study's primary outcome:** incidence of postoperative sore throat (POST) at 6 hours after extubation **Trial registry number:** NCT02039427
Notes	Two out of 4 groups relevant (ketorolac)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "using a computer-generated random assignment scheme"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "each study drug was made at the same volume (2 ml) by a nurse blinded to group assignment on the morning of surgery"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "at 1, 6 and 24 hours after extubation, the incidences and severities of sore throat, hoarseness and pain were assessed by an independent investigator unaware of group assignments"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "one hundred and ninety-two female patients who underwent thyroidectomy from October 2013 to October 2015 were consecutively enrolled in this study (Fig. 1). After randomized allocation, 12 patients were excluded because of steroid medication (one), anaphylactic reaction to antibiotic resulting in unexpected cancellation of surgery (one) and longer duration of surgery (two), withdrawal of the consent (one), and loss of follow-up (seven). Therefore, a total of 180 patients were included in the final analysis"
Selective reporting (reporting bias)	High risk	Judgement comment: NCT02039427 (prospective registration). Timing of assessment for the primary outcome (postoperative sore throat) was different between protocol and study report. The primary outcome was not PONV-related
Other bias	Unclear risk	Quote: "demographic, intubation and surgical characteristics were comparable among groups (Table 1)"

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Yang 2017 *(Continued)*

		Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear
Other bias	Unclear risk	Quote: "demographic, intubation and surgical characteristics were comparable among groups (Table 1)" Judgement comment: baseline characteristics (age, BMI, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Yeo 2009

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 45.2 ± 6.4 • *Weight (mean ± SD, median (IQR), median (range))*: 57.6 ± 8.3 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 175.8 • *Use of perioperative opioids (if yes, which?)*: none • *Type of surgery*: middle ear surgery (tympanoplasty or mastoidectomy) Dexamethasone • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 45.8 ± 9.1 • *Weight (mean ± SD, median (IQR), median (range))*: 59.5 ± 10.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0

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Yeo 2009 *(Continued)*

- *Type of general anaesthesia*: inhalational anaesthesia (isoflurane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 189.1
- *Use of perioperative opioids (if yes, which?)*: none
- *Type of surgery*: middle ear surgery (tympanoplasty or mastoidectomy)

Included criteria: ASA I or II, non-smoking, female, 19 to 62 years of age, undergoing middle ear surgery (tympanoplasty or mastoidectomy)

Excluded criteria: gastrointestinal disorder; history of previous PONV or motion sickness; had received antiemetic medication within 24 hours before surgery; had received steroid, opioid, benzodiazepine, or antipsychotic medication; pregnant or menstruating

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Placebo • *Dose*: 2 × 2 mL saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 35% (ondansetron) Dexamethasone • *Dose*: 10 mg dexamethasone, saline • *Time point of administration*: after induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (ondansetron)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Postoperative wound infection (during hospital stay)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (during hospital stay)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** no sponsorship **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Young Hoon Jeon

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Yeo 2009 *(Continued)*

Institution: Department of Anesthesiology, Kyungpook National University Hospital, Daegue, Republic of Korea

Email: jeon68@knu.ac.kr

Address: Department of Anesthesiology, Kyungpook National University Hospital, 200 Donduk-ro Jung-gu, Daegue, 700-721, Republic of Korea

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: incidence of PONV

Notes	Two out of 3 groups relevant (midazolam)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a computer-generated random number table, patients were randomly allocated to one of three groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the randomized patient selection process and the identity of the drugs used in the study were blinded to the patients, the anesthesiologists present during surgery"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the randomized patient selection process and the identity of the drugs used in the study were blinded to the patients, the anesthesiologists present during surgery, and the investigators who collected the postoperative data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "patient characteristics, duration of anesthesia and operation, surgical procedures, and duration of PACU stay were similar among the three groups (Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Yilmazlar 1996

Study characteristics

Methods	**Study design:** randomized controlled trial

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Yilmazlar 1996 *(Continued)*

Study grouping: 3 groups, monoprophylaxis

Participants

Baseline characteristics

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 42.5 ± 3.2
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 80
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 50 µg to 75 µg IV
- *Type of surgery*: thyroidectomy

Metoclopramide

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 43.2 ± 4.1
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 80
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 50 µg to 75 µg IV
- *Type of surgery*: thyroidectomy

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: NA
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 41.1 ± 2.8
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 85

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Yilmazlar 1996 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0/NA
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl 50 µg to 75 µg IV
- *Type of surgery*: thyroidectomy

Included criteria: ASA I or II, 22 to 60 years of age, scheduled for thyroidectomy with postoperative bed rest of at least 24 hours

Excluded criteria: nausea or emesis in the preoperative period, history of postoperative vomiting after previous anaesthesia, ASA III and IV

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness, duration of anaesthesia, non-smoker, peri-operative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: saline • *Time point of administration*: during anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: not defined Metoclopramide • *Dose*: 0.2 mg/kg • *Time point of administration*: during anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: not defined Tropisetron • *Dose*: 5 mg • *Time point of administration*: during anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: not defined
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** A. Yilmazlar **Institution:** Department of Anaesthesiology, Uludag University School of Medicine, Bursa, Turkey **Email:** NA **Address:** Department of Anaesthesiology, Uludag University School of Medicine, Corukle 16059, Bursa, Turkey **Language:** English **Duration of study:** NA

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Yilmazlar 1996 *(Continued)*

	Trial registry number: NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized" Judgement comment: insufficient information about the sequence generation process
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: "double-blind". No further statement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: "double-blind". No further statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "Table 1 summarizes the demographic data of the three groups, which were comparable with regard to age and sex. The three groups were not significantly different (P> 0.05). The number of patients vomiting..." Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Yilmazlar 2001

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, dose-finding study, monoprophylaxis
Participants	**Baseline characteristics** Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 20

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Yilmazlar 2001 *(Continued)*

- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 45.70 ± 12.10
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: breast surgery, thyroidectomy

Tropisetron (2 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 47.91 ± 19.18
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: breast surgery, thyroidectomy

Tropisetron (5 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 40.42 ± 15.03
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: inhalational anaesthesia (halothane, N_2O)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl
- *Type of surgery*: breast surgery, thyroidectomy

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Yilmazlar 2001 *(Continued)*

Included criteria: 22 to 64 years of age, undergoing surgery under general anaesthesia, ASA I or II, scheduled for thyroidectomy and breast surgery, when postoperative bed rest of at least 24 hours was the rule

Excluded criteria: nausea or emesis in the preoperative period, history of postoperative nausea and vomiting or motion sickness, ASA III or IV

Pretreatment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Placebo • *Dose*: 4 mL saline • *Time point of administration*: during anaesthesia induction • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.2 mg/kg metoclopramide IV Tropisetron (2 mg group) • *Dose*: 2 mg • *Time point of administration*: before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.2 mg/kg metoclopramide IV Tropisetron (5 mg group) • *Dose*: 5 mg • *Time point of administration*: before anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 0.2 mg/kg metoclopramide IV
Outcomes	*Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (2 to 4 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** inpatient, single-centre **Author's name:** A. Yılmazlar **Institution:** Department of Anaesthesiology and Intensive Care Medical School, Uludag˘University, Bursa, Turkey **Email:** ayyil@uludag.edu.tr; tunyil@ttnet.net.tr; tyilmazlar@hotmail.com **Address:** Department of Anaesthesiology and Intensive Care, Medical School, Uludag˘University,16059 Bursa, Turkey **Language:** English **Duration of study:** NA **Trial registry number:** NA

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Yilmazlar 2001 *(Continued)*

	Study's primary outcome: primary outcome measures were number of patients requesting a rescue antiemetic and/or experiencing a vomiting episode during the first 2 hours after the operation
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized into three groups" Judgement comment: no further information on randomization method provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: no information on blinding, but different time points of administration between study groups, so blinding of the anaesthesiologist is not possible
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "all three groups of patients were comparable with regard to age, sex and the type of surgery they required (Table 1)" Judgement comment: baseline characteristics (age): no; (weight, ASA): unclear. Potential effect modifiers (gender, history of PONV/motion sickness): no; (duration of anaesthesia, non-smoker, perioperative opioids): unclear

Yoon 2009

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: NA • *Analysed (n)*: 35

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Yoon 2009 *(Continued)*

- *Age (mean ± SD, median (IQR), median (range))*: 51 ± 4.8
- *Weight (mean ± SD, median (IQR), median (range))*: 57.1 ± 5.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 60
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 266.9
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil
- *Type of surgery*: mastoidectomy, tympanoplasty

Ramosetron (group R)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 35
- *Received treatment (n)*: NA
- *Analysed (n)*: 35
- *Age (mean ± SD, median (IQR), median (range))*: 51.43 ± 6.1
- *Weight (mean ± SD, median (IQR), median (range))*: 57.7 ± 7.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 57.1
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 263.2
- *Use of perioperative opioids (if yes, which?)*: intraoperative remifentanil
- *Type of surgery*: mastoidectomy, tympanoplasty

Included criteria: either sex, ASA I and II, scheduled middle ear surgery (mastoidectomy and tympanoplasty) under general anaesthesia with sevoflurane and remifentanil, 30 to 65 years of age

Excluded criteria: cardiovascular, respiratory, brain, renal, hepatic disease; pregnant women; severe obesity; usual vomiting or motion sickness; nausea or vomiting within 24 hours before surgery

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 4 mg • *Time point of administration*: before end of operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (0%) 10 mg metoclopramide Ramosetron (group R) • *Dose*: 0.3 mg • *Time point of administration*: before end of operation • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (0%) 10 mg metoclopramide

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Yoon 2009 *(Continued)*

Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Vomiting (6 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre **Author's name:** Sang Ho Jung **Institution:** Department of Anesthesiology and Pain Medicine, Maryknoll Hospital **Email:** inature7@naver.com **Address:** Maryknoll Hospital, Daecheong-dong 4ga, Jung-gu, Busan 600-730, Korea **Duration of study:** NA **Language:** Korean (Google Translator) **Study's primary outcome:** incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly assigned". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: insufficient information on blinding ("double-blinded")

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Yoon 2009 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: quote: "an anesthesiologist who did not know the patient's group visited the patient for 6 hours, 6-24 hours, and 24-48 hours postoperatively"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Yoon 2016

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Palonosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 145 • *Received treatment (n)*: NA • *Analysed (n)*: 132 • *Age (mean ± SD, median (IQR), median (range))*: 51.2 ± 11.1 • *Weight (mean ± SD, median (IQR), median (range))*: 60.1 ± 7.1 • *BMI (mean ± SD, median (IQR), median (range))*: 24.0 ± 3.5 • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 91 • *History of PONV/motion sickness (%)*: 12/55 • *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 150.4 • *Use of perioperative opioids (if yes, which?)*: 1 mg/kg fentanyl for induction, 1144.4 µg fentanyl via PCA for postoperative pain • *Type of surgery*: gynaecological oncology surgery Ramosetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 145 • *Received treatment (n)*: NA • *Analysed (n)*: 130 • *Age (mean ± SD, median (IQR), median (range))*: 49.8 ± 10.5 • *Weight (mean ± SD, median (IQR), median (range))*: 61.4 ± 9.9

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Yoon 2016 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 42.2 ± 3.8
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 88
- *History of PONV/motion sickness (%)*: 7/54
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 142.8
- *Use of perioperative opioids (if yes, which?)*: 1 mg/kg fentanyl for induction, 1101.0 µg fentanyl via PCA for postoperative pain
- *Type of surgery*: gynaecological oncology surgery

Included criteria: female, over 20 years of age, ASA I or II, undergoing gynaecological oncology surgery

Excluded criteria: history of substance abuse; hypersensitivity to medication; gastrointestinal, cardiovascular, respiratory, brain, kidney, liver disease; received a corticosteroid within 24 hours of surgery; pregnant women

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Palonosetron • *Dose*: 0.075 mg • *Time point of administration*: after anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (4%) 10 mg metoclopramide Ramosetron • *Dose*: 0.3 mg • *Time point of administration*: before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: (5%) 10 mg metoclopramide
Outcomes	*Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** South Korea **Setting:** inpatient, single-centre

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Yoon 2016 *(Continued)*

Author's name: Young Seok Jee

Institution: Department of Anesthesiology and Pain Medicine, Cheil General Hospital Women Healthcare Center, Dankook University College of Medicine

Email: jisaac@naver.com

Address: 17 Seoae-ro 1 gil, Jung-gu 04619, Korea

Duration of study: NA

Language: Korean (Google Translator)

Study's primary outcome: incidence of PONV

Trial registry number: NA

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: quote: "patients were randomly assigned to receive intravenous ramosetron 0.3 mg intravenously on the end of the procedure and 0.075 mg palonosetron intravenously immediately after induction of anesthesia using random allocation software (version 2.0)" (translated)
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: different time points of administration. We assume that anaesthesiologists were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: in total, 290 (145/145) participants were enrolled and 262 (132/130) were included in the analysis. Reasons for missing outcome data were not described
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Yu 2013

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis

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Yu 2013 *(Continued)*

Participants

Baseline characteristics

Tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 76
- *Received treatment (n)*: 76
- *Analysed (n)*: 76
- *Age (mean ± SD, median (IQR), median (range))*: 52.3 ± 13.4
- *Weight (mean ± SD, median (IQR), median (range))*: 63.2 ± 11.3
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 88.2
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 170.5
- *Use of perioperative opioids (if yes, which?)*: 324.3 µg fentanyl intraoperative, 7.2 mg postoperative morphine IM
- *Type of surgery*: modified radical mastectomy

Dexamethasone + tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 73
- *Received treatment (n)*: 73
- *Analysed (n)*: 73
- *Age (mean ± SD, median (IQR), median (range))*: 51.0 ± 14.5
- *Weight (mean ± SD, median (IQR), median (range))*: 64.7 ± 13.2
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 86.3
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 183.6
- *Use of perioperative opioids (if yes, which?)*: 315.7 µg fentanyl intraoperative, 5.8 mg postoperative morphine IM
- *Type of surgery*: modified radical mastectomy

Methylprednisolone + tropisetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 75
- *Received treatment (n)*: 75
- *Analysed (n)*: 75
- *Age (mean ± SD, median (IQR), median (range))*: 54.1 ± 12.2
- *Weight (mean ± SD, median (IQR), median (range))*: 64.3 ± 10.5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100

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Yu 2013 *(Continued)*

- *Non-smoker (%)*: 86.4
- *History of PONV/motion sickness (%)*: 0
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 176.6
- *Use of perioperative opioids (if yes, which?)*: 336.4 µg fentanyl intraoperative, 4.6 mg postoperative morphine IM
- *Type of surgery*: modified radical mastectomy

Included criteria: ASA I and II, undergoing modified radical mastectomy with general anaesthesia

Excluded criteria: history of PONV and motion sickness; had received drugs known to have antiemetic effects (phenothiazines, scopolamine, corticosteroids, and tricyclic antidepressants) in the 24 hours before surgery; pituitary or adrenal disease; diabetes; morbid obesity; allergy to study drug (tropisetron, dexamethasone, or methylprednisolone)

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Interventions	**Intervention characteristics** Tropisetron • *Dose*: 10 mg, saline • *Time point of administration*: after induction of anaesthesia, when the skin was sutured • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 13.2% (metoclopramide 10 mg) Dexamethasone + tropisetron • *Dose*: dexamethasone 8 mg, tropisetron 10 mg • *Time point of administration*: after induction of anaesthesia, when the skin was sutured • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2.7% (metoclopramide 10 mg) Methylprednisolone + tropisetron • *Dose*: methylprednisolone 40 mg, tropisetron 10 mg • *Time point of administration*: after induction of anaesthesia, when the skin was sutured • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 2.7% (metoclopramide 10 mg)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 1 week observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Shanghai Health Bureau Foundation of Youth (Shangaj, China), grant No. 20114y128; National Science Foundation for Youth (Beijing, China), grant No. 81200937 **Country:** China **Setting:** inpatient, single-centre **Author's name:** J. Zhang

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Yu 2013 *(Continued)*

Institution: Department of Anesthesia, Huashan Hospital, Fudan University, Shanghai, China

Email: anesth.huashan@gmail.com

Address: Department of Anesthesia, Huashan Hospital, Shanghai, China, 200040

Language: English

Duration of study: NA

Trial registry number: NA

Study's primary outcome: incidence of PONV

Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "all patients were randomly assigned using randomization table to one of the 3 groups"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the skin was sutured. The study drugs were prepared and given intravenously in equal volumes of 5 ml by a nursing staff not involved in either anesthesia or data collection"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "staff and a ward nursing staff, who were blinded to the drug administered, recorded the occurrence of PONV, the request and time of rescue antiemetic medication at 24, 48 and 72 hours postoperatively"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "...was statistically similar among 3 groups. There was no significant difference among groups with respect to intraoperative fluid requirement and total dose of fentanyl. The requirement of morphine given intramuscularly for postoperative analgesia was relative higher in group T compared with group TD and group TM, but the difference was not significant (P>0.05; Table I)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness): no; (perioperative opioids): yes

Yuksek 2003

Study characteristics

Methods	**Study design:** randomized controlled trial

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Yuksek 2003 *(Continued)*

Study grouping: 3 groups, monoprophylaxis

Participants

Baseline characteristics

Ondansetron

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 32.3 (20 to 42)
- *Weight (mean ± SD, median (IQR), median (range))*: 64.7 (45 to 77)
- *BMI (mean ± SD, median (IQR), median (range))*: 25.3 (17 to 29)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 74.6
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative morphine and fentanyl
- *Type of surgery*: gynaecological laparoscopy

Dexamethasone

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 31.7 (19 to 62)
- *Weight (mean ± SD, median (IQR), median (range))*: 60.5 (47 to 76)
- *BMI (mean ± SD, median (IQR), median (range))*: 24.6 (19 to 29)
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 64.3
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative morphine and fentanyl
- *Type of surgery*: gynaecological laparoscopy

Placebo

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 20
- *Received treatment (n)*: 20
- *Analysed (n)*: 20
- *Age (mean ± SD, median (IQR), median (range))*: 29.5 (19 to 60)
- *Weight (mean ± SD, median (IQR), median (range))*: 60.6 (45 to 77)
- *BMI (mean ± SD, median (IQR), median (range))*: 24.3 (19 to 29)
- *ASA I/II/III/IV (n)*: NA/NA/0/0

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Yuksek 2003 *(Continued)*

- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA/0
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 76.2
- *Use of perioperative opioids (if yes, which?)*: intraoperative fentanyl, postoperative morphine and fentanyl
- *Type of surgery*: gynaecological laparoscopy

Included criteria: ASA I or II, 19 to 62 years of age, undergoing general anaesthesia for elective gynaecological laparoscopy

Excluded criteria: antiemetic self-medication in the 48 hours before the operation, history of motion sickness, history of gastro-oesophageal reflux, body mass index (BMI) > 35, pregnancy

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Ondansetron • *Dose*: 4 mg • *Time point of administration*: 2 minutes before induction of anaesthesia, but after morphine/fentanyl bolus • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 10% (metoclopramide 10 mg IV) Dexamethasone • *Dose*: 8 mg • *Time point of administration*: 2 minutes before induction of anaesthesia, but after morphine/fentanyl bolus • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 20% (metoclopramide 10 mg IV) Placebo • *Dose*: 5 mL saline • *Time point of administration*: 2 minutes before induction of anaesthesia, but after morphine/fentanyl bolus • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 55% (metoclopramide 10 mg IV)
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 3 hours)* • Outcome type: dichotomous outcome *Vomiting (3 to 6 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome

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Yuksek 2003 *(Continued)*

	Subjects with any AE (0 to 24 hours) • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome
Identification	**Sponsorship source:** NA **Country:** Turkey **Setting:** outpatient, single-centre **Author's name:** M.S. Yuksek **Institution:** Department of Anaesthesiology and Reanimation, Atatürk University, Erzurum, Turkey **Email:** yuksek@hotmail.com **Address:** NA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated to one of three groups" Judgement comment: no further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "one nurse numbered all patients" Judgement comment: insufficient information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "one nurse numbered all patients and prepared the study medications in identical 5 ml syringes to ensure blinding of the anaesthetists..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients and investigators who collected the post-operative data were blind to the randomization"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all 60 patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported

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Yuksek 2003 *(Continued)*

Other bias	Unclear risk	Quote: "there was similarity among the groups with respect to patient characteristics (age, weight, height, BMI and last menstrual cycle) and surgical procedures (types of surgery, duration of anaesthesia, duration of surgery and duration of CO 2 insufflation; Table 1)" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of motion sickness): no; (history of PONV, non-smoker, perioperative opioids): unclear

Yun 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Ondansetron (group O) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 49 • *Received treatment (n)*: NA • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 38.8 ± 8.4 • *Weight (mean ± SD, median (IQR), median (range))*: 56.6 ± 6.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 92.9 • *Use of perioperative opioids (if yes, which?)*: 150 mg nalbuphine • *Type of surgery*: gynaecological laparoscopic surgery (total hysterectomy) Azasetron (group A) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 49 • *Received treatment (n)*: NA • *Analysed (n)*: 49 • *Age (mean ± SD, median (IQR), median (range))*: 39.4 ± 9.0 • *Weight (mean ± SD, median (IQR), median (range))*: 57.1 ± 8.0 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: 0 • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, sevoflurane)

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Yun 2010 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 90.6
- *Use of perioperative opioids (if yes, which?)*: 170 mg nalbuphine
- *Type of surgery*: gynaecological laparoscopic surgery (total hysterectomy)

Included criteria: ASA I or II, 20 to 65 years of age, undergoing general anaesthesia for gynaecological laparoscopic surgery (total hysterectomy)

Excluded criteria: use of antiemetics within 24 hours before surgery; presence of gastrointestinal disease; concurrent menstruation; history of motion sickness, smoking, or previous PONV

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Ondansetron (group O) • *Dose*: 8 mg • *Time point of administration*: at 5 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV Azasetron (group A) • *Dose*: 10 mg • *Time point of administration*: at 5 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV
Outcomes	*Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 48 hours)* • Outcome type: dichotomous outcome *Constipation (0 to 48 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 48 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** Korea **Setting:** inpatient, single-centre **Author's name:** Yoon Hee Kim **Institution:** Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, Seongnam **Email:** yhkim0404@cnu.ac.kr **Address:** Department of Anesthesiology and Pain Medicine, Chungnam National University Hospital, 640 Daesa-dong, Jung-gu, Daejeon 301-721, Korea **Duration of study:** NA **Language:** English

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Yun 2010 *(Continued)*

	Study's primary outcome: incidence of PONV **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "random numbers generated by a computer"
Allocation concealment (selection bias)	Unclear risk	Quote: "prepared the study drugs from instructions in numbered, sealed envelopes" Judgement comment: not stated; "sequentially numbered, opaque, and sealed envelopes" (SNOSE)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "from identical syringes" Quote: "a nurse, not participating in patient evaluation, prepared the study drugs from instructions in numbered, sealed envelopes"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients were interviewed by an anesthesiologist (who was blind to the study drug)"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Low risk	Quote: "patient groups did not show differences in age, body weight, height, operation time, anesthesia time, or the amount of infused solution (Table 1). All patients were non-smoking females who received laparoscopic gynecological surgery and postoperative pain control with opioid analgesics" Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Zarate 2000

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis, dose-finding study
Participants	**Baseline characteristics** Dolasetron (12.5 mg group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: -

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Zarate 2000 *(Continued)*

- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 82 ± 20
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 48
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 38/24
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 98
- *Use of perioperative opioids (if yes, which?)*: 1161 µg fentanyl intraoperative, 107 µg fentanyl in PACU
- *Type of surgery*: ENT procedure

Dolasetron (25 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 51
- *Received treatment (n)*: 51
- *Analysed (n)*: 51
- *Age (mean ± SD, median (IQR), median (range))*: 44 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 83 ± 19
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 45.10
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 27/16
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 91
- *Use of perioperative opioids (if yes, which?)*: 1256 µg fentanyl intraoperative, 103 µg fentanyl in PACU
- *Type of surgery*: ENT procedure

Ondansetron (4 mg group)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 49
- *Received treatment (n)*: 49
- *Analysed (n)*: 49
- *Age (mean ± SD, median (IQR), median (range))*: 45 ± 14
- *Weight (mean ± SD, median (IQR), median (range))*: 75 ± 17
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 42.86
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 31/12
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 95
- *Use of perioperative opioids (if yes, which?)*: 1000 µg fentanyl intraoperative, 77 µg fentanyl in PACU
- *Type of surgery*: ENT procedure

Ondansetron (8 mg group)

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Zarate 2000 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 50
- *Received treatment (n)*: 50
- *Analysed (n)*: 50
- *Age (mean ± SD, median (IQR), median (range))*: 46 ± 15
- *Weight (mean ± SD, median (IQR), median (range))*: 80 ± 18
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 40
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: 28/18
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 93
- *Use of perioperative opioids (if yes, which?)*: 1065 µg fentanyl intraoperative, 96 µg fentanyl in PACU
- *Type of surgery*: ENT procedure

Included criteria: ASA I and II, outpatient, 20 to 75 years of age, undergoing otolaryngological (ENT) procedures

Excluded criteria: had received any antiemetic medication within 24 hours before operation; pregnant; had clinically significant cardiovascular, neurological, renal, hepatic, gastrointestinal, or endocrinologic disease; history of drug abuse; > 100% above ideal body weight

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes

Interventions

Intervention characteristics

Dolasetron (12.5 mg group)

- *Dose*: 12.5 mg
- *Time point of administration*: within a 30 minute interval before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 30% (promethazine 6.25 mg, droperidol 1.25 mg, ondansetron)

Dolasetron (25 mg group)

- *Dose*: 25 mg
- *Time point of administration*: within a 30 minute interval before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 25.5% (promethazine 6.25 mg, droperidol 1.25 mg, ondansetron)

Ondansetron (4 mg group)

- *Dose*: 4 mg
- *Time point of administration*: within a 30 minute interval before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 22.4% (promethazine 6.25 mg, droperidol 1.25 mg, ondansetron)

Ondansetron (8 mg group)

- *Dose*: 8 mg
- *Time point of administration*: within a 30 minute interval before end of surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: 30% (promethazine 6.25 mg, droperidol 1.25 mg, ondansetron)

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Zarate 2000 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (in-hospital symptoms)* • Outcome type: dichotomous outcome *Vomiting (post discharge to 24 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Complete response (no PONV) in 24 hours* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** USA **Setting:** outpatient, single-centre **Author's name:** Paul F. White **Institution:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA **Email:** pwhite@mednet.swmed.edu **Address:** Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5161 Harry Hines Blvd., CS2.126, Dallas, TX 75235-9068, USA **Language:** English **Duration of study:** NA **Trial registry number:** NA **Study's primary outcome:** total costs for managing PONV
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a computer-generated random number schedule"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the study drug was prepared by the OR pharmacist according to a computer-generated random number schedule, diluted to a total volume of 5 mL and administered within a 30-min interval before the end of surgery"

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Zarate 2000 *(Continued)*

		Judgement comment: no further information on blinding of anaesthetists and participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a trained interviewer who was 'blinded' to the group assignment contacted all patients by telephone 24 h after discharge from the hospital to inquire about postdischarge side effects and the need for any therapeutic interventions at home"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	High risk	Quote: "there were no significant differences among the four treatment groups with respect to demographic data, including age, weight, sex, type and duration of surgery, incidence of motion sickness, or previous PONV (Table 2). In the female patients, there were no differences in the number of days from the start of their last menstrual cycle. The doses of anesthetic drugs including propofol, opioids, muscle relaxants (and their antagonists), steroids, and volume of perioperative IV fluid, did not differ among the four groups. There were also no significant differences in the times to eye opening, tracheal extubation, response to verbal commands, and orientation, the time to achieving discharge readiness criteria or the time to actual discharge among the four groups (Table 3). After discharge..." Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, history of PONV/motion sickness): no; (non-smoker): unclear; (perioperative opioids): yes

Zhang 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Tropisetron (group T) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 33 ± 7 • *Weight (mean ± SD, median (IQR), median (range))*: 52 ± 6 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA (propofol, remifentanil)

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Zhang 2012 *(Continued)*

- *Duration of anaesthesia or surgery (in min; as mean or median)*: 138
- *Use of perioperative opioids (if yes, which?)*: 5 μg/kg fentanyl at induction, intraoperative remifentanil, postoperative tramadol
- *Type of surgery*: gynaecological surgery

Tropisetron + penehyclidine (group TP)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 31 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 51 ± 7
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 134
- *Use of perioperative opioids (if yes, which?)*: 5 μg/kg fentanyl at induction, intraoperative remifentanil, postoperative tramadol
- *Type of surgery*: gynaecological surgery

Penehyclidine (group P)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 30 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 50 ± 5
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA (propofol, remifentanil)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 135
- *Use of perioperative opioids (if yes, which?)*: 5 μg/kg fentanyl at induction, intraoperative remifentanil, postoperative tramadol
- *Type of surgery*: gynaecological surgery

Included criteria: 18 to 43 years of age, weight between 40 and 72 kg, scheduled for gynaecological laparoscopic surgery with anticipated duration of 1.5 to 2.5 hours under general anaesthesia

Excluded criteria: pregnancy, hepatic or renal dysfunction, presence of gastrointestinal disease, smoking, allergic to research drugs, duration of surgery longer than 2.5 hours

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Interventions	**Intervention characteristics**

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Zhang 2012 *(Continued)*

	Tropisetron (group T) • *Dose*: 0.1 mg/kg • *Time point of administration*: just after surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: 32.5%, tropisetron 1 mg IV Tropisetron + penehyclidine (group TP) • *Dose*: tropisetron 0.1 mg/kg, penehyclidine 0.01 mg/kg • *Time point of administration*: tropisetron just after surgery, penehyclidine 20 to 40 minutes before anaesthesia induction as premedication • *Route of administration*: tropisetron IV, penehyclidine IM • *Rescue antiemetics (if yes, which?)*: 55%, tropisetron 1 mg IV Penehyclidine (group P) • *Dose*: 0.01 mg/kg • *Time point of administration*: 20 to 40 minutes before anaesthesia induction as premedication • *Route of administration*: IM • *Rescue antiemetics (if yes, which?)*: 12.5%, tropisetron 1 mg IV
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 2 hours)* • Outcome type: dichotomous outcome *Vomiting (12 to 24 hours)* • Outcome type: dichotomous outcome *Headache (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Z. Zhang **Institution:** Department of Anesthesiology, Nanfang Hospital, Southern Medical University **Email:** etee@qq.com **Address:** Department of Anesthesiology, Nanfang Hospital, Southern Medical University, 1838 Guangzhou Avenue North, Guangzhou 510515, Guangdong, People’s Republic of China **Duration of study:** NA **Language:** English **Study's primary outcome:** incidence of PONV

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Zhang 2012 *(Continued)*

	Trial registry number: NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were allocated to three groups equally (40 patients in each group) with the random numbers generated using the Rand function of Excel 2003 (Microsoft, Redmond, WA, USA)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "on complete recovery, patients were transferred to the gynecological ward and, to assess nausea and vomiting, they were visited at 2, 6, 12, and 24 h after the surgery by a nurse anesthetist who was unaware of the drugs involved in the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all patients (40 in each treatment group) enrolled in the study recovered from anesthesia after surgery" Judgement comment: 5 participants were excluded for prolonged surgery and 5 participants were added
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Quote: "the characteristics of the patients and the durations of surgery and anesthesia are shown in Table 1. There were no significant differences in these characteristics among the three groups" Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker): no; (history of PONV/motion sickness, perioperative opioids): unclear

Zhang 2013-1

Study characteristics

Methods	**Study design:** randomized controlled trial **Study grouping:** 4 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (sub-study I: sevoflurane) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40

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Zhang 2013-1 *(Continued)*

- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/18/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 42
- *Use of perioperative opioids (if yes, which?)*: 286 µg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Ondansetron (sub-study I: sevoflurane)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 7
- *Weight (mean ± SD, median (IQR), median (range))*: 64 ± 12
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 21/19/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: inhalational anaesthesia (sevoflurane)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 40
- *Use of perioperative opioids (if yes, which?)*: 291 µg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Placebo (sub-study I: sevoflurane + propofol)

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 36 ± 8
- *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 11
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 22/18/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (sevoflurane, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 39
- *Use of perioperative opioids (if yes, which?)*: 292 µg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Ondansetron (sub-study I: sevoflurane + propofol)

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Zhang 2013-1 *(Continued)*

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: NA
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: 37 ± 6
- *Weight (mean ± SD, median (IQR), median (range))*: 67 ± 13
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 23/17/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (sevoflurane, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 42
- *Use of perioperative opioids (if yes, which?)*: 290 µg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Included criteria: 25 to 45 years of age, ASA I or II, scheduled for elective gynaecological laparoscopy with general anaesthesia

Excluded criteria: body weight > 20% of ideal body weight (on the basis of body mass index recommended); impaired kidney or liver function; history of chronic cough, smoking, retching/vomiting, or moderate to severe nausea 24 hours before anaesthesia; chronic nausea or vomiting or upper respiratory tract infection during the previous 2 weeks

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, non-smoker): no; (history of PONV/motion sickness): unclear

Interventions	**Intervention characteristics** Placebo (sub-study I: sevoflurane) • *Dose*: saline • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (sub-study I: sevoflurane) • *Dose*: 8 mg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Placebo (sub-study I: sevoflurane + propofol) • *Dose*: saline • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (sub-study I: sevoflurane + propofol) • *Dose*: 8 mg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA

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Zhang 2013-1 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 8 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by an Outstanding Medical Professional Award from the Suzhou City Government (Suzhou, China) (no: RC0802) and by the ‘ 333 ’ project in Jiangsu province (Jiangsu, China) (no: BRA2011047) **Country:** China **Setting:** inpatient, single-centre **Author's name:** Qi-Feng Tang **Institution:** Department of Anesthesiology, Suzhou BenQ Medical Center, Nanjing Medical University, China **Email:** sztqf2001@yahoo.com.cn **Address:** Department of Anesthesiology, Suzhou BenQ Medical Center, Nanjing Medical University, Suzhou, Jiangsu Province, 215009, P.R. China **Duration of study:** NA **Language:** English **Study's primary outcome:** NA **Trial registry number:** NA
Notes	Six groups (3 different anaesthesia regimens) split into 2 sub-studies (inhalational/TIVA)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "the allocation sequences were sealed up in a set of sealed envelopes, and the observers as well as all the patients involved were blinded" Judgement comment: not stated; SNOSE
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement comment: no statement on blinding of anaesthetists

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Zhang 2013-1 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...recorded through direct questioning by one anesthesiologist unaware of the type of medications given to the patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, non-smoker): no; (history of PONV/motion sickness): unclear

Zhang 2013-2

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Placebo (sub-study II: propofol) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 38 ± 6 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 12 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: 24/16/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: 100 • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: TIVA • *Duration of anaesthesia or surgery (in min; as mean or median)*: 40 • *Use of perioperative opioids (if yes, which?)*: 299 µg fentanyl • *Type of surgery*: gynaecological laparoscopy Ondansetron (sub-study II: propofol) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: NA • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: 38 ± 8 • *Weight (mean ± SD, median (IQR), median (range))*: 65 ± 11

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Zhang 2013-2 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: 23/17/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: 100
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: TIVA
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 40
- *Use of perioperative opioids (if yes, which?)*: 284 µg fentanyl
- *Type of surgery*: gynaecological laparoscopy

Included criteria: 25 to 45 years of age, ASA I or II, scheduled for elective gynaecological laparoscopy with general anaesthesia

Excluded criteria: body weight > 20% of ideal body weight (on the basis of body mass index recommended); impaired kidney or liver function; history of chronic cough, smoking, retching/vomiting, or moderate to severe nausea 24 hours before anaesthesia; chronic nausea or vomiting or upper respiratory tract infection during previous 2 weeks

Pretreatment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, non-smoker): no; (history of PONV/motion sickness): unclear

Interventions	**Intervention characteristics** Placebo (sub-study II: propofol) • *Dose*: saline • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA Ondansetron (sub-study II: propofol) • *Dose*: 8 mg • *Time point of administration*: 30 minutes before end of surgery • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: NA
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (0 to 4 hours)* • Outcome type: dichotomous outcome *Vomiting (4 to 8 hours)* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** supported by an Outstanding Medical Professional Award from the Suzhou City Government (Suzhou, China) (no: RC0802) and by the ‘ 333 ’ project in Jiangsu province (Jiangsu, China) (no: BRA2011047)

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Zhang 2013-2 *(Continued)*

Country: China

Setting: inpatient, single-centre

Author's name: Qi-Feng Tang

Institution: Department of Anesthesiology, Suzhou BenQ Medical Center, Nanjing Medical University, China

Email: sztqf2001@yahoo.com.cn

Address: Department of Anesthesiology, Suzhou BenQ Medical Center, Nanjing Medical University, Suzhou, Jiangsu Province, 215009, P.R. China

Duration of study: NA

Language: English

Study's primary outcome: NA

Trial registry number: NA

Notes	Six groups (3 different anaesthesia regimens) split into 2 sub-studies (inhalational/TIVA)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated" Judgement comment: no information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Quote: "the allocation sequences were sealed up in a set of sealed envelopes, and the observers as well as all the patients involved were blinded" Judgement comment: not stated; SNOSE
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of anaesthetists
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "recorded through direct questioning by one anesthesiologist unaware of the type of medications given to the patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all patients completed the study"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight, ASA): no. Potential effect modifiers (gender, duration of anaesthesia, perioperative opioids, non-smoker): no; (history of PONV/motion sickness): unclear

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Zhou 2012

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis and combination prophylaxis
Participants	**Baseline characteristics** Dexamethasone (group D) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 56 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 47.7 ± 13.1 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 23.8 ± 3.2 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 74 • *Non-smoker (%)*: 78 • *History of PONV/motion sickness (%)*: 24 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 74.0 • *Use of perioperative opioids (if yes, which?)*: 156.6 µg fentanyl intraoperative • *Type of surgery*: thyroid surgery Tropisetron (group T) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 56 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 48.6 ± 12.0 • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: 23.0 ± 3.5 • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 78 • *Non-smoker (%)*: 78 • *History of PONV/motion sickness (%)*: 28 • *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl) • *Duration of anaesthesia or surgery (in min; as mean or median)*: 81.7 • *Use of perioperative opioids (if yes, which?)*: 168.0 µg fentanyl intraoperative • *Type of surgery*: thyroid surgery Dexamethasone + tropisetron (group DT) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 56 • *Received treatment (n)*: NA • *Analysed (n)*: 50 • *Age (mean ± SD, median (IQR), median (range))*: 47.4 ± 10.7 • *Weight (mean ± SD, median (IQR), median (range))*: NA

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Zhou 2012 *(Continued)*

- *BMI (mean ± SD, median (IQR), median (range))*: 22.9 ± 2.6
- *ASA I/II/III/IV (n)*: NA
- *Gender (female in %)*: 76
- *Non-smoker (%)*: 84
- *History of PONV/motion sickness (%)*: 20
- *Type of general anaesthesia*: balanced anaesthesia (sevoflurane, fentanyl)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: 78.7
- *Use of perioperative opioids (if yes, which?)*: 162.8 µg fentanyl intraoperative
- *Type of surgery*: thyroid surgery

Included criteria: undergoing thyroid surgery

Excluded criteria: had received antiemetic therapy within 48 hours before surgery; depression, chronic pain disorder, gastrointestinal disease, or insulin-dependent diabetes mellitus; pregnant or 18 years of age; had known malignant disease; had undergone previous thyroid or neck surgery; underwent extended lymphadenectomy because of positive findings in fresh frozen tissue analysis; not given standard anaesthesia and postoperative management

Pretreatment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Interventions	**Intervention characteristics** Dexamethasone (group D) • *Dose*: 8 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, tropisetron 5 mg IV, if symptoms persisted Tropisetron (group T) • *Dose*: 5 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, tropisetron 5 mg IV, if symptoms persisted Dexamethasone + tropisetron (group DT) • *Dose*: dexamethasone 8 mg, tropisetron 5 mg • *Time point of administration*: immediately before induction of anaesthesia • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: metoclopramide 10 mg IV, tropisetron 5 mg IV, if symptoms persisted
Outcomes	*Vomiting (0 to 6 hours)* • Outcome type: dichotomous outcome *Subjects with any AE (time point unknown)* • Outcome type: dichotomous outcome *Postoperative wound infection (0 to 30 days)* • Outcome type: dichotomous outcome *Headache (time point unknown)*

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Zhou 2012 *(Continued)*

- Outcome type: dichotomous outcome

Adverse events (general notes in the publication, 24 hours' observation)

- Outcome type: general notes on side effects

Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Zhiqian Hu **Institution:** Department of General Surgery, Changzheng Hospital, Second Military Medical University, Shanghai, China **Email:** czhuzq@yahoo.com.cn **Address:** Department of General Surgery, Changzheng Hospital, Second Military Medical University, No. 415 Fengyang Road, Shanghai 200003, People's Republic of China **Duration of study:** October 2009 to March 2010 **Language:** English **Study's primary outcome:** nausea, vomiting, and pain **Trial registry number:** ChiCTR-TRC-09000558
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a randomization list was prepared by a random number function of a computer spreadsheet"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "and identical syringes containing each drug were prepared by personnel not involved in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "for all patients, the same two investigators, who were blinded as to the group allocation, assessed the patients for nausea, vomiting, and pain"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "October 2009 and March 2010, a total of 246 patients underwent thyroidectomy at our institution. Among them, 168 patients consented to participate in the study. In all, 18 patients were excluded because a malignancy was detected intraoperatively and additional lymphadenectomy was required or because of protocol violations: 12 patients had a malignancy and underwent additional lymphadenectomy, four received additional steroids intraoperatively, and two received postoperative analgesic regimens that did not follow the protocol. Data from 150 patients..."
Selective reporting (reporting bias)	High risk	Judgement comment: ChiCTR-TRC-09000558 (prospective registration). The prospectively registered primary outcome in the protocol was described as

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Zhou 2012 *(Continued)*

		"nausea and vomiting 2, 4, 8, 16, 24, 36, 48, 72 h" and was changed into "nausea, vomiting and pain". Pain was introduced newly to the final study report. The time point "72h" as described in the protocol was omitted from the final study. Other time points were merged into "0–6 h after the operation and 6–48 h postoperatively"
Other bias	Unclear risk	Quote: "patient characteristics and operative data are summarized in Table 1. Treatment groups were similar with respect to patient characteristics and the operative and anesthesia management" Judgement comment: baseline characteristics (age, BMI): no; (ASA): unclear. Potential effect modifiers (gender, duration of anaesthesia, non-smoker, history of PONV/motion sickness, perioperative opioids): no

Zhu 2010

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 3 groups, monoprophylaxis, different routes of administration
Participants	**Baseline characteristics** Droperidol (PC6 group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: (23 to 66) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: NA • *Type of general anaesthesia*: combined anaesthesia (isoflurane, propofol) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: NA • *Type of surgery*: laparoscopic gynaecological surgery Droperidol (IV group) • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 40 • *Received treatment (n)*: 40 • *Analysed (n)*: 40 • *Age (mean ± SD, median (IQR), median (range))*: (21 to 65) • *Weight (mean ± SD, median (IQR), median (range))*: NA • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA/NA/0/0 • *Gender (female in %)*: 100

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Zhu 2010 *(Continued)*

- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (isoflurane, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic gynaecological surgery

Control

- *Assessed for eligibility (n)*: -
- *Enrolled (n)*: -
- *Randomized (n)*: 40
- *Received treatment (n)*: 40
- *Analysed (n)*: 40
- *Age (mean ± SD, median (IQR), median (range))*: (24 to 66)
- *Weight (mean ± SD, median (IQR), median (range))*: NA
- *BMI (mean ± SD, median (IQR), median (range))*: NA
- *ASA I/II/III/IV (n)*: NA/NA/0/0
- *Gender (female in %)*: 100
- *Non-smoker (%)*: NA
- *History of PONV/motion sickness (%)*: NA
- *Type of general anaesthesia*: combined anaesthesia (isoflurane, propofol)
- *Duration of anaesthesia or surgery (in min; as mean or median)*: NA
- *Use of perioperative opioids (if yes, which?)*: NA
- *Type of surgery*: laparoscopic gynaecological surgery

Included criteria: laparoscopic gynaecological surgery, ASA I and II

Excluded criteria: NA

Pretreatment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

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Interventions

Intervention characteristics

Droperidol (PC6 group)

- *Dose*: 2.5 mg
- *Time point of administration*: 20 minutes before surgery
- *Route of administration*: acupoint injection at neiguan PC6
- *Rescue antiemetics (if yes, which?)*: NA

Droperidol (IV group)

- *Dose*: 2.5 mg
- *Time point of administration*: 20 minutes before surgery
- *Route of administration*: IV
- *Rescue antiemetics (if yes, which?)*: NA

Control

- *Dose*: no treatment
- *Time point of administration*: -
- *Route of administration*: -
- *Rescue antiemetics (if yes, which?)*: NA

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Zhu 2010 *(Continued)*

Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *PONV (0 to 24 hours)* • Outcome type: dichotomous outcome *Sedation/drowsiness (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** NA **Country:** China **Setting:** inpatient, single-centre **Author's name:** Zhu Hong-Xia **Institution:** Department of Anesthesia, The Second Affiliated Hospital of Hebei North College **Email:** NA **Address:** Xuanhua 075100, China **Duration of study:** NA **Language:** Chinese (translated by Hong Sun) **Study's primary outcome:** NA **Trial registry number:** NA
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: quote: "randomly divided". No further information on sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: blinding impossible due to the nature of the different interventions
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: no statement on blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: no missing outcome data

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Zhu 2010 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, ASA): no; (weight): unclear. Potential effect modifiers (gender): no; (history of PONV/motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Zomers 1993

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** 2 groups, monoprophylaxis
Participants	**Baseline characteristics** Tropisetron • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: 35 • *Analysed (n)*: 35 • *Age (mean ± SD, median (IQR), median (range))*: 48 (27 to 73) • *Weight (mean ± SD, median (IQR), median (range))*: 66 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 52/NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 10 µg to 70 µg sufentanil, 20 µg to 70 µg naloxone • *Type of surgery*: gynaecological surgery Placebo • *Assessed for eligibility (n)*: - • *Enrolled (n)*: - • *Randomized (n)*: 35 • *Received treatment (n)*: 35 • *Analysed (n)*: 34 • *Age (mean ± SD, median (IQR), median (range))*: 47 (28 to 73) • *Weight (mean ± SD, median (IQR), median (range))*: 68 • *BMI (mean ± SD, median (IQR), median (range))*: NA • *ASA I/II/III/IV (n)*: NA • *Gender (female in %)*: 100 • *Non-smoker (%)*: NA • *History of PONV/motion sickness (%)*: 48/NA • *Type of general anaesthesia*: inhalational anaesthesia (N_2O, isoflurane) • *Duration of anaesthesia or surgery (in min; as mean or median)*: NA • *Use of perioperative opioids (if yes, which?)*: 10 µg to 80 µg sufentanil, 20 µg to 80 µg naloxone

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Zomers 1993 *(Continued)*

- *Type of surgery*: gynaecological surgery

Included criteria: non-pregnant women, 18 to 75 years of age, undergoing gynaecological surgery under general anaesthesia

Excluded criteria: day-case patients, confounding coexisting medical conditions, receiving concomitant medications that could interfere with evaluation of study drugs, in particular, phenothiazines and prokinetic drugs

Pretreatment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Interventions	**Intervention characteristics** Tropisetron • *Dose*: 5 mg • *Time point of administration*: 15 minutes before wound closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: domperidone 60 mg Placebo • *Dose*: NA • *Time point of administration*: 15 minutes before wound closure • *Route of administration*: IV • *Rescue antiemetics (if yes, which?)*: domperidone 60 mg
Outcomes	*Vomiting (0 to 24 hours)* • Outcome type: dichotomous outcome *Vomiting (PACU)* • Outcome type: dichotomous outcome *Vomiting (PACU release to 24 hours (on the ward))* • Outcome type: dichotomous outcome *Nausea (0 to 24 hours)* • Outcome type: dichotomous outcome *Adverse events (general notes in the publication, 24 hours' observation)* • Outcome type: general notes on side effects
Identification	**Sponsorship source:** Sandoz Pharma Ltd. provided the tropisetron and matching placebo **Country:** The Netherlands **Setting:** inpatient, single-centre **Author's name:** Paul J.W. Zomers **Institution:** Department of Anaesthesiologie, Ziekenhuis 'de Honte' **Email:** NA **Address:** Department of Anaesthesiologie, Ziekenhuis 'de Honte', 4535 PA Terneuzen, The Netherlands **Language:** English

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Zomers 1993 *(Continued)*

	Duration of study: NA **Trial registry number:** NA **Study's primary outcome:** primary efficacy endpoint was number of episodes of vomiting and nausea recorded by nurses and patients
Notes	None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "antiemetic treatment was randomized" Judgement comment: insufficient information on randomization provided
Allocation concealment (selection bias)	Unclear risk	Judgement comment: no statement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind" Judgement comment: insufficient information on blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "information on postoperative nausea and vomiting over the 24-h period after administration of the study medication was obtained from three sources: nursing observation in the recovery room and on the ward; the attending anaesthetist interviewed the patient on the day after the operation and completed a checklist; the patient completed a VAS score for self-assessment of nausea and vomiting and well-being on the day after surgery"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "we studied 70 patients; one patient given placebo was excluded because of missing data. The results are presented for 35 patients who received tropisetron and 34 who received placebo"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no reference to a study protocol or trial registry number reported
Other bias	Unclear risk	Judgement comment: baseline characteristics (age, weight): no; (ASA): unclear. Potential effect modifiers (gender, history of PONV): no; (history of motion sickness, duration of anaesthesia, non-smoker, perioperative opioids): unclear

Abbreviations: AE = adverse event; ASA = American Society of Anesthesiologists physical status classification system; BMI = body mass index; CABG = coronary artery bypass graft; ICU = intensive care unit; IM = intramuscular; IQR = interquartile range; IV = intravenous; n = number of participants; NA = not available; NSAIDs = non-steroidal anti-inflammatory drugs; PACU = post-anaesthesia care unit; PCA = patient-controlled analgesia; PO = per oral; PONV = postoperative nausea and vomiting; SD = standard deviation; SNOSE = sequentially numbered opaque sealed envelopes; TIVA = total intravenous anaesthesia.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aabakke 2014	Different baseline anaesthesia regimens in study arms
Abbasi 2009	Abstract only (e.g. conference proceeding)

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Study	Reason for exclusion
Abdelmalak 2013	Wrong outcomes
AbouZeid 2002	Retracted study
Adams 2009	Wrong population
Agah 2019	Regional or sedative anaesthesia
Ahlburg 2007	Meta-analysis
Ahmad 2019	Wrong outcomes
Ahn 2005	Paediatric population or mixed population (children and adults)
Albooghobeish 2017	Wrong or no eligible comparator
Alexander 1995	Wrong administration time point (after onset of PONV, therapy study)
Alfanek 2015	Regional or sedative anaesthesia
Ali 1995	Wrong outcomes
AliKhan 2013	Wrong study design
Alipour 2013	Wrong outcomes
Alon 1992	Paediatric population or mixed population (children and adults)
Alon 1994	Paediatric population or mixed population (children and adults)
Al Shehri 2004	Wrong administration time point (after onset of PONV, therapy study)
Altinok 2012	Abstract only (e.g. conference proceeding)
Ambesh 1999	Wrong outcomes
Anonymous 1994	Editorial, commentary, narrative review, etc.
Antonini 1994	Wrong outcomes
Apfel 2002	Paediatric population or mixed population (children and adults)
Arcioni 2002	Wrong administration time point (after onset of PONV, therapy study)
Arlia 1966	Wrong study design
Arndt 1997	Abstract only (e.g. conference proceeding)
Aronson 1986	Editorial, commentary, narrative review, etc.
Arsian 2000	Abstract only (e.g. conference proceeding)
Arslan 2011a	Wrong or no eligible comparator
Ascari 1999	Abstract only (e.g. conference proceeding)

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Study	Reason for exclusion
Asl 2011	Paediatric population or mixed population (children and adults)
Atsuta 2017	Wrong or no eligible comparator
Badaoui 2000	Editorial, commentary, narrative review, etc.
Bahmani 2015	Wrong study design
Bajaj 1980	Wrong intervention
Bakeer 2019	Regional or sedative anaesthesia
Banerjee 2014	Wrong outcomes
Barden 2020	Wrong outcomes
Barron 1984	Wrong administration time point (after onset of PONV, therapy study)
Barros-de-Oliveira 2002	Regional or sedative anaesthesia
Barry 2004	Editorial, commentary, narrative review, etc.
Barsoum 1990	Wrong administration time point (after onset of PONV, therapy study)
Bartlett 2013	Editorial, commentary, narrative review, etc.
Barton 1975	Paediatric population or mixed population (children and adults)
Batistaki 2019	Wrong outcomes
Battersby 1965	Paediatric population or mixed population (children and adults)
Bauer 1966	Wrong study design
Beattie 2002	Editorial, commentary, narrative review, etc.
Berg 1987	Paediatric population or mixed population (children and adults)
Berg 1995	Abstract only (e.g. conference proceeding)
Berg 1996	Paediatric population or mixed population (children and adults)
Berg 1996a	Paediatric population or mixed population (children and adults)
Berg 1996b	Paediatric population or mixed population (children and adults)
Bhutia 2009	Abstract only (e.g. conference proceeding)
Bilgin 1998	Wrong outcomes
Birmingham 2006	Different baseline anaesthesia regimens in study arms
Bjornholdt 2014	Wrong or no eligible comparator
Bock 2007	Wrong outcomes

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Study	Reason for exclusion
Boissieras 1967	Wrong study design
Bononi 2010	Wrong or no eligible comparator
Boonmak 2007	Wrong administration time point (after onset of PONV, therapy study)
Bosek 1992	Paediatric population or mixed population (children and adults)
Bouaggad 1999	Editorial, commentary, narrative review, etc.
Bouaggad 2007	Editorial, commentary, narrative review, etc.
Bouly 1993	Wrong outcomes
Boyer 2011	Abstract only (e.g. conference proceeding)
Braga 2019	Wrong administration time point (after onset of PONV, therapy study)
Breivik 1971	Wrong administration time point (after onset of PONV, therapy study)
Bridges 2006	Different baseline anaesthesia regimens in study arms
Brigandi 2015	Wrong population
Brookman 1997	Wrong outcomes
Browning 2004	Different baseline anaesthesia regimens in study arms
Burmeister 2003	Regional or sedative anaesthesia
Butrón 1996	Wrong intervention
Cade 1993	Editorial, commentary, narrative review, etc.
Campbell 1991	Paediatric population or mixed population (children and adults)
Carides 2007	Editorial, commentary, narrative review, etc.
Carlisle 2006b	Editorial, commentary, narrative review, etc.
Carr 1999	Wrong outcomes
Cavanaugh 1996	Abstract only (e.g. conference proceeding)
Celik 2015	Wrong or no eligible comparator
Chalya 2015	Wrong study design
Charuluxananan 2003	Regional or sedative anaesthesia
Chelly 1996	Abstract only (e.g. conference proceeding)
Chen 1998	Different baseline anaesthesia regimens in study arms
Cherian 2005	Wrong study design

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Study	Reason for exclusion
Chestnutt 1986	Paediatric population or mixed population (children and adults)
Cho 1998	Paediatric population or mixed population (children and adults)
Cho 2016	Wrong or no eligible comparator
Choi 2008a	Wrong administration time point (after onset of PONV, therapy study)
Choi 2012	Wrong administration time point (after onset of PONV, therapy study)
Choi 2014	Abstract only (e.g. conference proceeding)
Chopra 2009	Wrong administration time point (after onset of PONV, therapy study)
Clarke 1984	Editorial, commentary, narrative review, etc.
Cohen 1981	Abstract only (e.g. conference proceeding)
Cohen 1983	Wrong study design
Coloma 2001	Regional or sedative anaesthesia
Coloma 2002	Paediatric population or mixed population (children and adults)
Constenla 2004	Meta-analysis
Cowie 2010	Wrong outcomes
Cozanitis 1996	Wrong outcomes
Cramb 1989	Wrong outcomes
Cranwell Bruce 2009	Editorial, commentary, narrative review, etc.
Cruz 2008	Wrong or no eligible comparator
Culebras 2003	Wrong administration time point (after onset of PONV, therapy study)
Daftary 1998	Paediatric population or mixed population (children and adults)
DArcy 1998	Wrong study design
Das 2010	Abstract only (e.g. conference proceeding)
Davidson 1979	Wrong administration time point (after onset of PONV, therapy study)
Davies 1996	Wrong administration time point (after onset of PONV, therapy study)
Davis 1995	Paediatric population or mixed population (children and adults)
Davys 1957	Wrong study design
de Araujo 2020	Wrong or no eligible comparator
DeGroote 1996	Abstract only (e.g. conference proceeding)

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Study	Reason for exclusion
DeJohn 2013	Editorial, commentary, narrative review, etc.
Dejonckheere 1990	Wrong administration time point (after onset of PONV, therapy study)
Delatioglu 2009	Wrong outcomes
Dershwitz 1992	Wrong administration time point (after onset of PONV, therapy study)
Dershwitz 1998	Wrong outcomes
Deshpande 2017	Regional or sedative anaesthesia
Desmillieres 1977	Editorial, commentary, narrative review, etc.
Diamond 1985	Editorial, commentary, narrative review, etc.
Diamond 1988	Abstract only (e.g. conference proceeding)
Dimich 1991	Different baseline anaesthesia regimens in study arms
Dimitriou 1997	Abstract only (e.g. conference proceeding)
Dimitriou 1998	Abstract only (e.g. conference proceeding)
Dionne 1998	Regional or sedative anaesthesia
Dissanayake 2018	Regional or sedative anaesthesia
Dogliotti 1969	Wrong study design
Doksrod 2012	Wrong outcomes
DoVale 2010	Abstract only (e.g. conference proceeding)
Dresner 1998	Wrong administration time point (after onset of PONV, therapy study)
Driesschaert 1995	Abstract only (e.g. conference proceeding)
Du 2004	Wrong administration time point (after onset of PONV, therapy study)
Duarte 1985	Wrong study design
Dundee 1968	Wrong population
Dundee 1987	Editorial, commentary, narrative review, etc.
Dundee 1988	Abstract only (e.g. conference proceeding)
Dupeyron 1993	Wrong administration time point (after onset of PONV, therapy study)
Eberhart 1996	Different baseline anaesthesia regimens in study arms
Eberhart 1999c	Wrong or no eligible comparator
Eberhart 1999d	Wrong administration time point (after onset of PONV, therapy study)

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Study	Reason for exclusion
Eberhart 1999e	Wrong administration time point (after onset of PONV, therapy study)
Eberhart 2000	Wrong administration time point (after onset of PONV, therapy study)
Eberhart 2001	Paediatric population or mixed population (children and adults)
Ebrahim Soltani 2011	Paediatric population or mixed population (children and adults)
Eftekharian 2013	Paediatric population or mixed population (children and adults)
Egerton Warburton 2013	Wrong population
Einarsson 2008	Wrong or no eligible comparator
El-Boghdadly 2019	Regional or sedative anaesthesia
Elliott 1994	Wrong or no eligible comparator
Ellis 1970	Wrong outcomes
ElShobaki 2003	Wrong administration time point (after onset of PONV, therapy study)
Entezariasl 2013	Paediatric population or mixed population (children and adults)
Fang 2014	Wrong administration time point (after onset of PONV, therapy study)
Fassolt 1977	Wrong study design
Fassoulaki 1989	Paediatric population or mixed population (children and adults)
Fillinger 2002	Wrong administration time point (after onset of PONV, therapy study)
Fisher 1984	Different baseline anaesthesia regimens in study arms
Fitzpatrick 1987	Abstract only (e.g. conference proceeding)
Fonseca 2001	Paediatric population or mixed population (children and adults)
Foster 1996a	Regional or sedative anaesthesia
Fragen 1978	Wrong administration time point (after onset of PONV, therapy study)
Fragen 1979	Wrong administration time point (after onset of PONV, therapy study)
Franklyn 2019	Abstract only (e.g. conference proceeding)
Frelich 2020	Paediatric population or mixed population (children and adults)
Freymond 2002	Editorial, commentary, narrative review, etc.
Frighetto 1999	Wrong study design
Fry 1974	Wrong study design
Fry 1977	Wrong intervention

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Study	Reason for exclusion
Fu 2009	Regional or sedative anaesthesia
Fujii 1998	Authored by Fujii et al
Fujii 2008	Authored by Fujii et al
Fukushima 2001	Wrong administration time point (after onset of PONV, therapy study)
Gackle 1999	Abstract only (e.g. conference proceeding)
Gan 1995	Wrong administration time point (after onset of PONV, therapy study)
Gan 2002	Wrong or no eligible comparator
Gan 2005a	Editorial, commentary, narrative review, etc.
Gan 2009a	Wrong administration time point (after onset of PONV, therapy study)
Gandhi 2016	Abstract only (e.g. conference proceeding)
Gani 2010	Abstract only (e.g. conference proceeding)
Gani 2011	Abstract only (e.g. conference proceeding)
Ganjare 2013	Different baseline anaesthesia regimens in study arms
Gartner 2010	Wrong study design
Garzon 1993	Abstract only (e.g. conference proceeding)
Garzozi 2006	Paediatric population or mixed population (children and adults)
Gasbjerg 2020	Different baseline anaesthesia regimens in study arms
Gecaj Gashi 2012	Abstract only (e.g. conference proceeding)
Generali 2007	Regional or sedative anaesthesia
Generali 2010	Regional or sedative anaesthesia
Geng 2017	Wrong outcomes
George 2016	Abstract only (e.g. conference proceeding)
Ghaly 1987	Wrong outcomes
Ghosh 2009	Abstract only (e.g. conference proceeding)
Gibertini 1968	Wrong study design
Glaser 1999	Abstract only (e.g. conference proceeding)
Gougeon 1988	Regional or sedative anaesthesia
Grebenik 1996	Wrong administration time point (after onset of PONV, therapy study)

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Study	Reason for exclusion
Guldager 1983	Paediatric population or mixed population (children and adults)
Gunes 2003	Wrong administration time point (after onset of PONV, therapy study)
Gupta 2006a	Wrong study design
Gupta 2010	Paediatric population or mixed population (children and adults)
Gupta 2018	Wrong or no eligible comparator
Gurha 2012	Abstract only (e.g. conference proceeding)
Gürkan 2002	Regional or sedative anaesthesia
Gürses 2003	Wrong administration time point (after onset of PONV, therapy study)
Gutierrez Williams 2008	Wrong study design
Haapanen 2017	Wrong administration time point (after onset of PONV, therapy study)
Hahm 2010	Regional or sedative anaesthesia
Halvorsen 2003	Wrong administration time point (after onset of PONV, therapy study)
Ham 2016	Wrong administration time point (after onset of PONV, therapy study)
Hammond 1985	Editorial, commentary, narrative review, etc.
Han 2004	Wrong administration time point (after onset of PONV, therapy study)
Harmon 2000	Editorial, commentary, narrative review, etc.
Harper 1998	Editorial, commentary, narrative review, etc.
Harris 1991	Wrong administration time point (after onset of PONV, therapy study)
Hartrick 2010	Wrong study design
Hartsell 2005	Wrong administration time point (after onset of PONV, therapy study)
Hashemi 2015	Abstract only (e.g. conference proceeding)
Hayashi 2002	Wrong administration time point (after onset of PONV, therapy study)
Hee 2003	Wrong administration time point (after onset of PONV, therapy study)
Heffernan 2000	Editorial, commentary, narrative review, etc.
Helmers 1992	Wrong administration time point (after onset of PONV, therapy study)
Hendley 1991	Editorial, commentary, narrative review, etc.
Heyns 1961	Wrong or no eligible comparator
Hirs 2013	Wrong study design

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Study	Reason for exclusion
Ho 2010	Editorial, commentary, narrative review, etc.
Homaei 2012	Abstract only (e.g. conference proceeding)
Hong 2017	Wrong administration time point (after onset of PONV, therapy study)
Honkavaara 1994	Wrong intervention
Honkavaara 1995a	Paediatric population or mixed population (children and adults)
Honkavaara 1999	Paediatric population or mixed population (children and adults)
Horvath 1987	Wrong study design
Howat 1960	Wrong study design
Hsiao 2009	Editorial, commentary, narrative review, etc.
Huang 2012	Wrong administration time point (after onset of PONV, therapy study)
Huerta 2006	Editorial, commentary, narrative review, etc.
Huh 2006	Regional or sedative anaesthesia
Huh 2010	Wrong administration time point (after onset of PONV, therapy study)
Hunting 1997	Abstract only (e.g. conference proceeding)
Huston 1996	Abstract only (e.g. conference proceeding)
Hwang 2004	Wrong administration time point (after onset of PONV, therapy study)
Hwang 2004a	Wrong administration time point (after onset of PONV, therapy study)
Ionescu 2011	Wrong outcomes
Irjala 1996	Regional or sedative anaesthesia
Islam 2011	Paediatric population or mixed population (children and adults)
Isosu 1995	Wrong intervention
Jahromi 2013	Paediatric population or mixed population (children and adults)
Jain 2009	Wrong administration time point (after onset of PONV, therapy study)
Jain 2015	Regional or sedative anaesthesia
Jain 2016	Wrong or no eligible comparator
Jamshidi 2015	Wrong outcomes
Janknegt 1999a	Different baseline anaesthesia regimens in study arms
Jellish 2008	Wrong administration time point (after onset of PONV, therapy study)

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Study	Reason for exclusion
Jemia 2017	Abstract only (e.g. conference proceeding)
Jensen 1983	Wrong study design
Jirarattanaphochai 2007	Wrong intervention
Jo 2011	Wrong outcomes
Johns 2006	Different baseline anaesthesia regimens in study arms
Johnson 2009	Wrong population
Jokela 2010	Wrong administration time point (after onset of PONV, therapy study)
Jorgensen 1990	Wrong outcomes
Jose 2017	Wrong administration time point (after onset of PONV, therapy study)
Joshi 1993	Paediatric population or mixed population (children and adults)
Junge 2007	Editorial, commentary, narrative review, etc.
Kafali 1994	Wrong administration time point (after onset of PONV, therapy study)
Kainulainen 2018	Wrong administration time point (after onset of PONV, therapy study)
Kajac 1997	Abstract only (e.g. conference proceeding)
Kakodkar 2013	Editorial, commentary, narrative review, etc.
Kang 2009	Abstract only (e.g. conference proceeding)
Kang 2010	Regional or sedative anaesthesia
Karabulut 2018	Editorial, commentary, narrative review, etc.
Karaman 2013	Wrong administration time point (after onset of PONV, therapy study)
Karlidag 2002	Paediatric population or mixed population (children and adults)
Kasagi 2013	Wrong administration time point (after onset of PONV, therapy study)
Kassim 2018	Wrong outcomes
Katayama 1995	Wrong or no eligible comparator
Kathirvel 2001	Paediatric population or mixed population (children and adults)
Kaufmann 1994	Wrong administration time point (after onset of PONV, therapy study)
Kaul 1978	Wrong intervention
Kauste 1986	Paediatric population or mixed population (children and adults)
Kenny 1992	Wrong administration time point (after onset of PONV, therapy study)

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Study	Reason for exclusion
Kesecioglu 1991	Abstract only (e.g. conference proceeding)
Kessell 1974	Wrong intervention
Kessell 1997	Editorial, commentary, narrative review, etc.
Khalil 1999	Paediatric population or mixed population (children and adults)
Khan 2004	Editorial, commentary, narrative review, etc.
Khan 2011a	Paediatric population or mixed population (children and adults)
Kim 1997	Wrong administration time point (after onset of PONV, therapy study)
Kim 1998	Wrong outcomes
Kim 1998a	Wrong administration time point (after onset of PONV, therapy study)
Kim 2005d	Paediatric population or mixed population (children and adults)
Kim 2007a	Wrong administration time point (after onset of PONV, therapy study)
Kim 2007b	Wrong study design
Kim 2013c	Wrong administration time point (after onset of PONV, therapy study)
Kim 2014	Wrong outcomes
Kim 2016	Wrong administration time point (after onset of PONV, therapy study)
Kim 2017	Wrong intervention
Kim 2020	Wrong administration time point (after onset of PONV, therapy study)
Kirdak 2008	Regional or sedative anaesthesia
Kivalo 1970	Different baseline anaesthesia regimens in study arms
Kivalo 1976	Wrong administration time point (after onset of PONV, therapy study)
Kizilkaya 2005	Paediatric population or mixed population (children and adults)
Klahsen 1996	Wrong administration time point (after onset of PONV, therapy study)
Kleif 2017	Wrong or no eligible comparator
Koc 2007	Paediatric population or mixed population (children and adults)
Koh 2013	Regional or sedative anaesthesia
Kohler 1988	Wrong administration time point (after onset of PONV, therapy study)
Koivuranta 1997a	Wrong or no eligible comparator
Kolm 2006	Regional or sedative anaesthesia

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Study	Reason for exclusion
Koo 2001a	Wrong administration time point (after onset of PONV, therapy study)
Kooij 2006	Editorial, commentary, narrative review, etc.
Koposov 2011	Editorial, commentary, narrative review, etc.
Korttila 1985	Wrong administration time point (after onset of PONV, therapy study)
Korttila 2004	Meta-analysis
Koski 1990	Wrong or no eligible comparator
Kotake 2000	Regional or sedative anaesthesia
Kovac 1996	Paediatric population or mixed population (children and adults)
Kovac 1997	Wrong administration time point (after onset of PONV, therapy study)
Kovac 2005	Editorial, commentary, narrative review, etc.
Kranke 1997	Abstract only (e.g. conference proceeding)
Kreisler 2000	Different baseline anaesthesia regimens in study arms
Kuczkowski 2004	Editorial, commentary, narrative review, etc.
Kumar 2009	Editorial, commentary, narrative review, etc.
Kumar 2018	Wrong administration time point (after onset of PONV, therapy study)
Kushwaha 2007	Paediatric population or mixed population (children and adults)
Kuypers 2000	Abstract only (e.g. conference proceeding)
Kyriakides 1998	Abstract only (e.g. conference proceeding)
Laer 2001	Editorial, commentary, narrative review, etc.
Laffey 2002	Wrong administration time point (after onset of PONV, therapy study)
Lanza 1996	Abstract only (e.g. conference proceeding)
Lauretti 1997	Regional or sedative anaesthesia
Lauretti 2014	Regional or sedative anaesthesia
Le 1995	Abstract only (e.g. conference proceeding)
Lee 1995	Wrong outcomes
Lee 2015c	Abstract only (e.g. conference proceeding)
Lee 2015d	Wrong or no eligible comparator
Lee 2016	Wrong or no eligible comparator

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Study	Reason for exclusion
Lee 2017	Wrong administration time point (after onset of PONV, therapy study)
Lee 2017a	Wrong administration time point (after onset of PONV, therapy study)
Lee 2018	Regional or sedative anaesthesia
Lee 2020	Wrong outcomes
Leeser 1991	Wrong administration time point (after onset of PONV, therapy study)
Lei 2017	Wrong administration time point (after onset of PONV, therapy study)
Lei 2018	Wrong administration time point (after onset of PONV, therapy study)
Leksowski 2006	Wrong outcomes
Lencz 1990	Wrong administration time point (after onset of PONV, therapy study)
Lewaschiw 2005	Paediatric population or mixed population (children and adults)
Lewinski 1970	Wrong study design
Lewis 1994	Editorial, commentary, narrative review, etc.
Li 2019	Wrong administration time point (after onset of PONV, therapy study)
Li 2019a	Wrong administration time point (after onset of PONV, therapy study)
Li 2020	Wrong outcomes
Lien 1993	Wrong outcomes
Lim 2008	Wrong administration time point (after onset of PONV, therapy study)
Lin 1996	Regional or sedative anaesthesia
Lin 2005	Wrong administration time point (after onset of PONV, therapy study)
Liu 2003	Wrong administration time point (after onset of PONV, therapy study)
Lo 2005	Wrong administration time point (after onset of PONV, therapy study)
Loers 1973	Abstract only (e.g. conference proceeding)
Loper 1989	Regional or sedative anaesthesia
LopezHerrera 2000	Wrong administration time point (after onset of PONV, therapy study)
Lu 2006	Wrong intervention
Lu 2010	Wrong administration time point (after onset of PONV, therapy study)
Lu 2013	Wrong administration time point (after onset of PONV, therapy study)
Lund 2004	Wrong study design

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Study	Reason for exclusion
Lv 2013	Wrong or no eligible comparator
Ma 2009	Wrong outcomes
Maddali 2003a	Wrong intervention
Madenoglu 2003	Wrong administration time point (after onset of PONV, therapy study)
Madenoglu 2012	Wrong administration time point (after onset of PONV, therapy study)
Madsen 1992	Wrong study design
Maestre 1997	Paediatric population or mixed population (children and adults)
Malik 2019	Wrong outcomes
Malins 1994	Wrong outcomes
Manchikanti 1984	Wrong outcomes
Mangel 1959	Wrong study design
Mansfield 1997	Different baseline anaesthesia regimens in study arms
Marco 2013	Abstract only (e.g. conference proceeding)
Marcus 1964	Paediatric population or mixed population (children and adults)
Mathias 2004	Editorial, commentary, narrative review, etc.
Mathiesen 2008	Regional or sedative anaesthesia
Mathiesen 2013	Wrong study design
Mattila 2010	Regional or sedative anaesthesia
Mayzner Zawadzka 1996	Abstract only (e.g. conference proceeding)
Mazo 2012	Wrong intervention
McAuliffe 1995	Editorial, commentary, narrative review, etc.
McAuliffe 1997	Editorial, commentary, narrative review, etc.
McDevitt 2013	Editorial, commentary, narrative review, etc.
McKenzie 1993a	Wrong administration time point (after onset of PONV, therapy study)
McKenzie 1995	Wrong administration time point (after onset of PONV, therapy study)
Mehta 1984	Wrong outcomes
Mei 2014	Wrong outcomes
Melnick 1989	Editorial, commentary, narrative review, etc.

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Study	Reason for exclusion
Mendes 2009	Wrong outcomes
Migliavacca 1992	Wrong outcomes
Miles 1996	Abstract only (e.g. conference proceeding)
Miller 1988	Paediatric population or mixed population (children and adults)
Millo 2001	Wrong administration time point (after onset of PONV, therapy study)
Minobe 1981	Different baseline anaesthesia regimens in study arms
Mirakhur 1981	Editorial, commentary, narrative review, etc.
Mishra 2010	Paediatric population or mixed population (children and adults)
Modir 2019	Regional or sedative anaesthesia
Moeen 2017	Regional or sedative anaesthesia
Mohammad 2006	Paediatric population or mixed population (children and adults)
Monagle 1997	Paediatric population or mixed population (children and adults)
MontejanoMoran 1978	Different baseline anaesthesia regimens in study arms
Moon 2012	Wrong or no eligible comparator
Moon 2014	Wrong outcomes
Morimoto 1996	Wrong intervention
Morrison 1970	Wrong study design
Moscovici 1995	Wrong administration time point (after onset of PONV, therapy study)
Moslemi 2015	Wrong administration time point (after onset of PONV, therapy study)
Movafegh 2007	Regional or sedative anaesthesia
Mraovic 2010	Editorial, commentary, narrative review, etc.
Mukhopadhyay 2013	Regional or sedative anaesthesia
Naco 2012	Abstract only (e.g. conference proceeding)
Naji 1990	Regional or sedative anaesthesia
Najnigier 1997	Different baseline anaesthesia regimens in study arms
Nakajima 2015	Abstract only (e.g. conference proceeding)
Nam 2009	Wrong administration time point (after onset of PONV, therapy study)
Nam 2014	Abstract only (e.g. conference proceeding)

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Study	Reason for exclusion
Nam 2015	Different baseline anaesthesia regimens in study arms
Nazar 2009	Wrong outcomes
Nazar 2009a	Abstract only (e.g. conference proceeding)
Nazar 2009b	Abstract only (e.g. conference proceeding)
Nazar 2011	Wrong outcomes
NCT00231478	Paediatric population or mixed population (children and adults)
NCT01186029	Retracted study
NCT01819857	Wrong population
NCT02457195	Wrong study design
NCT02473042	Wrong or no eligible comparator
NCT02571075	Wrong intervention
NCT02941913	Wrong or no eligible comparator
NCT02947672	Wrong or no eligible comparator
NCT03035942	Regional or sedative anaesthesia
NCT03088696	Wrong intervention
NCT03125941	Wrong or no eligible comparator
NCT03197064	Wrong study design
NCT03202459	Wrong intervention
NCT03250494	Wrong or no eligible comparator
NCT03297021	Wrong or no eligible comparator
NCT03435003	Different baseline anaesthesia regimens in study arms
NCT03443778	Paediatric population or mixed population (children and adults)
NCT03583489	Wrong study design
NCT03588338	Wrong or no eligible comparator
NCT03603119	Wrong or no eligible comparator
NCT03758170	Wrong or no eligible comparator
NCT03763734	Wrong or no eligible comparator
NCT03763760	Wrong or no eligible comparator

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Study	Reason for exclusion
NCT03783182	Paediatric population or mixed population (children and adults)
NCT03933605	Wrong intervention
NCT03944681	Wrong study design
NCT04043247	Wrong intervention
NCT04054479	Paediatric population or mixed population (children and adults)
NCT04084912	Paediatric population or mixed population (children and adults)
NCT04123873	Wrong intervention
NCT04297293	Wrong study design
Ng 1997	Wrong administration time point (after onset of PONV, therapy study)
Nielsen 2008	Editorial, commentary, narrative review, etc.
Nikiforovlu 1999	Editorial, commentary, narrative review, etc.
Nikolajsen 2006	Editorial, commentary, narrative review, etc.
Ninger 2003	Editorial, commentary, narrative review, etc.
Nonaka 2008	Wrong study design
Nordin 2016	Wrong outcomes
Norred 2002	Editorial, commentary, narrative review, etc.
ODonovan 1984	Paediatric population or mixed population (children and adults)
Oh 2009	Paediatric population or mixed population (children and adults)
Okninska 1968	Wrong study design
Ongun 2000	Wrong administration time point (after onset of PONV, therapy study)
Ordy 1970	Wrong population
Ormel 2011	Wrong administration time point (after onset of PONV, therapy study)
Oshima 2002	Wrong intervention
Overdyk 1999	Wrong administration time point (after onset of PONV, therapy study)
Owczarzak 1997	Abstract only (e.g. conference proceeding)
Ozalp 1997	Wrong outcomes
Oztekin 2003	Wrong outcomes
Pacella 2001	Abstract only (e.g. conference proceeding)

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Study	Reason for exclusion
Paddock 1964	Different baseline anaesthesia regimens in study arms
Paech 2007	Wrong intervention
Pakpirom 2017	Different baseline anaesthesia regimens in study arms
Palazzo 1984	Editorial, commentary, narrative review, etc.
Palmer 1996	Editorial, commentary, narrative review, etc.
Panda 2004	Wrong outcomes
Pang 2002	Wrong administration time point (after onset of PONV, therapy study)
Pang 2020	Wrong administration time point (after onset of PONV, therapy study)
Panigrahi 2015	Wrong intervention
Panigrahi 2016	Regional or sedative anaesthesia
Papathanakos 2012	Abstract only (e.g. conference proceeding)
Park 1996	Wrong administration time point (after onset of PONV, therapy study)
Park 1997	Wrong administration time point (after onset of PONV, therapy study)
Park 1998	Wrong administration time point (after onset of PONV, therapy study)
Park 1998a	Wrong administration time point (after onset of PONV, therapy study)
Park 2010	Wrong or no eligible comparator
Parlow 1999	Wrong administration time point (after onset of PONV, therapy study)
Pauls 2015	Wrong outcomes
Paxton 1995	Paediatric population or mixed population (children and adults)
Peiying 2014	Wrong study design
Pergolizzi 2012	Editorial, commentary, narrative review, etc.
Pestel 1969	Editorial, commentary, narrative review, etc.
Pierre 2004	Wrong study design
Piper 2001	Retracted study
Piper 2002	Retracted study
Piper 2008	Paediatric population or mixed population (children and adults)
Pitkanen 1993	Regional or sedative anaesthesia
Polati 1995	Wrong outcomes

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Study	Reason for exclusion
Pourfakhr 2019	Wrong outcomes
Powell 2000	Editorial, commentary, narrative review, etc.
Pueyo 2003	Wrong administration time point (after onset of PONV, therapy study)
Pugh 1996	Wrong outcomes
Purkis 1965	Wrong outcomes
Rabbani 2010	Paediatric population or mixed population (children and adults)
Rae 1967	Wrong administration time point (after onset of PONV, therapy study)
Raeder 2005	Editorial, commentary, narrative review, etc.
Rahimzadeh 2014	Regional or sedative anaesthesia
Rainov 1996	Wrong intervention
Ramakrishna 2008	Editorial, commentary, narrative review, etc.
Ramesh 2011	Abstract only (e.g. conference proceeding)
Rasmussen 2008	Wrong outcomes
Rastogi 2008	Regional or sedative anaesthesia
Rauers 2010	Wrong outcomes
Razavizadeh 2017	Regional or sedative anaesthesia
Reddy 2001	Wrong outcomes
Refaat 2010	Abstract only (e.g. conference proceeding)
Reibaldi 2019	Regional or sedative anaesthesia
Riha 2009	Editorial, commentary, narrative review, etc.
Ritchie 2016	Editorial, commentary, narrative review, etc.
Robbie 1959	Wrong study design
Roberts 1995	Wrong administration time point (after onset of PONV, therapy study)
Robin 2001	Wrong outcomes
Rodary 1979	Wrong administration time point (after onset of PONV, therapy study)
Roh 2014	Wrong administration time point (after onset of PONV, therapy study)
Rosow 2008	Different baseline anaesthesia regimens in study arms
Russell 1992	Editorial, commentary, narrative review, etc.

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Study	Reason for exclusion
Ryu 2014	Wrong or no eligible comparator (some participants received dexamethasone; results not reported for dexamethasone-treated participants)
Sadighha 2008	Wrong study design
Sahjpaul 2003	Wrong administration time point (after onset of PONV, therapy study)
Said Ahmed 2008	Wrong administration time point (after onset of PONV, therapy study)
Sakamoto 2016	Wrong intervention
Salmenpera 1992	Wrong intervention
Sanansilp 2002	Wrong administration time point (after onset of PONV, therapy study)
Sanchez Ledesma 2002	Wrong administration time point (after onset of PONV, therapy study)
Sanchez Pena 1996	Wrong outcomes
Sansone 2011	Abstract only (e.g. conference proceeding)
Sarvestani 2013	Wrong outcomes
Scholtes 1991	Wrong administration time point (after onset of PONV, therapy study)
Schousboe 1998	Editorial, commentary, narrative review, etc.
Scuderi 2003	Editorial, commentary, narrative review, etc.
Scurr 1958	Wrong study design
Seervi 2019	Regional or sedative anaesthesia
SerranoMartinez 1998	Wrong outcomes
Severance 2006	Abstract only (e.g. conference proceeding)
Shahraki 2013	Regional or sedative anaesthesia
Sharma 1993	Wrong administration time point (after onset of PONV, therapy study)
Shin 2011	Abstract only (e.g. conference proceeding)
Shrestha 2014	Wrong outcomes
Sikka 2007	Editorial, commentary, narrative review, etc.
Silverberg 2012	Abstract only (e.g. conference proceeding)
Silverman 1992	Wrong administration time point (after onset of PONV, therapy study)
Simsa 2013	Different baseline anaesthesia regimens in study arms
Singh 2016	Abstract only (e.g. conference proceeding)

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Study	Reason for exclusion
Singla 2011	Abstract only (e.g. conference proceeding)
Sinha 1999	Paediatric population or mixed population (children and adults)
SivaRamaKrishna 2013	Abstract only (e.g. conference proceeding)
Skroubis 2016	Wrong outcomes
Sneyd 2009	Editorial, commentary, narrative review, etc.
Snow 1967	Paediatric population or mixed population (children and adults)
Song 2002	Regional or sedative anaesthesia
Song 2011	Wrong administration time point (after onset of PONV, therapy study)
Sood 2012	Abstract only (e.g. conference proceeding)
SoonIm 2012	Abstract only (e.g. conference proceeding)
Sousa 2014	Abstract only (e.g. conference proceeding)
Srivastava 2012a	Abstract only (e.g. conference proceeding)
Stamer 2001	Editorial, commentary, narrative review, etc.
Steegers 1982	Wrong outcomes
Steele 1971	Regional or sedative anaesthesia
Steinbrook 1996	Wrong study design
Stutchfield 2005	Regional or sedative anaesthesia
Su 2013	Different baseline anaesthesia regimens in study arms
Sultan 2014	Abstract only (e.g. conference proceeding)
Sustic 2005	Wrong administration time point (after onset of PONV, therapy study)
Suter 1958	Wrong study design
Talebpour 2014	Abstract only (e.g. conference proceeding)
Talebpour 2017	Wrong administration time point (after onset of PONV, therapy study)
Tammachote 2019	Regional or sedative anaesthesia
Tan 1998	Abstract only (e.g. conference proceeding)
Tang 1995	Paediatric population or mixed population (children and adults)
Tang 1996	Paediatric population or mixed population (children and adults)
Tatum 2009	Meta-analysis

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Study	Reason for exclusion
Tavlan 1996	Abstract only (e.g. conference proceeding)
Taylor 1962	Wrong outcomes
Taylor 1997	Wrong administration time point (after onset of PONV, therapy study)
Ternovyi 2003	Different baseline anaesthesia regimens in study arms
Teymourian 2015	Wrong outcomes
Tezcan 1996	Editorial, commentary, narrative review, etc.
Thagaard 2003	Wrong administration time point (after onset of PONV, therapy study)
Thomas 2000	Editorial, commentary, narrative review, etc.
Thomas 2006	Wrong or no eligible comparator
Thune 1995	Wrong study design
Tigga 2014	Abstract only (e.g. conference proceeding)
Tiippana 2008	Wrong outcomes
Tolksdorf 1984	Regional or sedative anaesthesia
Tornetta 1972	Different baseline anaesthesia regimens in study arms
Tornetta 1977	Paediatric population or mixed population (children and adults)
TorresHuerta 2001	Wrong administration time point (after onset of PONV, therapy study)
Toyonaga 2016	Wrong or no eligible comparator
Tracz 2015	Wrong outcomes
Trakya 1996	Wrong or no eligible comparator
Tramer 2005	Editorial, commentary, narrative review, etc.
Treen 1991	Wrong administration time point (after onset of PONV, therapy study)
Treschan 2005	Paediatric population or mixed population (children and adults)
Turner 2017	Abstract only (e.g. conference proceeding)
Turra 1973	Wrong study design
Tzeng 2002	Regional or sedative anaesthesia
Unseld 1996	Wrong intervention
Urias 2016	Abstract only (e.g. conference proceeding)
Usha 1996	Different baseline anaesthesia regimens in study arms

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Study	Reason for exclusion
Valami 2017	Wrong outcomes
Vanacker 1988	Wrong administration time point (after onset of PONV, therapy study)
VasconcelosPalacios 1983	Editorial, commentary, narrative review, etc.
Velickovic 2012	Abstract only (e.g. conference proceeding)
Vinson 2001	Wrong intervention
Visalyaputra 1998	Regional or sedative anaesthesia
Vollmer Larsen 1988	Wrong outcomes
Wakamiya 2019	Paediatric population or mixed population (children and adults)
Wakasugi 2015	Different baseline anaesthesia regimens in study arms
Walder 1994	Wrong administration time point (after onset of PONV, therapy study)
Walder 1995	Wrong administration time point (after onset of PONV, therapy study)
Wallenborn 2006	Different baseline anaesthesia regimens in study arms
Wallenborn 2009	Editorial, commentary, narrative review, etc.
Wallenborn 2010	Editorial, commentary, narrative review, etc.
Wang 1999c	Regional or sedative anaesthesia
Wang 2002c	Wrong outcomes
Warde 1995	Abstract only (e.g. conference proceeding)
Wasfie 2018	Wrong study design
Weber 1998	Regional or sedative anaesthesia
Weidmann 2001	Editorial, commentary, narrative review, etc.
Wenjie 2019	Abstract only (e.g. conference proceeding)
Whalley 1991	Wrong intervention
White 1999	Editorial, commentary, narrative review, etc.
White 2001	Wrong administration time point (after onset of PONV, therapy study)
White 2002	Editorial, commentary, narrative review, etc.
White 2002a	Wrong or no eligible comparator
White 2005a	Editorial, commentary, narrative review, etc.
Wig 2007	Wrong intervention

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Study	Reason for exclusion
Wilder Smith 1994	Regional or sedative anaesthesia
Williams 1993	Wrong administration time point (after onset of PONV, therapy study)
Williams 1999	Wrong administration time point (after onset of PONV, therapy study)
Wong 2010	Abstract only (e.g. conference proceeding)
Woodward 1993	Editorial, commentary, narrative review, etc.
Woodward 1999	Different baseline anaesthesia regimens in study arms
Wrench 1996	Wrong administration time point (after onset of PONV, therapy study)
Xu 2017	Wrong administration time point (after onset of PONV, therapy study)
Xu 2018	Wrong administration time point (after onset of PONV, therapy study)
Yalcyn 2004	Editorial, commentary, narrative review, etc.
Yang 1997	Wrong outcomes
Yang 2008	Wrong administration time point (after onset of PONV, therapy study)
Yang 2012	Wrong administration time point (after onset of PONV, therapy study)
Yelken 2003	Wrong outcomes
Yokoyama 1997	Paediatric population or mixed population (children and adults)
Yoo 2012	Abstract only (e.g. conference proceeding)
Yousef 2010	Wrong outcomes
Yu 2019	Wrong or no eligible comparator
Zahedi 2012	Wrong outcomes
Zahl 1993	Editorial, commentary, narrative review, etc.
Zainuddin 2016	Abstract only (e.g. conference proceeding)
Zajac 1996	Abstract only (e.g. conference proceeding)
Zajac 1997	Abstract only (e.g. conference proceeding)
Zajac 1998	Abstract only (e.g. conference proceeding)
Zajac 2000	Abstract only (e.g. conference proceeding)
Zghidi 2011	Abstract only (e.g. conference proceeding)
Zheng 2016	Wrong administration time point (after onset of PONV, therapy study)
Zhu 2015	Editorial, commentary, narrative review, etc.

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Abbreviations: PONV = postoperative nausea and vomiting.

Characteristics of studies awaiting classification *[ordered by study ID]*

Abdel Halim 2009

Methods	Randomized controlled trial
Participants	Patients undergoing unilateral modified radical mastectomy
Interventions	Preoperative administration of oral gabapentin 800 mg, IV dexamethasone 16 mg, both drugs together or no treatment
Outcomes	Pain, preoperative anxiety, haemodynamic response to intubation, opioid consumption
Notes	No full text available

Abusalem 2011

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy
Interventions	Dexamethasone 16 mg 2 hours before surgery
Outcomes	PONV, pain
Notes	Mail sent on 18th of January 2018; reasons for request were missing information about mean age with standard deviation or range of participants and type of anaesthesia regimen, no response received

ACTRN12615000540516

Methods	Randomized controlled trial
Participants	Patients who are presenting to preadmission clinic for single joint hip or knee arthroplasty; age > 18
Interventions	Dexamethasone (8 mg) first dose given immediately preoperatively and second dose given 24 hours post surgery or placebo
Outcomes	PONV, pain
Notes	Study status (completed), first posted (2015), missing information (anaesthesia regimen, outcomes)

Aleyasin 2014

Methods	Randomized controlled trial
Participants	Female patients undergoing myomectomy and hysterectomy surgeries

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Aleyasin 2014 *(Continued)*

Interventions	Granisetron 40 µg/kg or metoclopramide 0.2 mg/kg at end of surgery
Outcomes	PONV, patient satisfaction, sedation
Notes	Mail sent on 19th of March 2018 and again on 31st of July 2018; reason for request was missing information about type of anaesthesia regimen; no response received

Almustafa 2020

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic sleeve gastrectomy
Interventions	Dexamethasone 8 mg (nebulized) 1 hour before surgery and control (S) with saline nebulizer
Outcomes	Postoperative sore throat, nausea and vomiting
Notes	Study identified in search update; data will be included in next update of the review

Aydin 2019

Methods	Randomized controlled trial
Participants	Patients undergoing middle ear surgery
Interventions	0.075 mg palonosetron, 5 mg tropisetron, and 8 mg ondansetron were administered intravenously and compared
Outcomes	Pain, nausea, vomiting, headache, constipation
Notes	Study identified in search update; data will be included in next update of the review

Aziz 2011

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy, ASA I and II, 15 to 50 years of age
Interventions	Metoclopramide 10 mg IV or dexamethasone 8 mg IV at time of induction
Outcomes	PONV
Notes	Mail sent on 19th of March 2018; reason for request was missing information on age of participants; mail could not be delivered

Bilgen 2018

Methods	Randomized controlled trial

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Bilgen 2018 *(Continued)*

Participants	Patients undergoing laparoscopic gynaecological surgery or laparoscopic cholecystectomy, 18 to 60 years old, ASA I or II
Interventions	Aprepitant (40 mg) orally 1 to 2 hours before induction of anaesthesia and 2 mL saline intravenously (IV) within the last 30 minutes of surgery or oral placebo identical to aprepitant 1 to 2 hours before induction of anaesthesia and ondansetron (4 mg) IV within the last 30 minutes of surgery; all patients received dexamethasone (8 mg) IV after induction
Outcomes	PONV
Notes	Study identified after first search; data will be included in next update of the review

Biswas 2003a

Methods	Randomized controlled trial
Participants	Female patients undergoing laparoscopic tubal ligation, ASA I and II
Interventions	Ondansetron 4 mg IV or dexamethasone 8 mg IV or ondansetron 4 mg IV with dexamethasone 8 mg IV immediately before induction
Outcomes	PONV
Notes	Missing information about range of age; no contact details available

Blowey 2002

Methods	Randomized controlled trial
Participants	NA
Interventions	Metoclopramide or P6 acupressure
Outcomes	PONV
Notes	No full text available

Campbell 1990

Methods	Randomized controlled trial
Participants	Patients undergoing knee arthroscopy, laparoscopy, or dental extraction, ASA I or II, 18 to 59 years of age
Interventions	Droperidol 0.015 mg/kg IV or no treatment immediately after intubation
Outcomes	PONV, time to awakening, time to orientation
Notes	Missing information about study group sizes; no contact details available

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Carrascosa 1997

Methods	Randomized controlled trial
Participants	Patients undergoing maxillofacial surgery
Interventions	NA
Outcomes	NA
Notes	No full text available

Ceyhan 2004

Methods	Randomized controlled trial
Participants	Patients undergoing major orthopaedic surgery, 18 to 70 years of age
Interventions	Metoclopramide 10 mg IV 3 times a day or Reliefband to P6 acupuncture point or placebo and inactive Reliefband
Outcomes	PONV
Notes	No full text available

Champion 2018

Methods	Randomized controlled trial
Participants	Patients with planned non-emergent cardiac surgery
Interventions	4 mg betamethasone with/without 0.625 mg droperidol compared to control; control group was treated as per routine hospital practices
Outcomes	PONV, `drug-related` side effects
Notes	Study identified in search update; data will be included in next update of the review

Chan 1983

Methods	Randomized controlled trial
Participants	Female patients undergoing suction evacuation for termination of pregnancy
Interventions	Metoclopramide 10 mg IV at time of suction or prochlorperazine 6.25 mg IM with premedication or prochlorperazine 12.5 mg IM with premedication or no treatment
Outcomes	Vomiting
Notes	Missing information about range of age; no contact details available

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Charton 2018

Methods	Randomized controlled trial
Participants	Patients scheduled to undergo minor gynaecological, abdominal, or orthopaedic surgery under general anaesthesia for ambulatory surgery, 18 to 65 years of age, ≥ 2 Apfel risk factors
Interventions	Droperidol (0.625 or 1.25 mg) or ondansetron 4 mg
Outcomes	Akathisia, PONV
Notes	Study identified after the first search; data will be included in next update of the review

Chatterjee 2017

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy
Interventions	Dexamethasone 8 mg, palonosetron 0.075 mg, or dexamethasone 8 mg plus palonosetron 0.075 mg
Outcomes	PONV, need for rescue antiemetic
Notes	Study identified in search update; data will be included in next update of the review

Chen 2002

Methods	Randomized controlled trial
Participants	Patients undergoing gynaecological surgery
Interventions	Ondansetron and droperidol
Outcomes	PONV
Notes	No full text available

ChiCTR-TRC-09000671

Methods	Randomized controlled trial
Participants	Patients undergoing open gynaecological surgery, 18 to 60 years of age, ASA I and II
Interventions	Aprepitant or placebo
Outcomes	Complete response
Notes	Study status (completed), first posted (2005), missing information (anaesthesia regimen, time point of administration)

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ChiCTR-TRC-09000672

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic gynaecological surgery, 18 to 60 years of age, ASA I and II
Interventions	Cetirizine 1 hour preoperatively or dexamethasone and placebo
Outcomes	Complete response
Notes	Study status (completed), first posted (2005), missing information (anaesthesia regimen)

ChiCTR-TRC-09000739

Methods	Randomized controlled trial
Participants	Patients undergoing open gynaecological surgery, 18 to 65 years of age
Interventions	Aprepitant immediately before induction of anaesthesia or dexamethasone and aprepitant immediately before induction of anaesthesia
Outcomes	Complete response, pain, nausea
Notes	Study status (completed), first posted (2009), missing information (anaesthesia regimen)

Cho 2019

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic gynaecological surgery
Interventions	Ramosetron 0.3 mg, 0.45 mg, or 0.6 mg at end of surgery
Outcomes	Nausea severity, pain scores, adverse events, patient satisfaction
Notes	Study identified in search update; data will be included in next update of the review

Cooke 1979

Methods	Randomized controlled trial
Participants	Female patients between menarche and menopause undergoing caesarean section or non-obstetrical uterine dilatation and curettage or uterine evacuation
Interventions	Domperidone 4 mg or metoclopramide 10 mg or placebo
Outcomes	PONV, dizziness, drowsiness
Notes	Missing information about range of age; no contact details available

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Cosar 1997

Methods	Randomized controlled trial
Participants	Female adult patients undergoing major gynaecological surgery, ASA I and II
Interventions	Tropisetron 5 mg IV or placebo IV 15 minutes before end of surgery
Outcomes	PONV
Notes	Missing information about randomisation; no contact details available

CTRI/2012/05/002668

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy, ASA I and II, weight between 30 and 75 kg
Interventions	Metoclopramide (10 mg) and dexamethasone (5 mg) before operation or metoclopramide (10 mg) and dexamethasone (2.5 mg) before operation or metoclopramide (10 mg) and saline before operation
Outcomes	PONV
Notes	Study status (recruiting), first posted (2012), missing information (age, anaesthesia regimen)

CTRI/2013/03/003507

Methods	Randomized controlled trial
Participants	Participants over 18 years of age undergoing elective middle ear and nasal surgeries
Interventions	Oral and intravenous ondansetron administered at end of surgery
Outcomes	PONV, pruritus
Notes	Study status (recruiting), first posted (2013), missing information (anaesthesia regimen)

CTRI/2013/04/003570

Methods	Randomized controlled trial
Participants	Patients given elective general anaesthesia, 21 to 50 years of age
Interventions	Granisetron (1 mg/mL) 1 minute before induction of anaesthesia or metoclopramide (5 mg/mL) 1 minute before induction of anaesthesia
Outcomes	Pain, PONV
Notes	Study status (recruiting), first posted (2013), missing information (anaesthesia regimen)

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CTRI/2013/05/003630

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy, ASA I and II
Interventions	Palonosetron (0.075 mg) just before induction of anaesthesia or dexamethasone (8 mg) just before induction of anaesthesia or palonosetron (0.075 mg) and dexamethasone (8 mg) just before induction of anaesthesia
Outcomes	PONV
Notes	Study status (completed), first posted (2013), missing information (age, anaesthesia regimen)

CTRI/2014/11/005214

Methods	Randomized controlled trial
Participants	Patients scheduled for laparoscopic gynaecological surgery, 19 to 60 years of age, female, ASA I and II
Interventions	Palonosetron (0.15 mg), palonosetron (0.075 mg), palonosetron (0.075 mg) with dexamethasone (8 mg), and ondansetron (4 mg) administered intravenously before induction of anaesthesia
Outcomes	Nausea and vomiting at 6, 24, and 72 hours postoperatively
Notes	Study status (recruiting), first posted (2014), missing information (anaesthesia regimen)

CTRI/2014/12/005333

Methods	Randomized controlled trial
Participants	Patients scheduled for elective surgery, older than 18 years of age, breast cancer, ASA I to III
Interventions	Aprepitant (80 mg) 3 hours before induction of anaesthesia or dexamethasone (8 mg) at time of induction of anaesthesia
Outcomes	PONV, adverse reaction
Notes	Study status (completed), first posted (2014), missing information (anaesthesia regimen)

CTRI/2015/03/005616

Methods	Randomized controlled trial
Participants	Patients scheduled for elective intracranial surgery, ASA I and II, GCS 15
Interventions	Ondansetron (4 mg) given at the time of dural closure or palonosetron (0.075 mg) given at the time of dural closure

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CTRI/2015/03/005616 *(Continued)*

Outcomes	PONV, side effects
Notes	Study status (recruiting), first posted (2015), missing information (age, anaesthesia regimen, intervention)

CTRI/2015/09/006223

Methods	Randomized controlled trial
Participants	Patients undergoing open ovarian cancer surgery and requiring opioid-based PCA, 18 to 70 years of age, ASA I and II
Interventions	Palonosetron (0.075 mg) and dexamethasone (4 mg) given at time of wound closure; thereafter placebo drug will be given 3 times a day for 48 hours; or ondansetron (8 mg) and dexamethasone (4 mg) given at time of wound closure; thereafter, ondansetron 4 mg will be given 3 times a day for 48 hours
Outcomes	PONV, pain, adverse events
Notes	Study status (completed), first posted (2015), missing information (anaesthesia regimen, outcome details)

CTRI/2016/07/007108

Methods	Randomized controlled trial
Participants	Patients undergoing elective laparoscopic surgery under general anaesthesia, ASA I and II, 18 to 60 years of age
Interventions	Palonosetron (0.075 mg) or dexamethasone (8 mg) or palonosetron (0.075 mg) and dexamethasone (8 mg)
Outcomes	PONV, pain
Notes	Study status (closed), first posted (2016), missing information (anaesthesia regimen, time point of administration)

CTRI/2016/08/007195

Methods	Randomized controlled trial
Participants	Patients planned for laparoscopic sleeve gastrectomy, ASA I to III, BMI > 32.5 kg/m^2
Interventions	Palonosetron (1 mcg) 30 minutes before induction of anaesthesia and dexamethasone or ondansetron (0.1 mg/kg) and dexamethasone
Outcomes	PONV
Notes	Study status (completed), first posted (2016), missing information (anaesthesia regimen, age, time point of administration)

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CTRI/2017/03/007998

Methods	Randomized controlled trial
Participants	Patients undergoing middle ear surgery, ASA I and II, non-hypertensive and non-diabetic
Interventions	Ondansetron (8 mg) and dexamethasone (8 mg) before induction of anaesthesia or palonosetron (0.075 mg) and dexamethasone (8 mg) before induction of anaesthesia
Outcomes	PONV
Notes	Study status (recruiting), first posted (2017), missing information (anaesthesia regimen)

CTRI/2017/06/008769

Methods	Randomized controlled trial
Participants	Patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia, ASA I and II, 18 to 60 years of age, BMI < 30 kg/m^2
Interventions	Dexamethasone (2 mg) after induction of anaesthesia or dexamethasone (4 mg) after induction of anaesthesia or saline (1 mL) after induction of anaesthesia
Outcomes	PONV
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen)

CTRI/2017/08/009295

Methods	Randomized controlled trial
Participants	Patients scheduled for laparoscopic cholecystectomy
Interventions	Palonosetron (0.075 mg) 3 minutes before induction of anaesthesia or ondansetron (8 mg) 3 minutes before induction of anaesthesia
Outcomes	PONV, side effects
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen, age)

Dag 2020

Methods	Randomized controlled trial
Participants	Female patients between 19 and 70 years of age who were admitted for laparoscopic abdominal hysterectomy
Interventions	Placebo, haloperidol 2 mg, haloperidol 1 mg, haloperidol, haloperidol 0.25 mg

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Dag 2020 *(Continued)*

Outcomes	Heart rate, systolic arterial pressure, diastolic arterial pressure, level of sedation, visual analog scale values, antiemetic need, patient satisfaction, side effects
Notes	Study identified in search update; data will be included in next update of the review

Danner 2001

Methods	Randomized controlled trial
Participants	Patients undergoing thyroid surgery, ASA I to III
Interventions	Dolasetron 50 mg given orally 45 minutes before induction or dolasetron 12.5 mg given intravenously during induction or droperidol 1.25 mg given intravenously during induction or placebo
Outcomes	PONV (complete response, total response)
Notes	Mail sent on 4th of April 2018 and again on July 31st 2018; reason for request was missing information about mean age or range; no response received

DebanSingh 2009

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy, 18 to 65 years of age, ASA I and II
Interventions	Dexamethasone (8 mg) with granisetron (40 µg/kg) or granisetron (40 µg/kg) alone 1 minute before induction
Outcomes	PONV
Notes	No full text available

de Morais 2018

Methods	Randomized controlled trial
Participants	Patients scheduled for laparoscopic procedures to treat abdominal or pelvic cancer, 18 to 70 years of age, ASA status I or II, Apfel score of 3 or 4
Interventions	Oral starch (control group) or 80 mg oral aprepitant (treatment group) 1 hour before induction
Outcomes	PONV, adverse effects
Notes	Study identified after the first search; data will be included in next update of the review

Doenicke 2004

Methods	Randomized controlled trial

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Doenicke 2004 *(Continued)*

Participants	Patients undergoing surgery from different disciplines (general surgery, orthopaedic surgery, and urology)
Interventions	5 mg/kg cimetidine i.v. + 0.1 mg/kg dimetindene i.v. (20 minutes before induction of anaesthesia), 1.25 mg/kg ranitidine i.v. + 0.1 mg/kg dimetindene i.v. (20 minutes before induction of anaesthesia), 300 mg ranitidine p.o. + 0.1 mg/kg dimetindene i.v. (1 to 2 hours before induction of anaesthesia), 20 mL saline solution i.v. (20 minutes before induction of anaesthesia)
Outcomes	Nausea, vomiting
Notes	Study identified in search update; data will be included in next update of the review

Dundee 1966

Methods	Randomized controlled trial
Participants	Female patients undergoing minor gynaecological operation
Interventions	Cyclizine 50 mg IM or trimethobenzamide 200 mg IM as premedication before anaesthesia
Outcomes	PONV, drowsiness, apprehension, restlessness or excitement, dizziness, pain at injection site, tachycardia, hypotension
Notes	Missing information about range of age; no contact details available

Dundee 1974

Methods	Randomized controlled trial
Participants	Female patients undergoing minor gynaecological operation
Interventions	Metoclopramide 10 mg IM or metoclopramide 20 mg IM or placebo IM as premedication
Outcomes	PONV, drowsiness, apprehension, restlessness or excitement, dizziness
Notes	Missing information about range of age; no contact details available

Dundee 1975

Methods	Randomized controlled trial
Participants	Female patients undergoing minor gynaecological surgery
Interventions	Cyclizine 50 mg IM or perphenazine 2.5 mg IM or perphenazine 5 mg IM about 90 minutes before operating time
Outcomes	PONV, apprehension, restlessness
Notes	Missing information about range of age; no contact details available

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Eryilmaz 2008

Methods	Randomized controlled trial
Participants	Patients undergoing aesthetic surgery
Interventions	Ondansetron or metoclopramide as single drug prophylaxis in the postoperative recovery room
Outcomes	PONV
Notes	Mail sent on 10th of July 2018; reasons for request were missing information about randomisation and point of administration of antiemetics; no response received

EUCTR2004-004280-30-SE

Methods	Randomized controlled trial
Participants	Patients scheduled for inguinal hernia repair in Ludvika Hospital, 18 to 70 years of age
Interventions	Betamethasone or placebo
Outcomes	Pain
Notes	Study status (not yet recruiting), first posted (2004), missing information (anaesthesia regimen)

EUCTR2005-005928-13-IS

Methods	Randomized controlled trial
Participants	Patients scheduled to undergo gynaecological laparoscopic surgery at Landspitali University Hospital, female, older than 18 years of age
Interventions	Scopalamine or placebo
Outcomes	PONV, pain
Notes	Study status (recruiting), first posted (2006), missing information (anaesthesia regimen, comparator)

EUCTR2006-001761-42-LT

Methods	Randomized controlled trial
Participants	Patients scheduled to undergo open abdominal surgery or laparoscopically assisted vaginal hysterectomy requiring overnight hospital stay (24-hour hospital stay after surgery); general anaesthesia, including induction agents, narcotics, neuromuscular blocking agents, and maintenance with nitrous oxide (50% to 70%) with volatile anaesthetic; postoperative opioids by IM or IV route or by IV patient-controlled analgesia, older than 18 years of age
Interventions	Aprepitant (40 mg) or ondansetron (4 mg)

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EUCTR2006-001761-42-LT *(Continued)*

Outcomes	No vomiting, no nausea, complete response, side effects
Notes	Study status (not yet recruiting), first posted (2006), missing information (time point of administration)

EUCTR2010-019899-77-DK

Methods	Randomized controlled trial
Participants	Patients undergoing elective laparoscopic groin hernia repair, unilateral, ASA I and II, 18 to 85 years of age, male
Interventions	Dexamethasone (8 mg) or placebo
Outcomes	Pain, fatigue, PONV, nausea, vomiting
Notes	Study status (not yet recruiting), first posted (2010), missing information (anaesthesia regimen, time point of administration)

EUCTR2015-003956-32-SE

Methods	Randomized controlled trial
Participants	Patients having ambulatory surgery, older than 18 years of age, no pregnancy, ASA I and II
Interventions	Palonosetron or placebo
Outcomes	PONV, complete response, adverse events
Notes	Study status (recruiting), first posted (2016), missing information (anaesthesia regimen)

Gnanasekar 2018

Methods	Randomized controlled trial
Participants	Patients undergoing lower abdominal surgery in multiple specialties
Interventions	8 mg dexamethasone or 2 mL saline
Outcomes	Pain scores, morphine consumption, occurrence of nausea and vomiting
Notes	Study identified in search update; data will be included in next update of the review

Goutarel 1977

Methods	Randomized controlled trial
Participants	Patients undergoing general anaesthesia

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Goutarel 1977 *(Continued)*

Interventions	Metoclopramide or placebo
Outcomes	Postoperative vomiting
Notes	No full text available

Gu 1998

Methods	Randomized controlled trial
Participants	NA
Interventions	Droperidol injected different ways
Outcomes	PONV
Notes	No full text available

Gulhas 2003

Methods	Randomized controlled trial
Participants	Patients undergoing middle ear surgery
Interventions	Orally administered ginger (1 gr with 30 mL water) or ondansetron (8 mg with 30 mL water) tablet or placebo (only 30 mL water) 1 hour before surgery
Outcomes	PONV
Notes	No full text available

Gupta 2020

Methods	Randomized controlled trial
Participants	Patients undergoing upper abdominal surgery
Interventions	4 mg ondansetron or 0.075 mg palonosteron i.v. at end of surgery
Outcomes	Nausea, vomiting, need for rescue antiemetic
Notes	Study identified in search update; data will be included in next update of the review

Handley 1967

Methods	Randomized controlled trial

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Handley 1967 *(Continued)*

Participants	Female patients undergoing cervical dilatation or dilatation and curettage, younger than 60 years of age
Interventions	Metoclopramide 10 mg IM or perphenazine 5 mg IM or normal saline IM at end of surgery
Outcomes	PONV
Notes	Missing information about range of age; no contact details available

Heidari 2018

Methods	Randomized controlled trial
Participants	Adult patients undergoing laparoscopic cholecystectomy
Interventions	Dexamethasone (0.15 mg/kg), metoclopramide (10 mg), and placebo
Outcomes	Pain, nausea, vomiting, amount of anti-nausea drug administered
Notes	Study identified in search update; needs translation (Persian)

Hossain 2019

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy
Interventions	4 mg ondansetron, 0.075 mg palonosteron, or 2 mg granisetron i.v. before induction of anaesthesia
Outcomes	Nausea, vomiting
Notes	Study identified in search update; data will be included in next update of the review

Hussain 2011

Methods	Randomized controlled trial
Participants	Female patients undergoing laparoscopic cholecystectomy, 35 to 70 years of age, ASA I or II
Interventions	Ondansetron 4 mg IV, metoclopramide 10 mg IV, or saline 2 minutes before induction
Outcomes	Complete response, nausea, vomiting
Notes	No full text available

Hyman 2020

Methods	Randomized controlled trial

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Hyman 2020 *(Continued)*

Participants	Adult female patients ≤ 50 years of age, undergoing ambulatory gynaecological or plastic surgery
Interventions	Ondansetron (4 mg) plus dexamethasone (8 mg) with the addition of olanzapine relative to placebo
Outcomes	Nausea, vomiting, side effects
Notes	Study identified in search update; data will be included in next update of the review

Iannuzzi 1994

Methods	Randomized controlled trial
Participants	NA
Interventions	Ondansetron 4 mg or no treatment 5 to 10 minutes before induction
Outcomes	PONV
Notes	Missing information about study design; no contact details available

Ibrahim 1999

Methods	Randomized controlled trial
Participants	Patients undergoing middle ear surgery
Interventions	Ondansetron or placebo
Outcomes	PONV
Notes	No full text available

Imam 2004

Methods	Randomized controlled trial
Participants	Patients undergoing elective caesarean section under general anaesthesia
Interventions	IV ondansetron 4 mg with dexamethasone 8 mg or ondansetron 4 mg alone or placebo at induction
Outcomes	PONV
Notes	No full text available

IRCT138902253931N1

Methods	Randomized controlled trial

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IRCT138902253931N1 *(Continued)*

Participants	Patients undergoing laparoscopic cholecystectomy
Interventions	Dexamethasone (8 mg) 90 minutes before surgery or normal saline (2 cc) 90 minutes before surgery
Outcomes	PONV
Notes	Study status (completed), first posted (2010), missing information (anaesthesia regimen)

IRCT201008254505N1

Methods	Randomized controlled trial
Participants	Patients having elective inguinal hernia surgery, weight < 100 kg, 20 to 40 years of age, no severe or chronic illness, ASA I and II
Interventions	Metoclopramide (10 mg) before extubation and 6 hours after operation or dexamethasone (8 mg) before extubation and 6 hours after operation
Outcomes	Nausea, vomiting
Notes	Study status (completed), first posted (2010), missing information (anaesthesia regimen, outcomes)

IRCT201009084715N1

Methods	Randomized controlled trial
Participants	Patients undergoing elective cholecystectomy with laparoscopic method, 16 to 60 years of age
Interventions	Ondansetron (4 mg) and dexamethasone (8 mg) 5 minutes before end of surgery or metoclopramide (10 mg) and dexamethasone (8 mg) 5 minutes before end of surgery
Outcomes	Nausea, vomiting
Notes	Study status (completed), first posted (2010), missing information (anaesthesia regimen, age)

IRCT201012133181N3

Methods	Randomized controlled trial
Participants	Patients undergoing stapedectomy surgery who were referred to ENT clinic of Amiralam Hospital, ASA I and II, 15 to 62 years of age
Interventions	Dexamethasone (16 mg) a half hour before surgery or normal saline (4 mL) a half hour before surgery
Outcomes	PONV, vertigo
Notes	Study status (completed), first posted (2012), missing information (anaesthesia regimen, age)

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IRCT201105056392N1

Methods	Randomized controlled trial
Participants	Participants referred for elective laparoscopic cholecystectomy, 20 to 65 years or older
Interventions	Ondansetron (4 mg) immediately before receiving general anaesthesia or dexamethasone (8 mg) immediately before receiving general anaesthesia or ondansetron (4 mg) and dexamethasone (8 mg) immediately before receiving general anaesthesia
Outcomes	Nausea, vomiting
Notes	Study status (completed), first posted (2011), missing information (anaesthesia regimen)

IRCT201108067093N2

Methods	Randomized controlled trial
Participants	Patients having orthopaedic surgery under balanced anaesthesia, ASA I and II, 16 to 65 years of age, BMI < 30
Interventions	Ondansetron (4 mg) or metoclopramide (4 mg) or dexamethasone (4 mg) or ondansetron (4 mg) and metoclopramide (4 mg) or ondansetron (4 mg) and dexamethasone (4 mg) or metoclopramide (4 mg) and dexamethasone (4 mg) or placebo
Outcomes	PONV
Notes	Study status (completed), first posted (2012), missing information (anaesthesia regimen, age, time point of administration)

IRCT201108147324N1

Methods	Randomized controlled trial
Participants	Patients who are candidates for maxillofacial surgery, 18 to 50 years of age, undergoing IMF
Interventions	Ondansetron (0.15 mg/kg) 30 minutes before surgery or ondansetron (0.15 mg/kg) 30 minutes before end of surgery or metoclopramide (0.5 mg/kg) 30 minutes before surgery or metoclopramide (0.5 mg/kg) 30 minutes before end of surgery or placebo
Outcomes	Nausea, vomiting, vertigo
Notes	Study status (completed), first posted (2012), missing information (anaesthesia regimen)

IRCT201112088329N1

Methods	Randomized controlled trial
Participants	Patients undergoing general anaesthesia for elective laparoscopic cholecystectomy in Mostafa Khomeini Hospital, 18 to 60 years of age

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IRCT201112088329N1 *(Continued)*

Interventions	Dexamethasone (8 mg) or metoclopramide (10 mg) or normal saline (0.9%)
Outcomes	Vomiting, nausea
Notes	Study status (completed), first posted (2012), missing information (anaesthesia regimen, time point of administration)

IRCT201207223915N7

Methods	Randomized controlled trial
Participants	Patients are candidates for tympanoplasty, ASA I and II, 15 to 60 years of age
Interventions	Dexamethasone (8 mg) after intubation and granisetron (0.1 mg) 15 minutes before extubation or dexamethasone (8 mg) after intubation and granisetron (0.3 mg) 15 minutes before extubation or dexamethasone (8 mg) and ondansetron (4 mg) 15 minutes before extubation
Outcomes	PONV
Notes	Study status (completed), first posted (2012), missing information (anaesthesia regimen, age)

IRCT201208075225N2

Methods	Randomized controlled trial
Participants	Patients scheduled for tympanomastoidectomy under general anaesthesia, ASA I and II, 20 to 60 years of age
Interventions	Dexamethasone (8 mg) 1 hour before surgery and placebo 1 hour before surgery
Outcomes	PONV
Notes	Study status (completed), first posted (2012), missing information (anaesthesia regimen)

IRCT2014012511700N3

Methods	Randomized controlled trial
Participants	Patients who have an outpatient gynaecological diagnostic laparoscopy, 20 to 50 years of age, female, ASA I and II
Interventions	Dexamethasone (8 mg) before induction of anaesthesia or dexamethasone (8 mg) and ondansetron (4 mg) before induction of anaesthesia or ondansetron (4 mg) before induction of anaesthesia
Outcomes	PONV
Notes	Study status (completed), first posted (2014), missing information (anaesthesia regimen)

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IRCT2015042715281N3

Methods	Randomized controlled trial
Participants	Patients who were candidates for orthopaedic surgery, men, 16 to 65 years of age, ASA I and II
Interventions	Metoclopramide (10 mg) or granisetron (3 mg) or dexamethasone (8 mg)
Outcomes	PONV
Notes	Study status (completed), first posted (2015), missing information (anaesthesia regimen, age, time point of administration)

IRCT2016030126853N1

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy
Interventions	Dexamethasone (8 mg) 30 minutes before operation or no drugs
Outcomes	Pain, nausea
Notes	Study status (completed), first posted (2016), missing information (anaesthesia regimen, age)

IRCT2016120831302N1

Methods	Randomized controlled trial
Participants	Patients having laparoscopic cholecystectomy, female, 18 to 50 years of age, ASA I and II, 2 or more criteria of Apfel
Interventions	Ondansetron (4 mg) after anaesthetic induction and placed 1 hour before operation or aprepitant (80 mg) 1 hour before operation and placebo after anaesthetic induction or aprepitant (80 mg) 1 hour before operation and ondansetron (4 mg) after anaesthetic induction
Outcomes	PONV
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen)&&

IRCT2016122019359N8

Methods	Randomized controlled trial
Participants	Patients 15 to 60 years of age, ASA I and II
Interventions	Dexamethasone (0.1 mg/kg) or no prophylactic interventions
Outcomes	Nausea, vomiting

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IRCT2016122019359N8 *(Continued)*

Notes	Study status (completed), first posted (2016), missing information (anaesthesia regimen, age, time point of administration)

IRCT2017010923559N7

Methods	Randomized controlled trial
Participants	Patients with biliary colic pain or uncomplicated gallstone undergoing laparoscopic cholecystectomy, 18 to 65 years of age
Interventions	Intravenous dexamethasone (8 mg) with ondansetron or intravenous dexamethasone (8 mg) with Plasil (10 mg) during surgery
Outcomes	Nausea, vomiting, shivering within 24 hours postoperatively
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen)

IRCT2017011920588N5

Methods	Randomized controlled trial
Participants	Patients with strabismus surgery under general anaesthesia, ASA I and II, 18 to 65 years of age
Interventions	Ondansetron (0.05 mg/kg) or placebo (NaCl 0.9%) or metoclopramide (0.15 mg/kg)
Outcomes	Nausea, vomiting, side effects
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen, time point of administration)

IRCT2017020725732N13

Methods	Randomized controlled trial
Participants	Patients scheduled for laparoscopic cholecystectomy, 18 to 80 years of age, ASA I and II
Interventions	Dexamethasone (16 mg) before first surgery incision or ondansetron (4 mg) before first surgery incision or dexamethasone (8 mg) and ondansetron (4 mg) before first surgery incision
Outcomes	PONV
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen)

IRCT2017031433069N1

Methods	Randomized controlled trial

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IRCT2017031433069N1 *(Continued)*

Participants	Patients having elective gynaecological surgery under general anaesthesia, 18 to 45 years of age, ASA I and II, female
Interventions	Metcolopramide (10 mg) or ondansetron (4 mg)
Outcomes	Pain
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen, outcomes, randomization)

Isazadehfar 2016

Methods	Randomized controlled trial
Participants	Participants 6 to 81 years of age (majority over 18 years), ASA I and II, undergoing laparoscopic cholecystectomy
Interventions	Ondansetron (4 mg IV before induction of anaesthesia), dexamethasone (8 mg IV before induction of anaesthesia), placebo
Outcomes	Vomiting, nausea
Notes	Another publication by the same author (Isazadehfar 2017) reported identical baseline data for patients in the ondansetron group. Request to authors was sent but remains unanswered

Isazadehfar 2017

Methods	Randomized controlled trial
Participants	Participants 15 to 80 years of age (most over 18 years), ASA I or II, scheduled for elective laparoscopic cholecystectomy surgery
Interventions	Ondansetron (4 mg IV before anaesthesia induction), metoclopramide (10 mg IV before anaesthesia induction)
Outcomes	Vomiting, nausea
Notes	Another publication by the same author (Isazadehfar 2016) reported identical baseline data for patients in the ondansetron group. Request to authors was sent but remains unanswered

ISRCTN07711014

Methods	Randomized controlled trial
Participants	Patients undergoing day surgery with general anaesthesia
Interventions	Cyclizine (50 mg) at beginning of anaesthetic induction, ondansetron (4 mg) at beginning of anaesthetic induction, granisetron (1 mg) at beginning of anaesthetic induction, placebo
Outcomes	PONV

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ISRCTN07711014 *(Continued)*

Notes	Study status (completed), first posted (2005), missing information (anaesthesia regimen, age)

ISRCTN18556628

Methods	Randomized controlled trial
Participants	Patients undergoing daycase gynaecological laparoscopy, female, older than 18 years of age
Interventions	Cyclizine (50 mg) or dexamethasone (8 mg) and cyclizine (50 mg) or placebo (saline 0.9%)
Outcomes	Vomiting, retching, nausea, pain
Notes	Study status (completed), first posted (2005), missing information (anaesthesia regimen, outcomes, time point of administration)

ISRCTN21871435

Methods	Randomized controlled trial
Participants	Patients undergoing abdominal hysterectomy, female, ASA I to III
Interventions	NA
Outcomes	NA
Notes	Study status (completed), first posted (2003), missing information (anaesthesia regimen, age)

Janknegt 1999

Methods	Randomized controlled trial
Participants	NA
Interventions	Droperidol 1.25 mg IV or granisetron 1 mg IV or granisetron 1 mg IV with dexamethasone 5 mg IV
Outcomes	PONV
Notes	Missing information about anaesthesia regimen; no contact details available

Jensen 2020

Methods	Randomized controlled trial
Participants	Patients undergoing abdominal wall reconstruction
Interventions	125 mg methylprednisolone or placebo i.v. at induction of anaesthesia
Outcomes	Pain, nausea, fatigue

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Jensen 2020 *(Continued)*

Notes	Study identified in search update; data will be included in next update of the review

Jeyabalan 2019

Methods	Randomized controlled trial
Participants	Patients undergoing breast or thyroid surgery
Interventions	Ondansetron or aprepitant
Outcomes	PONV, patient satisfaction
Notes	Study identified in search update; data will be included in next update of the review&&

JPRN-UMIN000004167

Methods	Randomized controlled trial
Participants	Patients for surgical correction of bite, 18 to 40 years of age
Interventions	Aprepitant (125 mg) administered preoperatively or metoclopramide (10 mg) just before completion of surgery
Outcomes	Consumption of postoperative antiemetic agent
Notes	Study status (terminated), first posted (2010), missing information (anaesthesia regimen)

JPRN-UMIN000012365

Methods	Randomized controlled trial
Participants	Patients with breast cancer, 20 to 70 years of age, female
Interventions	Dexamethasone or saline
Outcomes	PONV
Notes	Study status (not yet recruiting), first posted (2013), missing information (anaesthesia regimen, time point of administration)

JPRN-UMIN000018532

Methods	Randomized controlled trial
Participants	Patients who received oral surgery, 20 to 80 years of age, ASA I to III
Interventions	Fosaprepitant (150 mg) before induction of anaesthesia or ondansetron (4 mg) before induction of anaesthesia

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JPRN-UMIN000018532 *(Continued)*

Outcomes	PONV
Notes	Study status (completed), first posted (2015), missing information (anaesthesia regimen)

JPRN-UMIN000024653

Methods	Randomized controlled trial
Participants	Patients who are surgery patients receiving antiemetics
Interventions	NA
Outcomes	PONV
Notes	Study status (completed), first posted (2016), missing information (no information provided)

Kamali 2018

Methods	Randomized controlled trial
Participants	Patients undergoing abdominal hysterectomy
Interventions	4 mg ondansetron or 2 mg haloperidol i.v.
Outcomes	Vomiting
Notes	Study identified in search update; data will be included in next update of the review

Karacinar 2009

Methods	Randomized controlled trial
Participants	Patients undergoing elective craniotomy
Interventions	Dexamethasone (4 mg, 8 mg, 16 mg) or placebo i.v. after intubation
Outcomes	Nausea, vomiting, blood glucose
Notes	Study identified in search update; needs translation (Turkish)

Kashmiri 2006

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy, ASA I and II
Interventions	Dexamethasone 8 mg or normal saline IV just before induction

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Kashmiri 2006 *(Continued)*

Outcomes	PONV
Notes	No full text available

KCT0000122

Methods	Randomized controlled trial
Participants	Patients undergoing craniotomy, older than 21 years of age
Interventions	Palonosetron (0.075 mg) immediately (no more than 5 minutes) before end of surgery or ondansetron (8 mg) immediately (no more than 5 minutes) before end of surgery or ramosetron (0.3 mg) immediately (no more than 5 minutes) before end of surgery
Outcomes	PONV, nausea
Notes	Study status (recruiting), first posted (2011), missing information (anaesthesia regimen)

KCT0000336

Methods	Randomized controlled trial
Participants	Patients undergoing elective pelviscopic gynaecological surgery or breast operation, 19 to 65 years of age, ASA I and II, female
Interventions	Palonosetron (0.075 mg) before end of surgery or ondansetron (8 mg) before end of surgery
Outcomes	Nausea, retching, vomiting, complete response, pain
Notes	Study status (recruiting), first posted (2012), missing information (anaesthesia regimen)

KCT0000487

Methods	Randomized controlled trial
Participants	Patients undergoing elective abdominal surgery, 20 to 70 years of age, ASA I and II
Interventions	Palonosetron (0.075 mg) at end of surgery or placebo
Outcomes	PONV, pain
Notes	Study status (recruiting), first posted (2012), missing information (anaesthesia regimen)

KCT0000809

Methods	Randomized controlled trial

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KCT0000809 *(Continued)*

Participants	Patients scheduled for elective operation under general anaesthesia, female, 20 to 70 years of age, PCA
Interventions	Ondansetron (8 mg) 30 minutes before end of surgery or palonosetron (0.075 mg) 30 minutes before end of surgery
Outcomes	PONV, side effects, nausea
Notes	Study status (completed), first posted (2013), missing information (anaesthesia regimen)

KCT0000899

Methods	Randomized controlled trial
Participants	Patients scheduled to undergo thyroidectomy under general anaesthesia in Chung-Ang University Hospital, 2 or more risk factors for PONV, 20 to 65 years of age, female
Interventions	Palonosetron (0.075 mg) 10 minutes before induction of general anaesthesia or dexamethasone (5 mg) or palonosetron (0.075 mg) and dexamethasone (5 mg)
Outcomes	PONV, pain
Notes	Study status (not yet recruiting), first posted (2013), missing information (anaesthesia regimen)

KCT0001740

Methods	Randomized controlled trial
Participants	Patients with knee osteoarthritis who were scheduled to undergo total knee arthroplasty, 55 to 85 years of age
Interventions	Dexamethasone (10 mg) 1 hour before total knee arthroplasty or no steroid injection before total knee arthroplasty
Outcomes	Pain, nausea
Notes	Study status (recruiting), first posted (2015), missing information (anaesthesia regimen, outcomes)

KCT0002433

Methods	Randomized controlled trial
Participants	Patients undergoing elective surgery under general anaesthesia, PCA, 20 to 70 years of age, female
Interventions	Palonosetron (0.075 mg) after induction of anaesthesia or palonosetron (0.075 mg) after induction of anaesthesia and aprepitant (80 mg) 2 to 3 hours before the operation
Outcomes	PONV, adverse effects
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen)

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Khan 2011

Methods	Randomized controlled trial
Participants	Female patients undergoing laparoscopic cholecystectomy, ASA I and II
Interventions	Ondansetron 2 mg IV before induction or metoclopramide 10 mg IV before induction
Outcomes	PONV
Notes	Mail sent on 10th of July 2018; reason for request was missing information about whether anaesthesia regimen was standardized for all patients and way of maintaining anaesthesia; no response received

Kim 2002

Methods	Randomized controlled trial
Participants	Patients undergoing elective operation under general anaesthesia, 15 to 65 years of age, ASA I and II
Interventions	Metoclopramide 5 mg IV or metoclopramide 10 mg IV or saline IV
Outcomes	Pain
Notes	Mail sent on 21st of March 2018; reason for request was missing information about maintenance of anaesthesia; mail could not be delivered

Kim 2003

Methods	Randomized controlled trial
Participants	Female patients undergoing pelviscopic gynaecological procedure
Interventions	Ondansetron 1 mg or ondansetron 4 mg or ondansetron 8 mg or saline at end of pelviscopic operation
Outcomes	PONV
Notes	No full text available

Kimya 1996

Methods	Randomized controlled trial
Participants	Patients undergoing gynaecological laparotomy and laparoscopy
Interventions	Ondansetron 8 mg IV or no treatment immediately before induction
Outcomes	PONV, adverse effects

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Kimya 1996 *(Continued)*

Notes	Missing information about study design; no contact details available

Kleif 2018

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic surgery for suspected appendicitis
Interventions	125 mg methylprednisolone plus 4 mg ondansetron or placebo plus 4 mg ondansetron i.v. before surgery
Outcomes	Pain, quality of recovery, side effects
Notes	Study identified in search update; data will be included in next update of the review

Klenke 2018

Methods	Randomized controlled trial
Participants	Patients undergoing general anaesthesia for gynaecological; ear, nose, and throat; or endocrine surgery (thyroid)
Interventions	Acustimulation/dexamethasone, acustimulation/vehicle, sham acustimulation/dexamethasone, sham acustimulation/vehicle
Outcomes	PONV
Notes	Study identified in search update; data will be included in next update of the review

Koff 1968

Methods	Randomized controlled trial
Participants	NA
Interventions	Metoclopramide
Outcomes	Post-anaesthetic vomiting and nausea
Notes	No full text available

Kranke 2018

Methods	Randomized controlled trial
Participants	Patients undergoing elective surgery (open or laparoscopic) under general anaesthesia, expected to last at least 1 hour, 18 years of age or older, at least 3 Apfel risk factors

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Kranke 2018 *(Continued)*

Interventions	Intravenous amisulpride (5 mg) or matching placebo at induction of general anaesthesia, in addition to 1 standard non-dopaminergic antiemetic
Outcomes	PONV, adverse events
Notes	Study identified after first search; data will be included in next update of the review

Kumar 2018a

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy
Interventions	8 mg ondansetron or 0.075 mg palonosetron
Outcomes	Nausea, retching, vomiting, rescue antiemetic, side effect profile, patient satisfaction scores
Notes	Study identified in search update; data will be included in next update of the review

Kwak 2019

Methods	Randomized controlled trial
Participants	Patients undergoing breast surgery
Interventions	Dexmedetomidine 0.5 µg/kg or combination of dexmedetomidine 0.5 µg/kg and dexamethasone 5 mg at 30 minutes before end of surgery
Outcomes	PONV
Notes	Study identified in search update; data will be included in next update of the review

LabradorGoyeneche 1998

Methods	Randomized controlled trial
Participants	Patients undergoing gynaecological surgery
Interventions	After induction tropisetron 2 mg IV unique dose or metoclopramide 10 mg IV each 8 hours during 24 hours
Outcomes	PONV, adverse episodes
Notes	No full text available

Laveneziana 1978

Methods	Randomized controlled trial

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Laveneziana 1978 *(Continued)*

Participants	Female patients undergoing total laparoscopic hysterectomy, between 41 and 68 years of age
Interventions	Haloperidol 2 mg IM or sulpiride 100 mg IM 1 hour before surgery
Outcomes	Vomiting
Notes	Missing information about study design; no contact details available

Lazar 1984

Methods	Randomized controlled trial
Participants	Patients undergoing stapes replacement operation, 21 to 69 years of age
Interventions	Transdermal scopolamine or identical placebo patch on the evening before the operation
Outcomes	PONV, side effects (dryness of mouth urine retention, drowsiness, blurred vision)
Notes	Missing information about anaesthesia regimen; no contact details available

Lee 2020a

Methods	Randomized controlled trial
Participants	Patients undergoing retromastoid craniectomy with microvascular decompression
Interventions	TDS patch or sham patch
Outcomes	Nausea, vomiting, use of antiemetics
Notes	Study identified in search update; data will be included in next update of the review

Li 1999

Methods	Randomized controlled trial
Participants	Patients undergoing cholecystectomy under abdominoscope
Interventions	Ondansetron 8 mg IV or saline
Outcomes	PONV
Notes	Missing information about range of age; no contact details available

Liberman 2000

Methods	Randomized controlled trial

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Liberman 2000 *(Continued)*

Participants	Patients undergoing laparoscopic cholecystectomy, 15 to 65 years of age
Interventions	Ondansetron 4 mg IV or placebo at induction of anaesthesia
Outcomes	PONV
Notes	Missing information about standard deviation of age; no contact details available

Lind 1970c

Methods	Randomized controlled trial
Participants	Patients undergoing vaginal surgery, gynaecological laparotomy, or varices surgery, 20 to 69 years of age
Interventions	Scopolamine with perphenazine 5 mg IM or scopolamine with thioproperazine IM 0.5 mg or 1 mg or 2 mg dose right after end of anaesthesia
Outcomes	PONV, requirement for postoperative analgesics, sedation, blood pressure
Notes	Missing information about study design and dose of scopolamine; no contact details available

Liu 2019

Methods	Randomized controlled trial
Participants	Adult patients undergoing total knee arthroplasty
Interventions	Dexamethasone or saline
Outcomes	Pain, vomiting, use of antiemetics, side effects
Notes	Study identified in search update; needs translation (Chinese)

Makhdoom 2009

Methods	Randomized controlled trial
Participants	Female patients undergoing middle ear surgery, mean age 32.6 years, ASA I and II
Interventions	Dexamethasone 10 mg IV or midazolam 0.075 mg/kg or a combination of both or normal saline IV before induction
Outcomes	PONV, sedation, pain
Notes	Mail sent on 19th of March 2018; reason for request was missing information about age range for included patients; mail could not be delivered

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Malak 2017

Methods	Randomized controlled trial
Participants	Patients undergoing elective laparoscopic cholecystectomy
Interventions	Ondansetron (4 mg), cyclizine (50 mg), or prochlorperazine (10 mg)
Outcomes	PONV, need for rescue antiemetics, adverse effects (e.g. headache, dizziness, sedation)
Notes	Study identified in search update; data will be included in next update of the review

McKenzie 1981

Methods	Randomized controlled trial
Participants	Female patients undergoing first trimester abortion, ASA I and II
Interventions	Droperidol 2.5 mg IM or hydroxyzine 100 mg IM or saline IM immediately after induction of anaesthesia
Outcomes	PONV, drowsiness
Notes	Missing information about range of age; no contact details available

McKenzie 1996

Methods	Randomized controlled trial
Participants	Female patients undergoing laparoscopic tubal banding, ASA I and II
Interventions	Droperidol 1.25 mg IV with ondansetron 4 mg IV or droperidol 1.25 mg IV with saline within 15 minutes after induction of anaesthesia
Outcomes	PONV, drowsiness, pain, adverse events
Notes	Missing information about range of age; no contact details available

McNeill 1995

Methods	Randomized controlled trial
Participants	Patients undergoing operation for spinal stenosis or herniated intervertebral disc
Interventions	Methylprednisolone 40 mg epidurally or placebo epidurally or morphine 5 mg epidurally or methylprednisolone 40 mg with morphine 5 mg epidurally at end of operation
Outcomes	Pain, nausea, itching, apnoea, urinary retention
Notes	Missing information about anaesthesia regimen and range of age; no contact details available

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Michaloudis 1993

Methods	Randomized controlled trial
Participants	Female patients undergoing laparoscopy, ASA I and II
Interventions	Droperidol 0.5 mg IV with metoclopramide 5 mg IV and hyoscine 0.1 mg IV or droperidol 1.25 mg IV and saline IV 10 minutes before end of surgery
Outcomes	PONV
Notes	Missing information about range of age

Mirhosseini 2011

Methods	Randomized controlled trial
Participants	Patients with severe left ventricle dysfunction undergoing coronary artery bypass graft surgery
Interventions	Methyprednisolone 5 mg/kg IV or normal saline after induction of anaesthesia
Outcomes	Postoperative atrial fibrillation, bleeding, infection, vomiting, respiratory and renal dysfunction, mortality, ICU and hospital stay
Notes	Mail sent on 21st of March 2018 and again on 31st of July 2018; reason for request was missing information about time point for assessment of vomiting and infection; no response received

Modir 2019a

Methods	Randomized controlled trial
Participants	Patients undergoing thympanomastoidectomy
Interventions	Dexamethasone (0.1 mg/kg) or metoclopramide (0.15 mg/kg) i.v.
Outcomes	PONV, vomiting
Notes	Study identified in search update; data will be included in next update of the review

Moradi 2019

Methods	Randomized controlled trial
Participants	Adult patients undergoing strabismus surgery
Interventions	0.1 mg/kg metoclopramide or 0.05 mg/kg ondansetron
Outcomes	Nausea, vomiting, drug complications, satisfaction
Notes	Study identified in search update; needs translation (Persian)

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Moradi Farsani 2017

Methods	Randomized controlled trial
Participants	Adult patients undergoing cataract surgery
Interventions	0.1 mg/kg metoclopramide or placebo
Outcomes	Pain, vomiting, use of antiemetics
Notes	Study identified in search update; needs translation (Persian)

Naghibi 2018

Methods	Randomized controlled trial
Participants	Adult patients undergoing cataract surgery
Interventions	Dexamethasone, ondansetron, or saline
Outcomes	Itching, nausea and vomiting
Notes	Study identified in search update; needs translation (Persian)

NCT00231777

Methods	Randomized controlled trial
Participants	Patients ≥ 18 years of age and scheduled to undergo open abdominal surgery or vaginal hysterectomy requiring overnight hospital stay (24-hour hospital stay after end of surgery)
Interventions	Fosaprepitant 40 mg IV or ondansetron 4 mg before surgery
Outcomes	Clinical adverse experiences, laboratory adverse experiences, drug-related clinical adverse experiences, serious clinical adverse experiences, constipation, arrhythmia, headache
Notes	Study protocol with study results; missing information on whether general anaesthesia was standardized for all groups; Sponsor Merck

NCT00445055

Methods	Randomized controlled trial
Participants	Patients scheduled for thyroid surgery, female, older than 18 years of age, Apfel score ≥ 2, ASA I and II
Interventions	Droperidol (0.625 mg) 30 minutes before end of anaesthesia or droperidol (2.5 mg) 30 minutes before end of anaesthesia or saline 30 minutes before end of anaesthesia
Outcomes	No vomiting, nausea, adverse events

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NCT00445055 *(Continued)*

Notes	Study status (terminated), first posted (2007), missing information (anaesthesia regimen)

NCT00674713

Methods	Randomized controlled trial
Participants	Patients scheduled for elective laparoscopic cholecystectomy, 18 to 70 years of age, ASA I and II
Interventions	Ondansetron plus sham acupuncture or saline solution plus sham acupuncture
Outcomes	PONV
Notes	Study status (completed), first posted (2008), missing information (anaesthesia regimen)

NCT00702442

Methods	Randomized controlled trial
Participants	Patients scheduled for laparoscopic cholecystectomy, older than 18 years of age
Interventions	Saline solution 30 minutes before surgery or droperidol (0.625 mg) 30 minutes before laparoscopic cholecystectomy
Outcomes	Vomiting, nausea, adverse events
Notes	Study status (completed), first posted (2008), missing information (anaesthesia regimen)

NCT00738621

Methods	Randomized controlled trial
Participants	Female patients undergoing ambulatory breast surgery under general anaesthesia, 18 to 65 years of age, 2 risk factors associated with PONV, ASA status I to III
Interventions	Oral aprepitant (40 mg) within 3 hours before induction, dexamethasone (4 mg) after induction and ondansetron (4 mg) at cessation of anaesthesia or oral aprepitant (40 mg) within 3 hours before induction, dexamethasone (4 mg) after induction and placebo at cessation of anaesthesia
Outcomes	Vomiting
Notes	Study identified after first search; data will be included in next update of the review

NCT00835965

Methods	Randomized controlled trial
Participants	Patients with high risk of PONV (≥ 2 risk factors for PONV), older than 18 years of age, ASA I to III

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NCT00835965 *(Continued)*

Interventions	Aprepitant (40 mg PO 1 time at least 1 hour before induction of anaesthesia) and dexamethasone (5 mg iv following endotracheal intubation) or aprepitant (40 mg PO 1 time at least 1 hour before induction of anaesthesia) and placebo dexamethasone
Outcomes	Incidence of nausea and vomiting, need for rescue medication
Notes	Study status (unknown), first posted (2009), missing information (anaesthesia regimen)

NCT01013012

Methods	Randomized controlled trial
Participants	Patients having spine surgery, 18 to 65 years of age, female
Interventions	Ramosetron (6 mcg) and saline (1 mL) or ramosetron (6 mcg) and dexamethasone (4 mg)
Outcomes	PONV
Notes	Study status (completed), first posted (2009), missing information (anaesthesia regimen, time point of administration)

NCT01022528

Methods	Randomized controlled trial
Participants	Patients scheduled for elective total abdominal hysterectomy (with or without salpingo-oophorectomy or minor bladder repair) or myomectomy through a lower transverse or low midline incision under general anaesthesia, incidental appendectomy and/or abdominal lipectomy, 18 to 65 years of age, female, non-lactating
Interventions	Dexamethasone (0.1 mg/kg) 1.5 hours before induction of anaesthesia or dexamethasone (0.2 mg/kg) 1.5 hours before induction of anaesthesia or saline
Outcomes	Pain
Notes	Study status (completed), first posted (2009), missing information (anaesthesia regimen)

NCT01055236

Methods	Randomized controlled trial
Participants	Patients scheduled for elective transabdominal hysterectomy under combined spinal-general anaesthesia, 18 to 60 years of age, ASA I and II, BMI < 35
Interventions	Hydroxyzine (75 mg) at least half hour before operation or placebo
Outcomes	Pruritus, PONV
Notes	Study status (completed), first posted (2010), missing information (outcome)

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NCT01149616

Methods	Randomized controlled trial
Participants	Participant over 18 years of age undergoing outpatient knee surgery
Interventions	Dexamethasone 8 mg IV or placebo, time point of administration unclear
Outcomes	Pain, nausea
Notes	Study protocol with study results. No information on anaesthesia regimen or time point of dexamethasone administration provided. Study terminated (investigators changed jobs, no longer affiliated with institution)

NCT01159548

Methods	Randomized controlled trial
Participants	Patients undergoing ambulatory gynaecological laparoscopic procedures ≥ 30 minutes in duration, 18 to 60 years of age, ASA I to III, ≥ 2 risk factors
Interventions	Promethazine (6.25 mg) or promethazine (3 mg) or saline
Outcomes	Absence of emetic episode
Notes	Study status (terminated), first posted (2010), missing information (anaesthesia regimen)

NCT01402622

Methods	Randomized controlled trial
Participants	Patients undergoing robot-assisted laparoscopic radical prostatectomy, 50 to 70 years of age, male, ASA I and II
Interventions	Ramosetron (0.3 mg) at end of surgery (balanced anaesthesia) or ramosetron (0.3 mg) at end of surgery (TIVA) or no antiemetic prophylaxis (TIVA)
Outcomes	PONV
Notes	Study status (completed), first posted (2011), missing information (anaesthesia regimen)

NCT01427127

Methods	Randomized controlled trial
Participants	Patients scheduled for laparoscopic colorectal surgery, 20 to 70 years of age, ASA I or II
Interventions	Ramosetron (0.3 mg) at end of surgery and 24 hours after surgery or saline at end of surgery and 24 hours after surgery

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NCT01427127 *(Continued)*

Outcomes	PONV
Notes	Study status (unknown), first posted (2011), missing information (anaesthesia regimen, study design)

NCT01524731

Methods	Randomized controlled trial
Participants	Patients scheduled for non-oncological gynaecological laparotomy, 18 to 80 years of age, female
Interventions	Ondansetron (4 mg) before tracheal extubation and saline immediately after induction of anaesthesia or ondansetron (4 mg) before tracheal extubation and dexamethasone (4 mg) immediately after induction of anaesthesia or ondansetron (4 mg) before tracheal extubation and dexamethasone (8 mg) immediately after induction of anaesthesia
Outcomes	PONV, pain
Notes	Study status (completed), first posted (2012), missing information (anaesthesia regimen)

NCT01612702

Methods	Randomized controlled trial
Participants	Participants over 18 years of age, undergoing total knee arthroplasty
Interventions	Ramosetron (NA) + dexamethasone (10 mg IV, 1 hour before surgery) or placebo
Outcomes	PONV, pain, wound complications, any AE, serious adverse events
Notes	Study protocol with study results; anaesthesia regimen and details on ramosetron administration (dose/time point) unclear

NCT01637545

Methods	Randomized controlled trial
Participants	Patients considered as surgical candidates with facial bone fracture, age (child, adult, older adult)
Interventions	Ramosetron (0.3 mg) just before beginning of surgery or ramosetron (0.3 mg) after end of surgery or regular antiemetics if patient wants
Outcomes	PONV
Notes	Study status (terminated), first posted (2012), missing information (anaesthesia regimen, age)

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NCT01679093

Methods	Randomized controlled trial
Participants	Patients undergoing thyroidectomy without lymph node dissection, 18 to 70 years of age, ASA I to III, Apfel score equal to 2
Interventions	Ondansetron (4 mg) after induction of anaesthesia or droperidol (1.25 mg) after induction of anaesthesia or dexamethasone (4 mg) after induction of anaesthesia
Outcomes	Pain, PONV
Notes	Study status (completed), first posted (2012), missing information (anaesthesia regimen)

NCT01811251

Methods	Randomized controlled trial
Participants	Patients undergoing lumbar slipped disc surgery, 18 to 85 years of age, ASA I to III
Interventions	Dexamethasone (20 mg/5 mL) or placebo
Outcomes	Pain, PONV, side effects
Notes	Study status (completed), first posted (2013), missing information (anaesthesia regimen)

NCT02011659

Methods	Randomized controlled trial
Participants	Patients undergoing gynaecological laparoscopic surgery, 18 to 70 years of age, female, ASA I and II, non-smoker
Interventions	Ramosetron or placebo
Outcomes	PONV, adverse events
Notes	Study status (unknown), first posted (2013), missing information (anaesthesia regimen)

NCT02234466

Methods	Randomized controlled trial
Participants	Patients undergoing general anaesthesia for elective breast surgery, 18 to 80 years of age, ASA I to III
Interventions	Dexamethasone (two 4 mg tabs) 2 hours pre-induction and ondansetron (6 mg) at time of skin closure or gelatin pill and ondansetron (6 mg) at time of skin closure
Outcomes	PONV
Notes	Study status (unknown), first posted (2014), missing information (anaesthesia regimen)

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NCT02304250

Methods	Randomized controlled trial
Participants	Patients having elective total thyroidectomy or hemithyroidectomy with lymphadenectomy for thyroid cancer, 18 to 65 years of age
Interventions	Dexamethasone (5 mg) after general anaesthesia induction or saline (1 mL) after general anaesthesia induction
Outcomes	Pain, PONV, side effects
Notes	Study status (completed), first posted (2014), missing information (anaesthesia regimen)

NCT02416115

Methods	Randomized controlled trial
Participants	Patients scheduled for gynaecological surgery under general anaesthesia and postoperative analgesia with a PCA device, age (child, adult, older adult), female, ASA I and II
Interventions	Ramosetron (0.3 mg) 30 minutes before end of surgery or saline 30 minutes before surgery
Outcomes	PONV
Notes	Study status (completed), first posted (2015), missing information (anaesthesia regimen, age)

NCT02431286

Methods	Randomized controlled trial
Participants	Patients submitted to breast cancer surgery, non-smokers, female, 18 to 70 years of age
Interventions	Aprepitant (80 mg) 1 hour before surgery and palonosetron (0.075 mg) and dexamethasone (4 mg) administered intraoperatively or saline 1 hour before surgery and palonosetron (0.075 mg) and dexamethasone (4 mg) administered intraoperatively
Outcomes	PONV, pain
Notes	Study status (unknown), first posted (2015), missing information (anaesthesia regimen)

NCT02510157

Methods	Randomized controlled trial
Participants	Patients scheduled for laparoscopic cholecystectomy, 18 to 70 years of age, duration of operation < 3 hours
Interventions	Dexamethasone before induction of anaesthesia or saline before induction of anaesthesia

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NCT02510157 *(Continued)*

Outcomes	Pain, PONV
Notes	Study status (completed), first posted (2015), missing information (anaesthesia regimen)

NCT02525848

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic gynaecological surgery under general anaesthesia, 18 to 45 years of age, ASA I and II
Interventions	Dexamethasone (8 mg) 2 minutes before induction of anaesthesia or dexamethasone (8 mg) 2 minutes before induction of anaesthesia and aprepitant (80 mg) 1 hour before induction of anaesthesia
Outcomes	PONV, side effects
Notes	Study status (completed), first posted (2015), missing information (anaesthesia regimen)

NCT02541019

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy, older than 60 years of age, ASA I to III, female
Interventions	Palonosetron (75 mcg) 1 minute before anaesthesia induction or ondansetron (4 mg) 1 minute before anaesthesia induction and 4 mg 3 times a day during 2 days after surgery
Outcomes	PONV, nausea, complete response, adverse events
Notes	Study status (completed), first posted (2015), missing information (outcome)

NCT02594241

Methods	Randomized controlled trial
Participants	Patients with ventral incisional hernia with horizontal fascial defect > 10 cm described at computed tomography scan or clinical assessment, planned elective open hernia repair, older than 18 years of age
Interventions	Methylprednisolone (125 mg) immediately after induction of general anaesthesia or saline (100 mL) 2 hours before surgery
Outcomes	Pain, nausea, vomiting, complications
Notes	Study status (unknown), first posted (2015), missing information (anaesthesia regimen)

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NCT02711449

Methods	Randomized controlled trial
Participants	Patients having laparoscopy for suspected appendicitis, older than 18 years of age, ASA I to III
Interventions	Methylprednisolone (125 mg) approximately 30 minutes before skin incision or saline (0.9%) approximately 30 minutes before skin incision
Outcomes	Pain, side effects, PONV
Notes	Study status (completed), first posted (2016), missing information (anaesthesia regimen, outcome)

NCT02744495

Methods	Randomized controlled trial
Participants	Patients with non-emergent cardiac surgery, older than 18 years of age
Interventions	Betamethasone (4 mg) and/or droperidol (0.625 mg) immediately after cardiac surgery
Outcomes	PONV, pain, side effects, QTc interval
Notes	Study status (completed), first posted (2016), missing information (anaesthesia regimen)

NCT02744508

Methods	Randomized controlled trial
Participants	Patients undergoing minor orthopaedic surgery, 20 to 65 years of age
Interventions	Palonosetron or palonosetron and dexamethasone
Outcomes	PONV
Notes	Study status (completed), first posted (2016), missing information (anaesthesia regimen, time point of administration)

NCT02755116

Methods	Randomized controlled trial
Participants	Patients undergoing ambulatory surgery
Interventions	10 mg olanzapine or placebo
Outcomes	Nausea, vomiting
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized); if eligible, data will be included in next update of the review

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NCT02767882

Methods	Randomized controlled trial
Participants	Patients scheduled for elective primary unilateral total knee replacement, 18 to 80 years of age, ASA I to III, Chinese patients
Interventions	Dexamethasone (2 mL) or dexamethasone (4 mL) or saline (4 mL)
Outcomes	Pain
Notes	Study status (unknown), first posted (2016), missing information (anaesthesia regimen)

NCT02803788

Methods	Randomized controlled trial
Participants	Patients undergoing elective laparoscopic cholecystectomy, female, 20 to 40 years of age, ASA I and II
Interventions	Ondansetron (4 mg) and dexamethasone (8 mg) just before extubation or ramosetron (0.3 mg) just before extubation
Outcomes	Nausea, vomiting, adverse effect, pain
Notes	Study status (unknown), first posted (2016), missing information (anaesthesia regimen)

NCT02809378

Methods	Randomized controlled trial
Participants	Female patients undergoing thyroidectomy, ASA I or II, 20 to 60 years of age
Interventions	Palonosetron (0.075 mg) before anaesthesia induction or no treatment
Outcomes	PONV
Notes	Study identified after first search; data will be included in next update of the review

NCT02849483

Methods	Randomized controlled trial
Participants	Patients scheduled for gynaecological laparoscopic surgery, 20 to 70 years of age, ASA I and II
Interventions	Ramosetron or saline
Outcomes	Complications
Notes	Study status (recruiting), first posted (2016), missing information (anaesthesia regimen, outcome, time point of administration)

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NCT02884180

Methods	Randomized controlled trial
Participants	Patients scheduled for unilateral, revision TKA: total and major partial revisions were included (i.e. revisions including femoral and/or tibial component(s)); older than 18 years of age; ASA I to III; BMI > 18 and < 45; women in the fertile age (i.e. until 1 year after menopause) must have negative urine human chorionic gonadotropin (HCG) pregnancy test
Interventions	Dexamethasone (24 mg) after start of anaesthesia or saline isotonic after start of anaesthesia
Outcomes	Pain, adverse events, nausea, vomiting, dizziness
Notes	Study status (recruiting), first posted (2016), missing information (anaesthesia regimen)

NCT02966041

Methods	Randomized controlled trial
Participants	Patients (elective and urgent) with cardiac surgery procedures requiring cardiopulmonary bypass, older than 19 years of age
Interventions	Ondansetron (4 mg) or saline (2 mL) at time of discontinuation of propofol infusion
Outcomes	PONV, rescue PONV medication, PON, POV, ventricular arrhythmias
Notes	Study status (completed), first posted (2016), missing information (anaesthesia regimen)

NCT02968082

Methods	Randomized controlled trial
Participants	Patients have hemi-facial spasm or trigeminal neuralgia, undergo microvascular decompression (MVD), understand study objectives and voluntarily consent to participation, 18 to 65 years of age, ASA I and II
Interventions	Scopolamine (1.5 mg) or placebo
Outcomes	Nausea
Notes	Study status (unknown), first posted (2016), missing information (anaesthesia regimen)

NCT03034733

Methods	Randomized controlled trial
Participants	Patients having primary total knee replacement surgery, ASA I to III, 18 to 90 years of age
Interventions	Dexamethasone (0.15 mg/kg) intraoperative, dexamethasone (0.25 mg/kg) intraoperative, saline (0.9%) intraoperative

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NCT03034733 *(Continued)*

Outcomes	Pain, nausea, vomiting, wound complication/infection
Notes	Study status (recruiting), first posted (2017), missing information (anaesthesia regimen)

NCT03094442

Methods	Randomized controlled trial
Participants	Patients scheduled for minimally invasive sacrocolpopexy with or without concomitant anti-incontinence procedure and with or without concomitant hysterectomy, ASA I and II, older than 18 years of age
Interventions	Dexamethasone (8 mg) administered at time of induction of general anaesthesia or normal saline 0.9%
Outcomes	Pain, PONV, side effects
Notes	Study status (recruiting), first posted (2017), missing information (anaesthesia regimen)

NCT03141645

Methods	Randomized controlled trial
Participants	Patients having elective laparoscopic cholecystectomy, 18 to 70 years of age, ASA I to III
Interventions	Ondansetron (8 mg) 15 minutes before finishing operation or placebo/no intervention or Ringer's lactate solution (10 mL/kg) 15 minutes before starting operation
Outcomes	PONV
Notes	Study status (recruiting), first posted (2017), missing information (anaesthesia regimen)

NCT03218553

Methods	Randomized controlled trial
Participants	Patients having major surgery (> 90 minutes and realized under general anaesthesia) of the abdomen, pelvis, thorax, face/neck; vascular surgery in a patient older than 65 years; or major surgery (> 90 minutes and realized under general anaesthesia) of the abdomen, pelvis, thorax, face/neck, vascular surgery in a patient older than 50 years; risk factor for cardiac or respiratory disease; medical history of smoke; renal impairment; active smoking; blood losses > 500 mL, emergency surgery, 50 to 90 years of age
Interventions	Dexamethasone (0.2 mg/kg at end of surgical procedure, second dose 0.2 mg/kg 24 hours after surgery) or placebo (at end of surgical procedure, second dose 24 hours after surgery)
Outcomes	Sepsis/infection
Notes	Study status (recruiting), first posted (2017), missing information (anaesthesia regimen, outcome)

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NCT03278522

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic gynaecological surgery, age > 19 to 99 years, female
Interventions	Ramosetron (0.6 mg) at anaesthesia induction or ramosetron (0.6 mg) at end of surgery or placebo
Outcomes	QTc interval change
Notes	Study status (completed), first posted (2017), missing information (comparator)

NCT03338400

Methods	Randomized controlled trial
Participants	Patients undergoing outpatient vaginal prolapse surgery
Interventions	Dexamethasone or saline
Outcomes	Nausea, vomiting, quality of recovery
Notes	Study protocol identified in search update; missing information about anaesthesia details; if eligible, data will be included in next update of the review

NCT03403517

Methods	Randomized controlled trial
Participants	Patients undergoing open liver resection
Interventions	Methylprednisolone or dexamethasone
Outcomes	Postoperative complications
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized); if eligible, data will be included in next update of the review

NCT03409835

Methods	Randomized controlled trial
Participants	Patients undergoing gynaecological surgery
Interventions	Ramosetron or saline
Outcomes	Nausea, vomiting, pain, patient satisfaction
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized); if eligible, data will be included in next update of the review

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NCT03459248

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy
Interventions	Metoclopramide plus ondansetron or metoclopramide alone
Outcomes	PONV, patient satisfaction
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized, age); if eligible, data will be included in next update of the review

NCT03586817

Methods	Randomized controlled trial
Participants	Patients undergoing video-laparoscopic cholecystectomy
Interventions	Palonosetron or fosaprepitant
Outcomes	Complete response, nausea, vomiting
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized); if eligible, data will be included in next update of the review

NCT03631004

Methods	Randomized controlled trial
Participants	Patients undergoing medium and large surgeries in the thoracic or abdominal region (mastectomy, breast plastic surgery, hysterectomy, annexectomy, gynaecological pelvic surgery, colectomy, rectosigmoidectomy)
Interventions	Olanzapine or placebo
Outcomes	Nausea, vomiting, retching, side effects
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized); if eligible, data will be included in next update of the review

NCT03685032

Methods	Randomized controlled trial
Participants	Patients undergoing microvascular decompression surgery
Interventions	Dexamethasone, ondansetron, or saline
Outcomes	PONV, pain

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NCT03685032 *(Continued)*

Notes	Study protocol identified in search update; missing information about anaesthesia details; if eligible, data will be included in next update of the review

NCT03874936

Methods	Randomized controlled trial
Participants	Patients undergoing operation for hip dysplasia
Interventions	Dexamethasone or saline
Outcomes	Pain, morphine consumption, nausea, vomiting, side effects
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized); if eligible, data will be included in next update of the review

NCT03901768

Methods	Randomized controlled trial
Participants	Patients undergoing total knee surgery
Interventions	Dexamethasone or placebo
Outcomes	Pain
Notes	Study protocol identified in search update; missing information about anaesthesia details; if eligible, data will be included in next update of the review

NCT04013386

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic sleeve gastrectomy
Interventions	Dexamethasone plus aprepitant or dexamethasone alone
Outcomes	PONV
Notes	Study protocol identified in search update; missing information about anaesthesia details; if eligible, data will be included in next update of the review

NCT04027751

Methods	Randomized controlled trial
Participants	Patients undergoing elective non-cardiac surgery

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NCT04027751 *(Continued)*

Interventions	Tropisetron or placebo
Outcomes	Delirium, nausea, vomiting, side effects
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized); if eligible, data will be included in next update of the review

NCT04195204

Methods	Randomized controlled trial
Participants	Patients undergoing cardiac surgery
Interventions	Tropisetron or placebo
Outcomes	Delirium, nausea, vomiting, side effects
Notes	Study protocol identified in search update; missing information about anaesthesia details (standardized); if eligible, data will be included in next update of the review

PACTR201510001174606

Methods	Randomized controlled trial
Participants	Patients are candidates for laparoscopic cholecystectomy, 20 to 70 years of age
Interventions	Dexamethasone or placebo
Outcomes	PONV
Notes	Study status (NA), first posted (2015), missing information (anaesthesia regimen, time point of administration)

PACTR201707002398224

Methods	Randomized controlled trial
Participants	Patients coming for elective breast surgery, ASA I and II, 18 to 70 years of age, female
Interventions	Dexamethasone or saline
Outcomes	PONV, pain
Notes	Study status (completed), first posted (2017), missing information (anaesthesia regimen, time point of administration)

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Pandit 1986

Methods	Randomized controlled trial
Participants	Adult female patients undergoing laparoscopic examination or laparoscopic tubal cauterization, ASA I and II
Interventions	Study phase 1: cimetidine 300 mg orally 2 hours before operation with metoclopramide 10 mg IV about 15 minutes before induction or cimetidine 300 mg orally 2 hours before operation with placebo IV about 15 minutes before induction or placebo orally 2 hours before operation with metoclopramide 10 mg IV about 15 minutes before induction or placebo orally 2 hours before operation with placebo IV 15 minutes before induction Study phase 2: cimetidine 300 mg orally approximately 160 minutes beforehand, followed by metoclopramide 10 mg or 20 mg or placebo about 30 minutes before induction
Outcomes	PONV, pH of gastric juice, residual gastric volume
Notes	Missing information about time point of outcome assessment; no contact details available

Park 2018

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic colectomy for colorectal cancer
Interventions	0.3 mg ramosetron i.v. or saline (placebo)
Outcomes	PONV, pain, total amount of patient-controlled analgesia used, recovery of bowel function
Notes	Study identified in search update; data will be included in next update of the review

Paul 1985

Methods	Randomized controlled trial
Participants	Adult patients undergoing elective surgery
Interventions	Metoclopramide 10 mg IV or no treatment 5 to 10 minutes before end of anaesthesia
Outcomes	Vomiting, side effects
Notes	Missing information about study design; no contact details available

Paul 2018

Methods	Randomized controlled trial
Participants	Patients undergoing ear or nose surgery
Interventions	0.075 mg palonosetron i.v. or 8 mg dexamethasone i.v.

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Paul 2018 *(Continued)*

Outcomes	PONV
Notes	Study identified in search update; data will be included in next update of the review

Rajnikant 2019

Methods	Randomized controlled trial
Participants	Patients undergoing ear or nose surgery
Interventions	0.075 mg palonosetron i.v. or 8 mg dexamethasone i.v.
Outcomes	PONV
Notes	Study identified in search update; data will be included in next update of the review

RBR-4mjv6r

Methods	Randomized controlled trial
Participants	Patients undergoing elective laparoscopic cholecystectomy, 20 to 65 years of age, ASA I and II
Interventions	Palonosetron (0.075 mg) before anaesthesia induction or ondansetron (8 mg) before anaesthesia induction and 8 and 16 hours after surgery
Outcomes	PONV
Notes	Study status (recruiting), first posted (2017), missing information (anaesthesia regimen, outcome)

RBR-55mp5z

Methods	Randomized controlled trial
Participants	Patients undergoing elective laparoscopic gastroplasty, 20 to 65 years of age, ASA I and II, BMI ≥ 35 kg/m^2
Interventions	Palonosetron (0.075 mg) before anaesthesia induction or ondansetron (8 mg) before anaesthesia induction and 8 and 16 hours after surgery
Outcomes	PONV
Notes	Study status (recruiting), first posted (2016), missing information (anaesthesia regimen, outcome)

Reddy 2019

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystetomy

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Reddy 2019 *(Continued)*

Interventions	Palonosetron i.v. or ramosetron i.v.
Outcomes	PONV, adverse effects
Notes	Study identified in search update; data will be included in next update of the review

Roy 1977

Methods	Randomized controlled trial
Participants	NA
Interventions	Prochlorperazine
Outcomes	Postoperative sickness
Notes	No full text available

Rudra 1987

Methods	Randomized controlled trial
Participants	Female patients undergoing tubal ligation
Interventions	Metoclopramide 10 mg IM or normal saline IM 30 minutes before cessation of anaesthesia
Outcomes	PONV, dizziness, blood pressure, pulse, emergence delirium, extrapyramidal manifestation
Notes	Missing information about range of age and study design; no contact details available

Rust 1995

Methods	Randomized controlled trial
Participants	Female patients undergoing major gynaecological surgery
Interventions	Ondansetron 4 mg IV or metoclopramide 10 mg IV or placebo immediately before induction of anaesthesia
Outcomes	PONV
Notes	Missing information about anaesthesia regimen and range of age; no contact details available

Sajedi 2008

Methods	Randomized controlled trial

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Sajedi 2008 *(Continued)*

Participants	Patients undergoing elective orthopaedic surgery, 18 to 65 years of age, weight 50 to 70 kg, ASA I and II
Interventions	Granisetron 40 µg/kg IV or meperidine 0.4 mg/kg IV or saline 0.9% IV at end of surgery
Outcomes	Post-anaesthesia shivering, blood pressure, heart rate, core temperature, sedation, nausea, vomiting, respiratory depression
Notes	Mail sent on the 10th of July 2018; reason for request was missing information about time point for assessment of postoperative vomiting; no response received

Schettini 1989

Methods	Randomized controlled trial
Participants	Participants between 18 and 40 years of age
Interventions	L-sulpiride 50 mg or l-sulpiride 100 mg or droperidol 5 mg or control
Outcomes	Vomiting, prolactin secretion, headache, visual disturbance
Notes	Missing information about anaesthesia regimen; no contact details available

Schietroma 2010

Methods	Randomized controlled trial
Participants	Adult participants undergoing laparoscopic Nissen fundoplication
Interventions	Dexamethasone 8 mg plus promethazine 0.5 mg/kg IV before induction or promethazine 0.5 mg/kg IV alone before induction
Outcomes	Postoperative wound infection
Notes	Several clinical studies from the study author (Mario Schietroma) were retracted or were listed in the Retraction Watch Database

Schietroma 2013

Methods	Randomized controlled trial
Participants	Adult participants undergoing total thyroidectomy or total lobectomy
Interventions	Dexamethasone 8 mg plus promethazine 0.5 mg/kg IV before induction or promethazine 0.5 mg/kg IV alone before induction
Outcomes	Postoperative wound infection
Notes	Retracted study; listed in the Retraction Watch Database

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Schnaider 2008

Methods	Randomized controlled trial
Participants	Female patients undergoing total abdominal hysterectomy with adnexectomy under general anaesthesia with epidural block, 20 to 50 years of age, ASA I and II
Interventions	Metoclopramide 20 mg IV or dexamethasone 8 mg IV or droperidol 1.25 mg IV or ondansetron 8 mg IV or dexamethasone 8 mg and ondansetron 4 mg IV or droperidol 1.25 mg and ondansetron 4 mg IV or dexamethasone 8 mg and droperidol 0.625 mg and ondansetron 4 mg IV after venipuncture but before epidural puncture
Outcomes	PONV
Notes	Mail sent on 10th of July 2018; reason for request was missing information about study design; no response received

Shah 2011

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy, 18 to 60 years of age, ASA I and II
Interventions	Dexamethasone 8 mg IV or saline IV 2 hours before the operation
Outcomes	PONV, pain
Notes	Mail sent on 20th of March 2018 and again on 31st of July 2018; reason for request was missing information about type of anaesthesia; no response received

Sharma 2019

Methods	Randomized controlled trial
Participants	Patients undergoing middle ear surgery
Interventions	Palonosetron i.v. or ondansetron i.v.
Outcomes	PONV, nausea, vomiting, QT prolongation
Notes	Study identified in search update; data will be included in next update of the review

Shetty 2015

Methods	Randomized controlled trial
Participants	Patients undergoing elective middle ear surgery, 15 to 60 years of age, ASA I and II, scheduled to be hospitalized for 36 hours after surgery
Interventions	Ondansetron 4 mg IV or ramosetron 0.3 mg IV after the operation

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Shetty 2015 *(Continued)*

Outcomes	PONV, headache, drowsiness, dizziness, itching
Notes	Mail sent on 21st of March 2018 and again on 31st of July 2018; reason for request was missing information about time point af administration of study drugs and type of anaesthesia; no response received

Simogai 2016

Methods	Randomized controlled trial
Participants	NA
Interventions	Dexamethasone or combined diphenhydramine and diprophylline
Outcomes	PONV
Notes	No full text available

Singh 2008

Methods	Randomized controlled trial
Participants	Adult patients undergoing laparoscopic cholecystectomy
Interventions	Dexamethasone 10 mg IV (3 mL) or normal saline (3 mL)
Outcomes	PONV
Notes	No full text available

Singh 2011

Methods	Randomized controlled trial
Participants	Patients undergoing elective surgery under general anaesthesia, 21 to 50 years of age, ASA I and II
Interventions	Granisetron 2 mg IV or magnesium sulfate 2.48 mmol or nitroglycerine 200 µg or normal saline before injection of propofol
Outcomes	Pain
Notes	Mail sent on 18th of January; reason for request was missing information about time point of assessment of nausea; no response received

Sirajuddin 2014

Methods	Randomized controlled trial

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Sirajuddin 2014 *(Continued)*

Participants	Female patients undergoing breast surgery
Interventions	Metoclopramide (0.15 mg/kg) alone or metoclopramide (0.15 mg/kg) with dimenhydrinate (1 mg/kg) after induction
Outcomes	PONV
Notes	No full text available

Snow 1965

Methods	Randomized controlled trial
Participants	Patients undergoing elective surgery for retinal detachment
Interventions	Hydroxyzine 50 mg IM or prochlorperazine 5 mg IM or no treatment upon arrival in the recovery room
Outcomes	PONV, restlessness
Notes	Missing information about mean age and administration of study drugs before onset of PONV; no contact details available

Srivastava 2012

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy under general anaesthesia, 20 to 60 years of age, ASA I and II
Interventions	Metoclopramide 10 mg IV or ondansetron 4 mg IV or granisetron 3 mg IV before induction of anaesthesia
Outcomes	PONV, pain, patient satisfaction, adverse effects
Notes	No full text available

Stefanov 2005

Methods	Randomized controlled trial
Participants	Female patients undergoing laparoscopic cholecystectomy
Interventions	Dexamethasone or placebo
Outcomes	Vomiting
Notes	No full text available

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Tahir 2018

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic abdominal surgery
Interventions	Palonosetron i.v. or granisetron i.v.
Outcomes	PONV
Notes	Study identified in search update; data will be included in next update of the review

Tantawy 2008

Methods	Randomized controlled trial
Participants	Patients undergoing major pelvic oncological surgery
Interventions	Epidural dexamethasone 4 mg with morphine 4 mg or morphine 4 mg alone
Outcomes	Pain, morphine-related side effects
Notes	No full text available

Thongrong 2018

Methods	Randomized controlled trial
Participants	Patients undergoing microvascular decompression surgery
Interventions	Dexamethasone i.v. or ondansetron i.v.
Outcomes	PONV
Notes	Study identified in search update; data will be included in next update of the review

Tokat 1994

Methods	Randomized controlled trial
Participants	Female patients undergoing gynaecological surgery, ASA I and II
Interventions	Ondansetron 4 mg IV or placebo 30 minutes before surgery and 8 hours after surgery
Outcomes	PONV, blood pressure, pulse
Notes	Missing information about randomisation; no contact details available

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Tolksdorf 1985

Methods	Randomized controlled trial
Participants	Female patients undergoing minor gynaecological surgery, 21 to 77 years of age
Interventions	Transdermal scopolamine or identical placebo patch
Outcomes	PONV
Notes	Missing information about randomization; no contact details available

Top 1996

Methods	Randomized controlled trial
Participants	NA
Interventions	Ondansetron 4 mg or ondansetron 4 mg with dexamethasone 8 mg 5 minutes before induction
Outcomes	PONV, sleep manner
Notes	Missing information about study design; no contact details available

Tornetta 1969

Methods	Randomized controlled trial
Participants	Adult patients undergoing elective surgery
Interventions	Study part 1: metoclopramide 10 mg IM or placebo IM at end of operation Study part 2: metoclopramide 20 mg IV or metoclopramide 30 mg IV or metoclopramide 50 mg IV before emergence from anaesthesia Study part 3: metoclopramide 20 mg IM or prochlorperazine 10 mg IM or placebo before emergence from anaesthesia
Outcomes	PONV, blood pressure, pulse, time of emergence
Notes	Missing information about anaesthesia regimen; no contact details available

Tuhanioglu 2018

Methods	Randomized controlled trial
Participants	Patients undergoing tonsillectomy
Interventions	Dexamethasone or saline
Outcomes	Pain, vomiting

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Tuhanioglu 2018 *(Continued)*

Notes	Study identified in search update; data will be included in next update of the review

Tuncer 2002

Methods	Randomized controlled trial
Participants	Patients undergoing major orthopaedic surgery with at least 24 hours bed rest, over 18 years of age, ASA I and II
Interventions	Dexamethasone 150 µg/kg IV or normal saline IV before the start of PCA, which was started in the recovery room
Outcomes	PONV, pain
Notes	Mail sent on 21st of March 2018 and again on 31st of July 2018; reason for request was missing information about randomization and time point of administration of study drugs; no response received

Tur 1994

Methods	Randomized controlled trial
Participants	Patients undergoing gynaecological, ear nose and throat, or ophthalmic surgery, 16 to 75 years of age
Interventions	Oral ondansetron 4 mg and 1 mg/kg pethidine IM or only pethidine 1 mg/kg IM for premedication
Outcomes	PONV
Notes	Missing information about study design; no contact details available

Tur 1995

Methods	Randomized controlled trial
Participants	Adult patients, 17 to 65 years of age
Interventions	Oral ondansetron in doses of 4 mg or 8 mg or 16 mg or no treatment preoperatively
Outcomes	Postoperative vomiting
Notes	Missing information about study design; no contact details available

Turan 2006

Methods	Randomized controlled trial

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Turan 2006 *(Continued)*

Participants	Adult patients undergoing elective surgery under general anaesthesia that was expected to last at least 1 hour, at least 2 risk factors
Interventions	Intraoperative 80% oxygen or 30% oxygen and also ondansetron 4 mg or not, dexamethasone 4 mg or not, droperidol 1.25 mg or not
Outcomes	PONV
Notes	Mail sent on 18th of January 2018; reason for request was missing information about outcome data; no response received

Usmani 2003

Methods	Randomized controlled trial
Participants	Patients undergoing elective middle ear surgery, ASA I and II
Interventions	Ondansetron 0.1 mg/kg IV or dexamethasone 0.15 mg/kg IV or ondansetron 0.1 mg/ kg IV with dexamethasone 0.15 mg/kg IV 10 minutes before induction of anaesthesia
Outcomes	PONV, headache, dizziness, erythema at injection site, perineal itching
Notes	Missing information about range of age; no contact details available

Ventriglia 1993

Methods	Randomized controlled trial
Participants	Patients undergoing abdominal surgery
Interventions	Ondansetron 4 mg IV or physiological solution at the moment of induction
Outcomes	PONV
Notes	No full text available

Vimlati 2002

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic cholecystectomy
Interventions	Ondansetron 4 mg IV before starting anaesthesia or ondansetron 4 mg IV at end of operation or control
Outcomes	PONV
Notes	Missing information about range of age; no contact details available

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Viriyaroj 2015

Methods	Randomized controlled trial
Participants	Patients undergoing elective laparoscopic cholecystectomy
Interventions	Dexamethasone 8 mg IV 60 to 90 minutes before surgery or normal saline 60 to 90 minutes before surgery
Outcomes	Pain, PONV, analgesic consumption, antiemetic requirement, erythrocyte sedimentation, C-reactive protein
Notes	No full text available

Wang 2002

Methods	Randomized controlled trial
Participants	Patients undergoing elective surgery
Interventions	Ondansetron 8 mg or tropisetron 3 mg or ondansetron 8 mg plus dexamethasone 10 mg or tropisetron 3 mg plus dexamethasone 10 mg
Outcomes	PONV, wound healing
Notes	Mail sent on 20th of March 2018; reason for request was missing information about age range, type of anaesthesia, time point for assessment of PONV; mail could not be delivered

Wang 2020

Methods	Randomized controlled trial
Participants	Patients undergoing cardiac surgery
Interventions	Ondansetron or placebo
Outcomes	PONV, headache, arrhythmia
Notes	Study identified in search update; data will be included in next update of the review

Winning 1977

Methods	Randomized controlled trial
Participants	Patients undergoing minor gynaecological or urological surgery, average age of 32.7 years
Interventions	Droperidol 5 mg IM or diphenidol 40 mg IM or saline IM 1 hour before anaesthesia
Outcomes	PONV, giddiness, drowsiness, weakness, confusion
Notes	Missing information about study design; no contact details available

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Wittayapairoj 2017

Methods	Randomized controlled trial
Participants	Patients undergoing lumbar spine surgery
Interventions	0.2 mg/kg dexamethasone or normal saline
Outcomes	Morphine consumption, pain, adverse events
Notes	Study identified in search update; data will be included in next update of the review

Wu 1998

Methods	Randomized controlled trial
Participants	Patients undergoing gynaecological surgery
Interventions	Droperidol epidural or droperidol intravenous
Outcomes	PONV
Notes	No full text available

Wu 2018

Methods	Randomized controlled trial
Participants	Patients undergoing total knee arthroplasty
Interventions	Dexamethasone or normal saline
Outcomes	Pain, postoperative complications
Notes	Study identified in search update; data will be included in next update of the review

Yan 2019

Methods	Randomized controlled trial
Participants	Patients undergoing laparoscopic radical resection
Interventions	Palonosetron or tropisetron
Outcomes	Abdominal distension, nausea, vomiting, ECG, blood oxygen, heart rate, respiratory frequency, mental and neurological symptoms
Notes	Study identified in search update; needs translation (Chinese)

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Yao 2002

Methods	Randomized controlled trial
Participants	Female patients undergoing hysterectomy, ASA I and II
Interventions	Epidural saline or epidural 2% lidocaine 10 mL combined with 2.5 µg/mL fentanyl 30 minutes before skin incision followed by 0.125% ropivacaine and 2 µg/mL fentanyl infusion at 9 mL/h to the end of surgery or epidural 2% lidocaine 10 mL combined with 2.5 µg/mL fentanyl and 0.15 mg/mL droperidol 30 minutes before incision followed by 0.125% ropivacaine and 2 µg/mL fentanyl infusion at 9 mL/h to end of surgery
Outcomes	Pain, nausea, pruritus, motor block
Notes	No full text available

Yoo 2018

Methods	Randomized controlled trial
Participants	Patients undergoing elective surgery under general anaesthesia
Interventions	Aprepitant plus palonosetron or palonosteron alone
Outcomes	Nausea, vomiting
Notes	Study identified in search update; data will be included in next update of the review

Zafar 2018

Methods	Randomized controlled trial
Participants	Patients undergoing open appendectomy
Interventions	Dexamethasone plus dimenhydrinate or dimenhydrinate alone
Outcomes	Nausea, vomiting
Notes	Study identified in search update; data will be included in next update of the review

Zarate 2001

Methods	Randomized controlled trial
Participants	Patients undergoing ambulatory ear, nose, and throat surgery
Interventions	Metoclopramide
Outcomes	PONV
Notes	No full text available

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Zhang 2016

Methods	Randomized controlled trial
Participants	Patients undergoing thyroid surgery
Interventions	Dexamethasone 0.1 mg/kg or same volume of saline at induction of anaesthesia
Outcomes	Pain, PONV
Notes	No full text available

Abbreviations: ASA = American Society of Anesthesiologists physical status classification system; BMI = body mass index; IM = intramuscular; IMF = intermaxillary fixation; IV = intravenous; NA = not available; PONV = postoperative nausea and vomiting; IV = intravenous; TIVA = total intravenous anaesthesia.

DATA AND ANALYSES

Comparison 1. Amisulpride versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Vomiting within 0 to 24 hours	2	841	Risk Ratio (IV, Random, 95% CI)	0.71 [0.52, 0.98]
1.1.1 Low dose	1	76	Risk Ratio (IV, Random, 95% CI)	0.83 [0.38, 1.80]
1.1.2 Recommended dose	2	694	Risk Ratio (IV, Random, 95% CI)	0.69 [0.38, 1.25]
1.1.3 High dose	1	71	Risk Ratio (IV, Random, 95% CI)	0.44 [0.19, 1.00]
1.2 Serious adverse events	2	904	Risk Ratio (IV, Random, 95% CI)	0.83 [0.38, 1.85]
1.2.1 Low dose	1	76	Risk Ratio (IV, Random, 95% CI)	0.97 [0.04, 22.74]
1.2.2 Recommended dose	2	757	Risk Ratio (IV, Random, 95% CI)	0.62 [0.11, 3.43]
1.2.3 High dose	1	71	Risk Ratio (IV, Random, 95% CI)	0.68 [0.07, 7.05]
1.3 Any adverse event	2	904	Risk Ratio (IV, Random, 95% CI)	0.97 [0.90, 1.06]
1.3.1 Low dose	1	76	Risk Ratio (IV, Random, 95% CI)	0.95 [0.75, 1.22]
1.3.2 Recommended dose	2	757	Risk Ratio (IV, Random, 95% CI)	0.98 [0.90, 1.08]
1.3.3 High dose	1	71	Risk Ratio (IV, Random, 95% CI)	0.93 [0.72, 1.20]
1.4 Headache	2	904	Risk Ratio (IV, Random, 95% CI)	1.56 [0.80, 3.08]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4.1 Low dose	1	76	Risk Ratio (IV, Random, 95% CI)	2.90 [0.16, 51.41]
1.4.2 Recommended dose	2	757	Risk Ratio (IV, Random, 95% CI)	1.50 [0.73, 3.06]
1.4.3 High dose	1	71	Risk Ratio (IV, Random, 95% CI)	1.76 [0.09, 35.02]
1.5 Sedation/drowsiness	1	689	Risk Ratio (IV, Random, 95% CI)	Not estimable
1.5.1 Recommended dose	1	689	Risk Ratio (IV, Random, 95% CI)	Not estimable
1.6 Extrapyramidal symptoms	1	689	Risk Ratio (IV, Random, 95% CI)	Not estimable
1.6.1 Recommended dose	1	689	Risk Ratio (IV, Random, 95% CI)	Not estimable
1.7 Constipation	2	904	Risk Ratio (IV, Random, 95% CI)	1.12 [0.71, 1.75]
1.7.1 Low dose	1	76	Risk Ratio (IV, Random, 95% CI)	0.93 [0.21, 4.22]
1.7.2 Recommended dose	2	757	Risk Ratio (IV, Random, 95% CI)	1.15 [0.70, 1.89]
1.7.3 High dose	1	71	Risk Ratio (IV, Random, 95% CI)	1.02 [0.23, 4.60]

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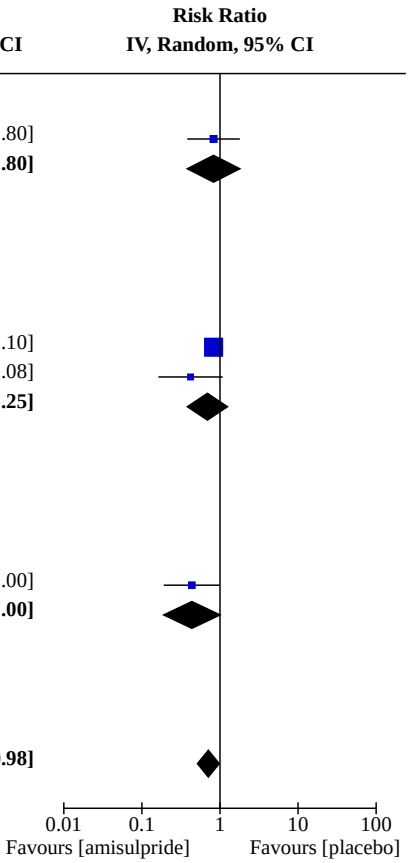
Analysis 1.1. Comparison 1: Amisulpride versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Amisulpride Events	Amisulpride Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Low dose						
Kranke 2013	16	58	6	18	14.9%	0.83 [0.38 , 1.80]
Subtotal (95% CI)		**58**		**18**	**14.9%**	**0.83 [0.38 , 1.80]**
Total events:	16		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.48 (P = 0.63)						
1.1.2 Recommended dose						
Gan 2017	68	315	81	311	61.5%	0.83 [0.63 , 1.10]
Kranke 2013	7	50	6	18	10.4%	0.42 [0.16 , 1.08]
Subtotal (95% CI)		**365**		**329**	**71.9%**	**0.69 [0.38 , 1.25]**
Total events:	75		87			
Heterogeneity: Tau² = 0.10; Chi² = 1.81, df = 1 (P = 0.18); I² = 45%						
Test for overall effect: Z = 1.23 (P = 0.22)						
1.1.3 High dose						
Kranke 2013	9	53	7	18	13.2%	0.44 [0.19 , 1.00]
Subtotal (95% CI)		**53**		**18**	**13.2%**	**0.44 [0.19 , 1.00]**
Total events:	9		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.96 (P = 0.05)						
Total (95% CI)		**476**		**365**	**100.0%**	**0.71 [0.52 , 0.98]**
Total events:	100		100			
Heterogeneity: Tau² = 0.02; Chi² = 3.61, df = 3 (P = 0.31); I² = 17%						
Test for overall effect: Z = 2.10 (P = 0.04)						
Test for subgroup differences: Chi² = 1.29, df = 2 (P = 0.52), I² = 0%						



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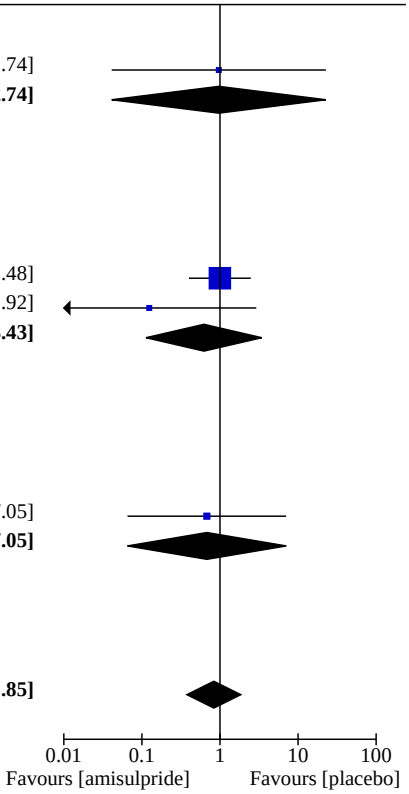
Analysis 1.2. Comparison 1: Amisulpride versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Amisulpride Events	Amisulpride Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
1.2.1 Low dose						
Kranke 2013	1	58	0	18	6.3%	0.97 [0.04 , 22.74]
Subtotal (95% CI)		**58**		**18**	**6.3%**	**0.97 [0.04 , 22.74]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.98)						
1.2.2 Recommended dose						
Gan 2017	9	345	9	344	75.8%	1.00 [0.40 , 2.48]
Kranke 2013	0	50	1	18	6.3%	0.12 [0.01 , 2.92]
Subtotal (95% CI)		**395**		**362**	**82.2%**	**0.62 [0.11 , 3.43]**
Total events:	9		10			
Heterogeneity: Tau² = 0.76; Chi² = 1.54, df = 1 (P = 0.21); I² = 35%						
Test for overall effect: Z = 0.54 (P = 0.59)						
1.2.3 High dose						
Kranke 2013	2	53	1	18	11.5%	0.68 [0.07 , 7.05]
Subtotal (95% CI)		**53**		**18**	**11.5%**	**0.68 [0.07 , 7.05]**
Total events:	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.32 (P = 0.75)						
Total (95% CI)		**506**		**398**	**100.0%**	**0.83 [0.38 , 1.85]**
Total events:	12		11			
Heterogeneity: Tau² = 0.00; Chi² = 1.58, df = 3 (P = 0.66); I² = 0%						
Test for overall effect: Z = 0.45 (P = 0.66)						
Test for subgroup differences: Chi² = 0.06, df = 2 (P = 0.97), I² = 0%						



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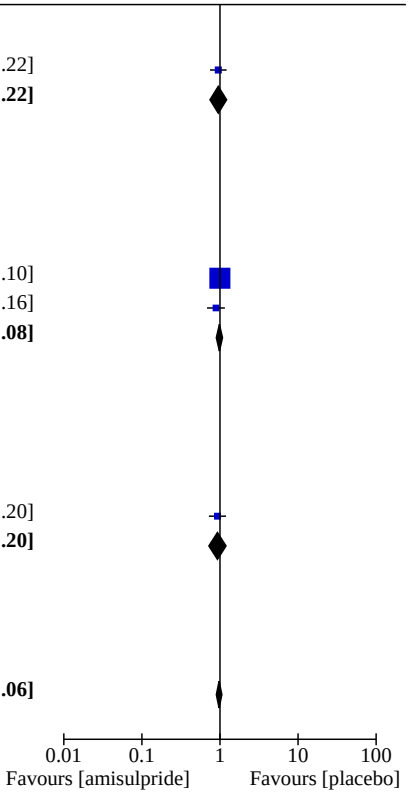
Analysis 1.3. Comparison 1: Amisulpride versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Amisulpride Events	Amisulpride Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
1.3.1 Low dose						
Kranke 2013	46	58	15	18	10.8%	0.95 [0.75 , 1.22]
Subtotal (95% CI)		**58**		**18**	**10.8%**	**0.95 [0.75 , 1.22]**
Total events:	46		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.40 (P = 0.69)						
1.3.2 Recommended dose						
Gan 2017	243	345	243	344	69.7%	1.00 [0.91 , 1.10]
Kranke 2013	37	50	15	18	9.3%	0.89 [0.68 , 1.16]
Subtotal (95% CI)		**395**		**362**	**79.0%**	**0.98 [0.90 , 1.08]**
Total events:	280		258			
Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 1 (P = 0.42); I² = 0%						
Test for overall effect: Z = 0.36 (P = 0.72)						
1.3.3 High dose						
Kranke 2013	41	53	15	18	10.2%	0.93 [0.72 , 1.20]
Subtotal (95% CI)		**53**		**18**	**10.2%**	**0.93 [0.72 , 1.20]**
Total events:	41		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.58 (P = 0.56)						
Total (95% CI)		**506**		**398**	**100.0%**	**0.97 [0.90 , 1.06]**
Total events:	367		288			
Heterogeneity: Tau² = 0.00; Chi² = 0.87, df = 3 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.63 (P = 0.53)						
Test for subgroup differences: Chi² = 0.22, df = 2 (P = 0.90), I² = 0%						



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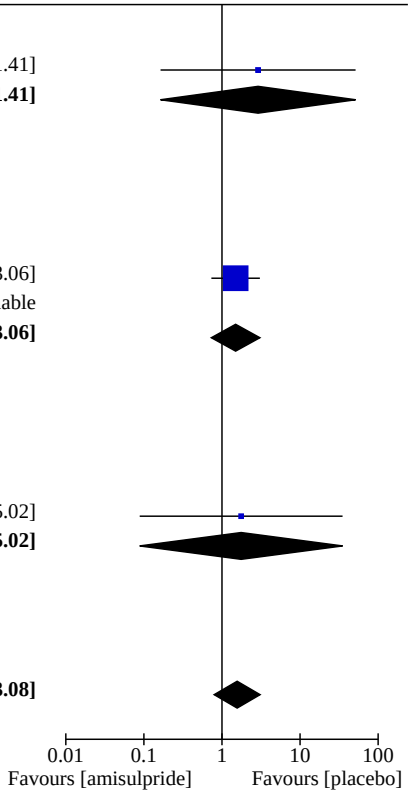
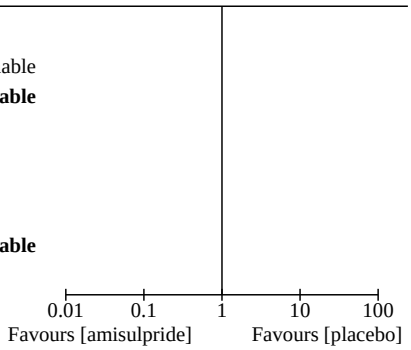
Analysis 1.4. Comparison 1: Amisulpride versus placebo, Outcome 4: Headache

Study or Subgroup	Amisulpride Events	Amisulpride Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
1.4.1 Low dose						
Kranke 2013	4	58	0	18	5.5%	2.90 [0.16 , 51.41]
Subtotal (95% CI)		**58**		**18**	**5.5%**	**2.90 [0.16 , 51.41]**
Total events:	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.73 (P = 0.47)						
1.4.2 Recommended dose						
Gan 2017	18	345	12	344	89.4%	1.50 [0.73 , 3.06]
Kranke 2013	0	50	0	18		Not estimable
Subtotal (95% CI)		**395**		**362**	**89.4%**	**1.50 [0.73 , 3.06]**
Total events:	18		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.10 (P = 0.27)						
1.4.3 High dose						
Kranke 2013	2	53	0	18	5.1%	1.76 [0.09 , 35.02]
Subtotal (95% CI)		**53**		**18**	**5.1%**	**1.76 [0.09 , 35.02]**
Total events:	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
Total (95% CI)		**506**		**398**	**100.0%**	**1.56 [0.80 , 3.08]**
Total events:	24		12			
Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 2 (P = 0.91); I² = 0%						
Test for overall effect: Z = 1.30 (P = 0.19)						
Test for subgroup differences: Chi² = 0.20, df = 2 (P = 0.91), I² = 0%						



Analysis 1.5. Comparison 1: Amisulpride versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Amisulpride Events	Amisulpride Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
1.5.1 Recommended dose						
Gan 2017	0	345	0	344		Not estimable
Subtotal (95% CI)		**345**		**344**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**345**		**344**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



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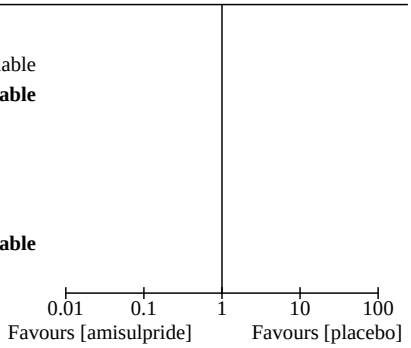
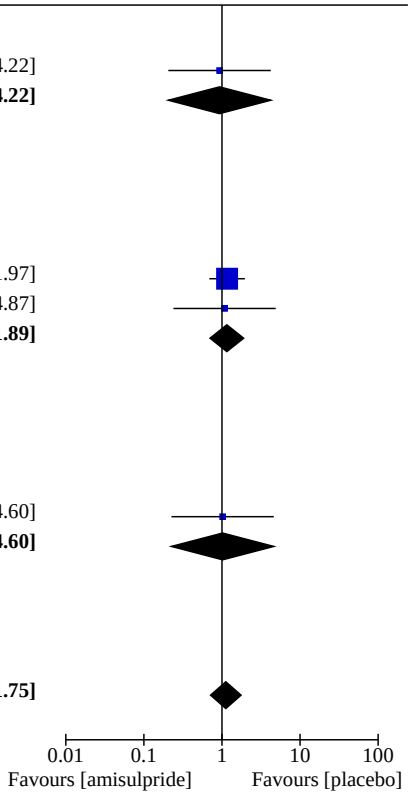
Analysis 1.6. Comparison 1: Amisulpride versus placebo, Outcome 6: Extrapyramidal symptoms

Study or Subgroup	Amisulpride Events	Amisulpride Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
1.6.1 Recommended dose						
Gan 2017	0	345	0	344		Not estimable
Subtotal (95% CI)		**345**		**344**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**345**		**344**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 1.7. Comparison 1: Amisulpride versus placebo, Outcome 7: Constipation

Study or Subgroup	Amisulpride Events	Amisulpride Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
1.7.1 Low dose						
Kranke 2013	6	58	2	18	8.8%	0.93 [0.21 , 4.22]
Subtotal (95% CI)		**58**		**18**	**8.8%**	**0.93 [0.21 , 4.22]**
Total events:	6		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.09 (P = 0.93)						
1.7.2 Recommended dose						
Gan 2017	28	345	24	344	73.4%	1.16 [0.69 , 1.97]
Kranke 2013	6	50	2	18	8.9%	1.08 [0.24 , 4.87]
Subtotal (95% CI)		**395**		**362**	**82.3%**	**1.15 [0.70 , 1.89]**
Total events:	34		26			
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.93); I² = 0%						
Test for overall effect: Z = 0.57 (P = 0.57)						
1.7.3 High dose						
Kranke 2013	6	53	2	18	8.9%	1.02 [0.23 , 4.60]
Subtotal (95% CI)		**53**		**18**	**8.9%**	**1.02 [0.23 , 4.60]**
Total events:	6		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.98)						
Total (95% CI)		**506**		**398**	**100.0%**	**1.12 [0.71 , 1.75]**
Total events:	46		30			
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 3 (P = 0.99); I² = 0%						
Test for overall effect: Z = 0.49 (P = 0.62)						
Test for subgroup differences: Chi² = 0.09, df = 2 (P = 0.96), I² = 0%						



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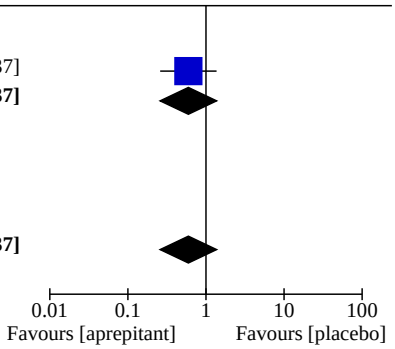
Comparison 2. Aprepitant versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Vomiting within 0 to 24 hours	1	94	Risk Ratio (IV, Random, 95% CI)	0.59 [0.26, 1.37]
2.1.1 Recommended dose	1	94	Risk Ratio (IV, Random, 95% CI)	0.59 [0.26, 1.37]
2.2 Headache	1	120	Risk Ratio (IV, Random, 95% CI)	0.33 [0.06, 1.92]
2.2.1 High dose	1	120	Risk Ratio (IV, Random, 95% CI)	0.33 [0.06, 1.92]

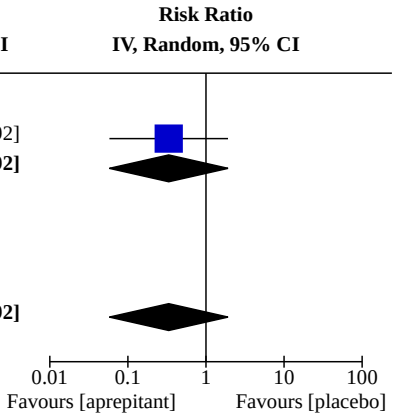
Analysis 2.1. Comparison 2: Aprepitant versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Aprepitant Events	Aprepitant Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
2.1.1 Recommended dose						
NCT00888329	6	35	17	59	100.0%	0.59 [0.26 , 1.37]
Subtotal (95% CI)		**35**		**59**	**100.0%**	**0.59 [0.26 , 1.37]**
Total events:	6		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.22 (P = 0.22)						
Total (95% CI)		**35**		**59**	**100.0%**	**0.59 [0.26 , 1.37]**
Total events:	6		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.22 (P = 0.22)						
Test for subgroup differences: Not applicable						



Analysis 2.2. Comparison 2: Aprepitant versus placebo, Outcome 2: Headache

Study or Subgroup	Aprepitant Events	Aprepitant Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
2.2.1 High dose						
Jung 2013	2	80	3	40	100.0%	0.33 [0.06 , 1.92]
Subtotal (95% CI)		**80**		**40**	**100.0%**	**0.33 [0.06 , 1.92]**
Total events:	2		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.23 (P = 0.22)						
Total (95% CI)		**80**		**40**	**100.0%**	**0.33 [0.06 , 1.92]**
Total events:	2		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.23 (P = 0.22)						
Test for subgroup differences: Not applicable						



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Comparison 3. Dexamethasone versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Vomiting within 0 to 24 hours	43	4804	Risk Ratio (IV, Random, 95% CI)	0.50 [0.44, 0.56]
3.1.1 Low dose	3	220	Risk Ratio (IV, Random, 95% CI)	0.65 [0.41, 1.04]
3.1.2 Recommended dose	15	2051	Risk Ratio (IV, Random, 95% CI)	0.55 [0.44, 0.67]
3.1.3 High dose	31	2382	Risk Ratio (IV, Random, 95% CI)	0.43 [0.36, 0.51]
3.1.4 NA dose	1	151	Risk Ratio (IV, Random, 95% CI)	0.42 [0.22, 0.82]
3.2 Serious adverse events	3	376	Risk Ratio (IV, Random, 95% CI)	1.01 [0.15, 7.01]
3.2.1 High dose	2	225	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.2.2 NA dose	1	151	Risk Ratio (IV, Random, 95% CI)	1.01 [0.15, 7.01]
3.3 Any adverse event	6	1152	Risk Ratio (IV, Random, 95% CI)	0.78 [0.53, 1.16]
3.3.1 High dose	6	1152	Risk Ratio (IV, Random, 95% CI)	0.78 [0.53, 1.16]
3.4 Headache	13	1678	Risk Ratio (IV, Random, 95% CI)	0.90 [0.59, 1.37]
3.4.1 Recommended dose	3	193	Risk Ratio (IV, Random, 95% CI)	0.96 [0.20, 4.53]
3.4.2 High dose	10	1334	Risk Ratio (IV, Random, 95% CI)	0.91 [0.57, 1.44]
3.4.3 NA dose	1	151	Risk Ratio (IV, Random, 95% CI)	0.76 [0.18, 3.28]
3.5 Sedation/drowsiness	9	1290	Risk Ratio (IV, Random, 95% CI)	1.01 [0.92, 1.11]
3.5.1 Recommended dose	1	96	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.5.2 High dose	8	1194	Risk Ratio (IV, Random, 95% CI)	1.01 [0.92, 1.11]
3.6 Extrapyramidal symptoms	4	1031	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.6.1 Recommended dose	3	266	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.6.2 High dose	2	765	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.7 Constipation	3	327	Risk Ratio (IV, Random, 95% CI)	0.75 [0.14, 3.91]
3.7.1 Recommended dose	1	96	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.7.2 High dose	1	80	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.95]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.7.3 NA dose	1	151	Risk Ratio (IV, Random, 95% CI)	1.01 [0.15, 7.01]
3.8 Postoperative wound infection	24	3199	Risk Ratio (IV, Random, 95% CI)	1.21 [0.34, 4.30]
3.8.1 Low dose	1	102	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.8.2 Recommended dose	5	253	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.8.3 High dose	20	2533	Risk Ratio (IV, Random, 95% CI)	1.27 [0.30, 5.29]
3.8.4 NA dose	2	311	Risk Ratio (IV, Random, 95% CI)	1.01 [0.06, 15.91]
3.9 Arrhythmia	3	189	Risk Ratio (IV, Random, 95% CI)	0.82 [0.43, 1.54]
3.9.1 Recommended dose	2	80	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.9.2 High dose	1	109	Risk Ratio (IV, Random, 95% CI)	0.82 [0.43, 1.54]
3.10 Visual disturbances	1	40	Risk Ratio (IV, Random, 95% CI)	0.83 [0.30, 2.29]
3.10.1 High dose	1	40	Risk Ratio (IV, Random, 95% CI)	0.83 [0.30, 2.29]
3.11 QT prolongation	1	149	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.11.1 Recommended dose	1	149	Risk Ratio (IV, Random, 95% CI)	Not estimable

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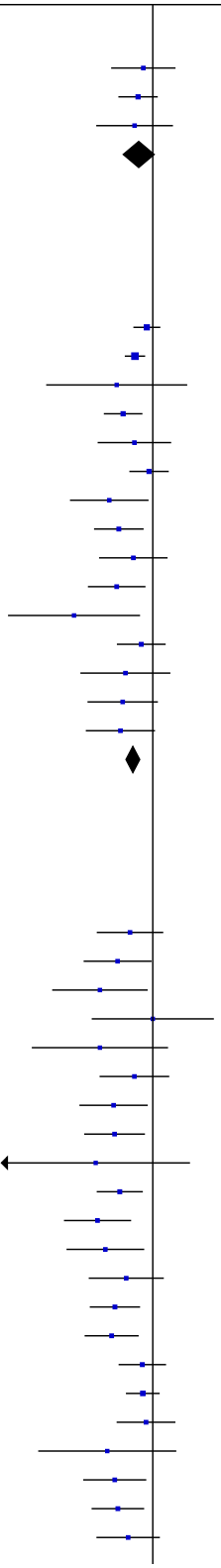
Analysis 3.1. Comparison 3: Dexamethasone versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.1.1 Low dose						
Lee Y 2004	9	36	4	12	1.4%	0.75 [0.28 , 2.00]
Liu 1999	23	60	6	10	3.8%	0.64 [0.35 , 1.16]
Wang 2000c	10	87	3	15	1.0%	0.57 [0.18 , 1.85]
Subtotal (95% CI)		**183**		**37**	**6.2%**	**0.65 [0.41 , 1.04]**
Total events:	42		13			
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 2 (P = 0.94); I² = 0%						
Test for overall effect: Z = 1.79 (P = 0.07)						
3.1.2 Recommended dose						
Apfel 2004-1	33	172	40	174	8.1%	0.83 [0.55 , 1.26]
Apfel 2004-2	51	340	89	345	14.2%	0.58 [0.43 , 0.79]
Cekmen 2003	1	15	3	15	0.3%	0.33 [0.04 , 2.85]
Chu 2008	12	74	30	75	4.0%	0.41 [0.23 , 0.73]
Daabiss 2008	4	30	7	30	1.1%	0.57 [0.19 , 1.75]
Hemmati 2014	14	46	15	44	3.8%	0.89 [0.49 , 1.63]
Huang 2001	3	39	11	38	1.0%	0.27 [0.08 , 0.88]
Lee Y 2001	8	45	11	22	2.4%	0.36 [0.17 , 0.76]
Lee Y 2004	7	38	4	12	1.3%	0.55 [0.19 , 1.57]
Liu 1999	6	30	6	10	1.8%	0.33 [0.14 , 0.80]
Rimaitis 2010	1	51	11	51	0.3%	0.09 [0.01 , 0.68]
Smith 2008	10	72	14	71	2.5%	0.70 [0.34 , 1.48]
Wang 2000c	4	43	3	14	0.7%	0.43 [0.11 , 1.71]
Wang 2002a	4	39	10	39	1.2%	0.40 [0.14 , 1.17]
Wang 2002b	4	38	11	39	1.2%	0.37 [0.13 , 1.07]
Subtotal (95% CI)		**1072**		**979**	**43.8%**	**0.55 [0.44 , 0.67]**
Total events:	162		265			
Heterogeneity: Tau² = 0.02; Chi² = 16.22, df = 14 (P = 0.30); I² = 14%						
Test for overall effect: Z = 5.74 (P < 0.00001)						
3.1.3 High dose						
Alghanem 2010	5	60	10	60	1.3%	0.50 [0.18 , 1.38]
Bianchin 2007	4	36	12	37	1.3%	0.34 [0.12 , 0.96]
Bisgaard 2003	2	40	10	40	0.6%	0.20 [0.05 , 0.86]
Demirhan 2013	2	20	2	20	0.4%	1.00 [0.16 , 6.42]
Entezariasl 2010	1	25	5	25	0.3%	0.20 [0.03 , 1.59]
Erhan 2008	4	20	7	20	1.2%	0.57 [0.20 , 1.65]
Feo 2006	4	49	14	52	1.3%	0.30 [0.11 , 0.86]
Kim 2007	5	50	16	50	1.6%	0.31 [0.12 , 0.79]
Koo 2001	0	12	3	15	0.2%	0.18 [0.01 , 3.11]
Lee 2003	9	83	24	81	2.8%	0.37 [0.18 , 0.74]
Lee Y 2001	4	43	11	22	1.3%	0.19 [0.07 , 0.52]
Lee Y 2002	3	43	13	44	1.0%	0.24 [0.07 , 0.77]
Lee Y 2004	9	74	3	11	1.0%	0.45 [0.14 , 1.40]
Liu 1998	6	30	19	30	2.3%	0.32 [0.15 , 0.68]
Liu 1999	6	30	7	10	2.0%	0.29 [0.13 , 0.65]
Lopez Olaondo 1996	8	25	11	25	2.6%	0.73 [0.35 , 1.50]
Mathiesen 2009	14	37	20	39	5.2%	0.74 [0.44 , 1.23]
Mathiesen 2011	7	43	9	45	1.7%	0.81 [0.33 , 1.99]
Mitra 1998	1	20	4	20	0.3%	0.25 [0.03 , 2.05]
Murphy 2011a	5	60	13	49	1.5%	0.31 [0.12 , 0.82]
Nielsen 2015	7	77	20	76	2.1%	0.35 [0.16 , 0.77]
Sistla 2009	5	36	10	34	1.5%	0.47 [0.18 , 1.24]
Thimmasettaiah 2012	7	75	7	25	1.5%	0.33 [0.13 , 0.86]



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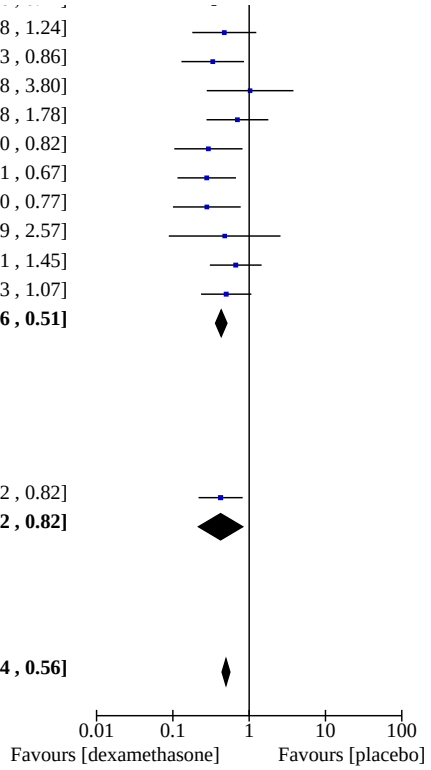
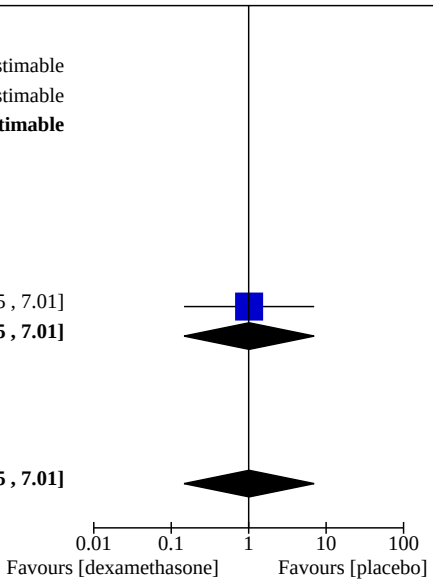
Analysis 3.1. (Continued)

Sistla 2009	5	36	10	34	1.5%	0.47 [0.18 , 1.24]
Thimmasettaiah 2012	7	75	7	25	1.5%	0.33 [0.13 , 0.86]
Tolver 2012	4	36	4	37	0.8%	1.03 [0.28 , 3.80]
Tzeng 2000	6	38	9	40	1.6%	0.70 [0.28 , 1.78]
Wang 1999a	4	40	13	38	1.3%	0.29 [0.10 , 0.82]
Wang 1999b	5	38	18	38	1.8%	0.28 [0.11 , 0.67]
Wang 2000b	4	41	14	40	1.3%	0.28 [0.10 , 0.77]
Wang 2000c	3	44	2	14	0.5%	0.48 [0.09 , 2.57]
Yeo 2009	8	40	12	40	2.2%	0.67 [0.31 , 1.45]
Yuksek 2003	6	20	12	20	2.4%	0.50 [0.23 , 1.07]
Subtotal (95% CI)		**1285**		**1097**	**46.9%**	**0.43 [0.36 , 0.51]**
Total events:	158		334			
Heterogeneity: Tau² = 0.00; Chi² = 25.35, df = 30 (P = 0.71); I² = 0%						
Test for overall effect: Z = 9.68 (P < 0.00001)						
3.1.4 NA dose						
Eberhart 2006	10	75	24	76	3.1%	0.42 [0.22 , 0.82]
Subtotal (95% CI)		**75**		**76**	**3.1%**	**0.42 [0.22 , 0.82]**
Total events:	10		24			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.54 (P = 0.01)						
Total (95% CI)		**2615**		**2189**	**100.0%**	**0.50 [0.44 , 0.56]**
Total events:	372		636			
Heterogeneity: Tau² = 0.00; Chi² = 47.88, df = 49 (P = 0.52); I² = 0%						
Test for overall effect: Z = 11.74 (P < 0.00001)						
Test for subgroup differences: Chi² = 4.78, df = 3 (P = 0.19), I² = 37.3%						



Analysis 3.2. Comparison 3: Dexamethasone versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.2.1 High dose						
Bianchin 2007	0	36	0	37		Not estimable
Tarantino 2015	0	76	0	76		Not estimable
Subtotal (95% CI)		**112**		**113**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.2.2 NA dose						
Eberhart 2006	2	75	2	76	100.0%	1.01 [0.15 , 7.01]
Subtotal (95% CI)		**75**		**76**	**100.0%**	**1.01 [0.15 , 7.01]**
Total events:	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
Total (95% CI)		**187**		**189**	**100.0%**	**1.01 [0.15 , 7.01]**
Total events:	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
Test for subgroup differences: Not applicable						



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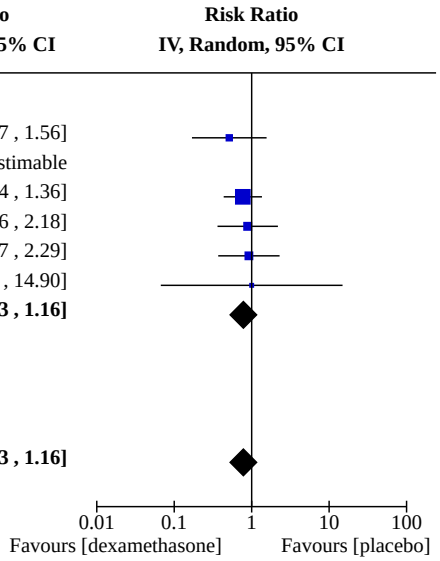
Analysis 3.3. Comparison 3: Dexamethasone versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.3.1 High dose						
Bianchin 2007	4	36	8	37	12.5%	0.51 [0.17 , 1.56]
Chen 2006	0	350	0	350		Not estimable
Murphy 2011a	16	60	17	49	47.7%	0.77 [0.44 , 1.36]
Tarantino 2015	8	76	9	76	19.1%	0.89 [0.36 , 2.18]
Tzeng 2000	7	38	8	40	18.5%	0.92 [0.37 , 2.29]
Yuksek 2003	1	20	1	20	2.1%	1.00 [0.07 , 14.90]
Subtotal (95% CI)		**580**		**572**	**100.0%**	**0.78 [0.53 , 1.16]**
Total events:	36		43			
Heterogeneity: Tau² = 0.00; Chi² = 0.79, df = 4 (P = 0.94); I² = 0%						
Test for overall effect: Z = 1.23 (P = 0.22)						
Total (95% CI)		**580**		**572**	**100.0%**	**0.78 [0.53 , 1.16]**
Total events:	36		43			
Heterogeneity: Tau² = 0.00; Chi² = 0.79, df = 4 (P = 0.94); I² = 0%						
Test for overall effect: Z = 1.23 (P = 0.22)						
Test for subgroup differences: Not applicable						



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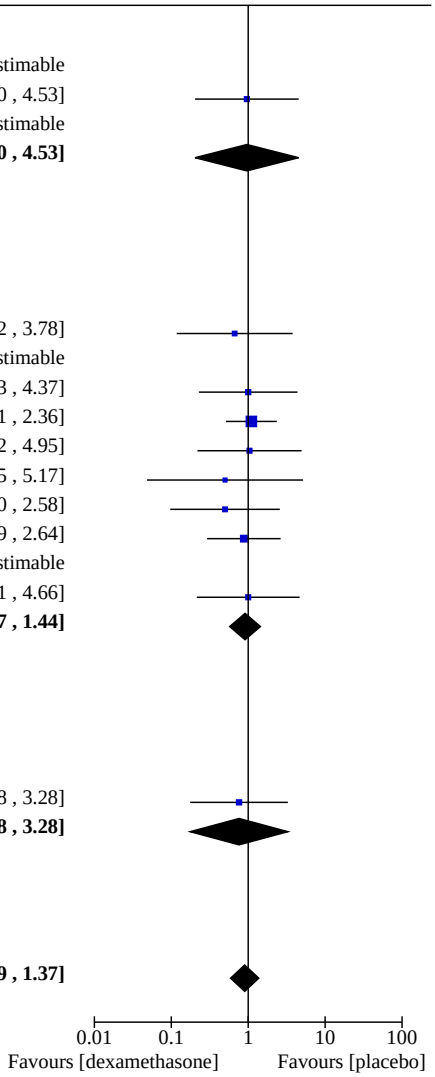
Analysis 3.4. Comparison 3: Dexamethasone versus placebo, Outcome 4: Headache

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.4.1 Recommended dose						
Khafagy 2010	0	30	0	30		Not estimable
Lee HS 2004	4	25	2	12	7.4%	0.96 [0.20 , 4.53]
Olajumoke 2013	0	48	0	48		Not estimable
Subtotal (95% CI)		**103**		**90**	**7.4%**	**0.96 [0.20 , 4.53]**
Total events:	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.05 (P = 0.96)						
3.4.2 High dose						
Bilgin 2010	2	40	3	40	5.9%	0.67 [0.12 , 3.78]
Chen 2006	0	350	0	350		Not estimable
Demirhan 2013	3	20	3	20	8.2%	1.00 [0.23 , 4.37]
Kim 2007	11	50	10	50	30.7%	1.10 [0.51 , 2.36]
Lee HS 2004	4	25	2	13	7.3%	1.04 [0.22 , 4.95]
Lopez Olaondo 1996	1	25	2	25	3.3%	0.50 [0.05 , 5.17]
Nesek Adam 2007	2	40	4	40	6.6%	0.50 [0.10 , 2.58]
Tzeng 2000	5	38	6	40	14.7%	0.88 [0.29 , 2.64]
Yang 2017	0	43	0	45		Not estimable
Yeo 2009	3	40	3	40	7.5%	1.00 [0.21 , 4.66]
Subtotal (95% CI)		**671**		**663**	**84.3%**	**0.91 [0.57 , 1.44]**
Total events:	31		33			
Heterogeneity: Tau² = 0.00; Chi² = 1.19, df = 7 (P = 0.99); I² = 0%						
Test for overall effect: Z = 0.40 (P = 0.69)						
3.4.3 NA dose						
Eberhart 2006	3	75	4	76	8.3%	0.76 [0.18 , 3.28]
Subtotal (95% CI)		**75**		**76**	**8.3%**	**0.76 [0.18 , 3.28]**
Total events:	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
Total (95% CI)		**849**		**829**	**100.0%**	**0.90 [0.59 , 1.37]**
Total events:	38		39			
Heterogeneity: Tau² = 0.00; Chi² = 1.25, df = 9 (P = 1.00); I² = 0%						
Test for overall effect: Z = 0.49 (P = 0.62)						
Test for subgroup differences: Chi² = 0.06, df = 2 (P = 0.97), I² = 0%						



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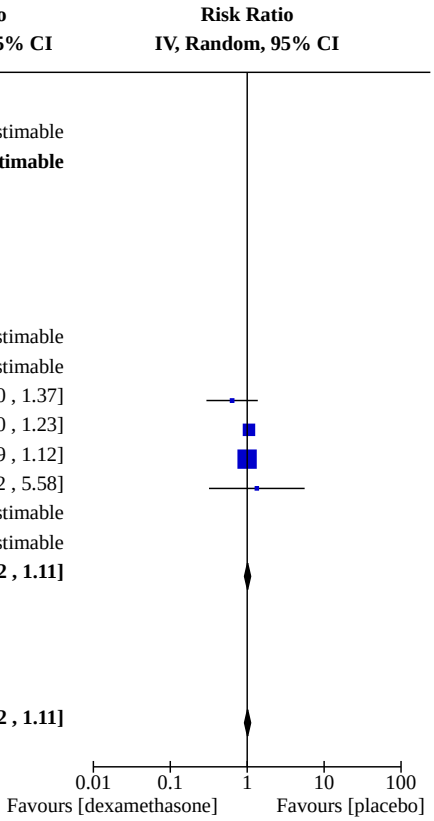
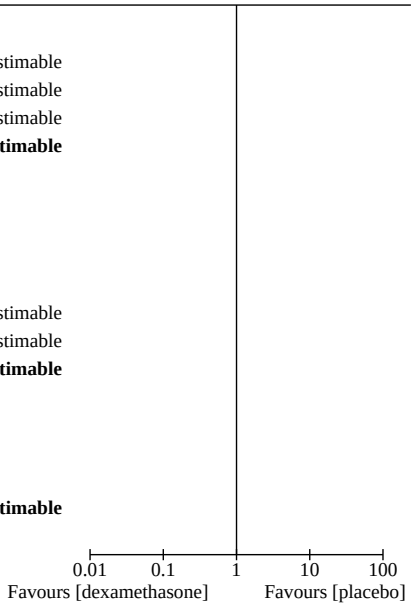
Analysis 3.5. Comparison 3: Dexamethasone versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.5.1 Recommended dose						
Olajumoke 2013	0	48	0	48		Not estimable
Subtotal (95% CI)		**48**		**48**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.5.2 High dose						
Bilgin 2010	0	40	0	40		Not estimable
Chen 2006	0	350	0	350		Not estimable
Lopez Olaondo 1996	7	25	11	25	1.4%	0.64 [0.30 , 1.37]
Mathiesen 2009	34	37	34	39	34.5%	1.05 [0.90 , 1.23]
Mathiesen 2011	40	43	42	45	63.7%	1.00 [0.89 , 1.12]
Nesek Adam 2007	4	40	3	40	0.4%	1.33 [0.32 , 5.58]
Yeo 2009	0	40	0	40		Not estimable
Yuksek 2003	0	20	0	20		Not estimable
Subtotal (95% CI)		**595**		**599**	**100.0%**	**1.01 [0.92 , 1.11]**
Total events:	85		90			
Heterogeneity: Tau² = 0.00; Chi² = 1.88, df = 3 (P = 0.60); I² = 0%						
Test for overall effect: Z = 0.24 (P = 0.81)						
Total (95% CI)		**643**		**647**	**100.0%**	**1.01 [0.92 , 1.11]**
Total events:	85		90			
Heterogeneity: Tau² = 0.00; Chi² = 1.88, df = 3 (P = 0.60); I² = 0%						
Test for overall effect: Z = 0.24 (P = 0.81)						
Test for subgroup differences: Not applicable						



Analysis 3.6. Comparison 3: Dexamethasone versus placebo, Outcome 6: Extrapyramidal symptoms

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.6.1 Recommended dose						
Chu 2008	0	74	0	75		Not estimable
Contreras Dominguez 2008	0	25	0	25		Not estimable
Lee Y 2001	0	45	0	22		Not estimable
Subtotal (95% CI)		**144**		**122**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.6.2 High dose						
Chen 2006	0	350	0	350		Not estimable
Lee Y 2001	0	43	0	22		Not estimable
Subtotal (95% CI)		**393**		**372**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**537**		**494**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



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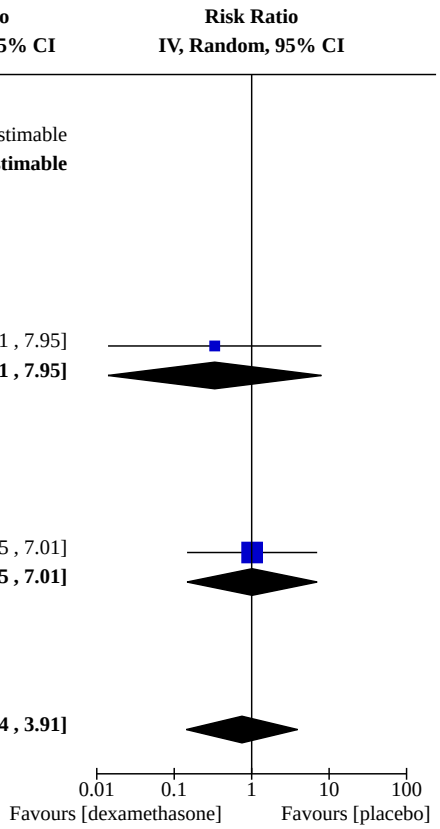
Analysis 3.7. Comparison 3: Dexamethasone versus placebo, Outcome 7: Constipation

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.7.1 Recommended dose						
Olajumoke 2013	0	48	0	48		Not estimable
Subtotal (95% CI)		**48**		**48**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.7.2 High dose						
Bilgin 2010	0	40	1	40	27.1%	0.33 [0.01 , 7.95]
Subtotal (95% CI)		**40**		**40**	**27.1%**	**0.33 [0.01 , 7.95]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
3.7.3 NA dose						
Eberhart 2006	2	75	2	76	72.9%	1.01 [0.15 , 7.01]
Subtotal (95% CI)		**75**		**76**	**72.9%**	**1.01 [0.15 , 7.01]**
Total events:	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
Total (95% CI)		**163**		**164**	**100.0%**	**0.75 [0.14 , 3.91]**
Total events:	2		3			
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 1 (P = 0.56); I² = 0%						
Test for overall effect: Z = 0.34 (P = 0.73)						
Test for subgroup differences: Chi² = 0.34, df = 1 (P = 0.56), I² = 0%						



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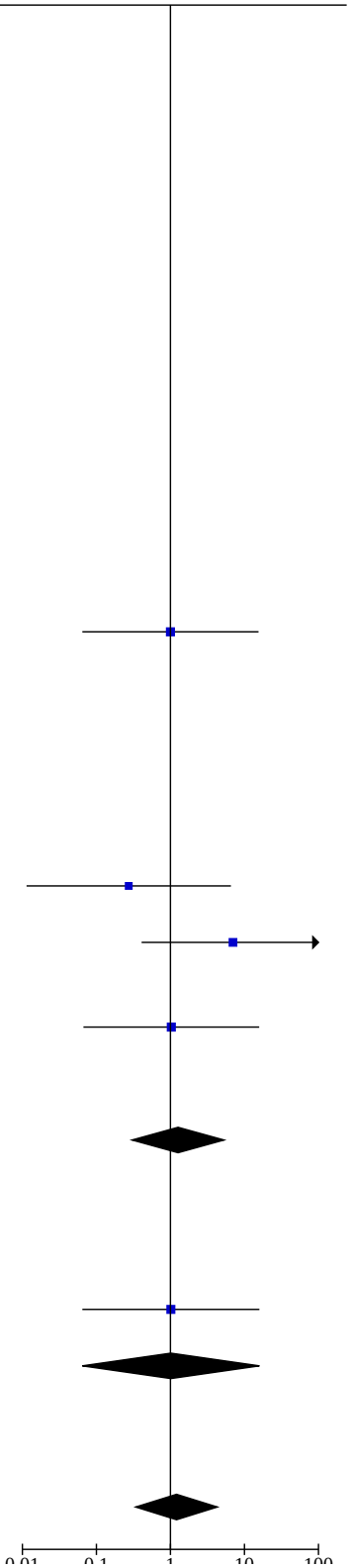
Analysis 3.8. Comparison 3: Dexamethasone versus placebo, Outcome 8: Postoperative wound infection

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.8.1 Low dose						
Wang 2000c	0	87	0	15		Not estimable
Subtotal (95% CI)		**87**		**15**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.8.2 Recommended dose						
Daabiss 2008	0	30	0	30		Not estimable
Ionescu 2014	0	22	0	20		Not estimable
Lee Y 2001	0	45	0	22		Not estimable
Thangaswamy 2010	0	18	0	9		Not estimable
Wang 2000c	0	43	0	14		Not estimable
Subtotal (95% CI)		**158**		**95**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.8.3 High dose						
Areeruk 2016	0	25	0	24		Not estimable
Bianchin 2007	0	36	0	37		Not estimable
Bisgaard 2003	1	44	1	44	21.4%	1.00 [0.06 , 15.49]
Chen 2006	0	350	0	350		Not estimable
Dimov 2004	0	143	0	146		Not estimable
Feo 2006	0	49	0	52		Not estimable
Feroci 2011	0	51	0	51		Not estimable
Fukami 2009	0	40	0	40		Not estimable
Lee Y 2001	0	43	0	22		Not estimable
Liu 2001	0	40	0	40		Not estimable
Manaa 2012	0	52	0	52		Not estimable
Murphy 2011a	0	60	1	49	15.9%	0.27 [0.01 , 6.56]
Sanchez Rodriguez 2010	0	105	0	105		Not estimable
Seki 2005	3	10	0	10	19.9%	7.00 [0.41 , 120.16]
Tarantino 2015	0	76	0	76		Not estimable
Thangaswamy 2010	0	19	0	9		Not estimable
Tolver 2012	1	36	1	37	21.5%	1.03 [0.07 , 15.82]
Wang 2000c	0	44	0	14		Not estimable
Worni 2008	0	37	0	35		Not estimable
Yeo 2009	0	40	0	40		Not estimable
Subtotal (95% CI)		**1300**		**1233**	**78.8%**	**1.27 [0.30 , 5.29]**
Total events:	5		3			
Heterogeneity: Tau² = 0.00; Chi² = 2.33, df = 3 (P = 0.51); I² = 0%						
Test for overall effect: Z = 0.32 (P = 0.75)						
3.8.4 NA dose						
Eberhart 2006	1	75	1	76	21.2%	1.01 [0.06 , 15.91]
Hefni 2014	0	120	0	40		Not estimable
Subtotal (95% CI)		**195**		**116**	**21.2%**	**1.01 [0.06 , 15.91]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
Total (95% CI)		**1740**		**1459**	**100.0%**	**1.21 [0.34 , 4.30]**
Total events:	6		4			
Heterogeneity: Tau² = 0.00; Chi² = 2.35, df = 4 (P = 0.67); I² = 0%						



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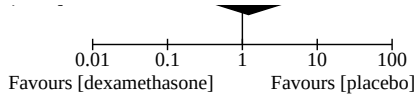
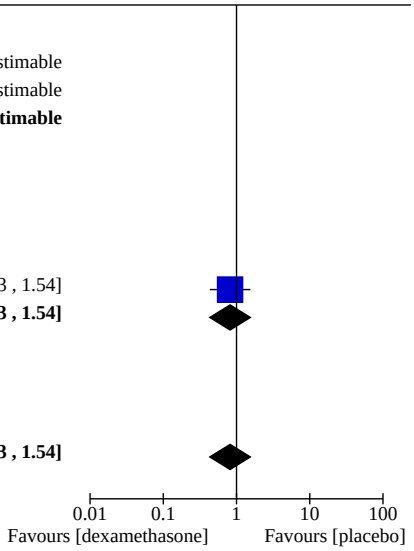
Analysis 3.8. (Continued)

Total events: 6 4
Heterogeneity: Tau² = 0.00; Chi² = 2.35, df = 4 (P = 0.67); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.89), I² = 0%



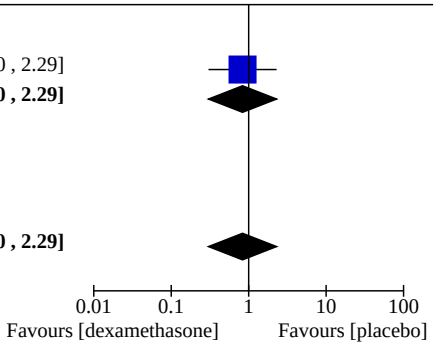
Analysis 3.9. Comparison 3: Dexamethasone versus placebo, Outcome 9: Arrhythmia

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.9.1 Recommended dose						
Cekmen 2003	0	15	0	15		Not estimable
Contreras Dominguez 2008	0	25	0	25		Not estimable
Subtotal (95% CI)		**40**		**40**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.9.2 High dose						
Murphy 2011a	14	60	14	49	100.0%	0.82 [0.43 , 1.54]
Subtotal (95% CI)		**60**		**49**	**100.0%**	**0.82 [0.43 , 1.54]**
Total events:	14		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.62 (P = 0.53)						
Total (95% CI)		**100**		**89**	**100.0%**	**0.82 [0.43 , 1.54]**
Total events:	14		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.62 (P = 0.53)						
Test for subgroup differences: Not applicable						



Analysis 3.10. Comparison 3: Dexamethasone versus placebo, Outcome 10: Visual disturbances

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.10.1 High dose						
Demirhan 2013	5	20	6	20	100.0%	0.83 [0.30 , 2.29]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**0.83 [0.30 , 2.29]**
Total events:	5		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.72)						
Total (95% CI)		**20**		**20**	**100.0%**	**0.83 [0.30 , 2.29]**
Total events:	5		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.72)						
Test for subgroup differences: Not applicable						



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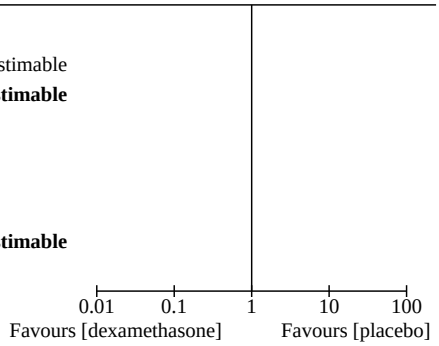
Analysis 3.11. Comparison 3: Dexamethasone versus placebo, Outcome 11: QT prolongation

Study or Subgroup	Dexamethasone Events	Dexamethasone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
3.11.1 Recommended dose						
Chu 2008	0	74	0	75		Not estimable
Subtotal (95% CI)		**74**		**75**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**74**		**75**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						

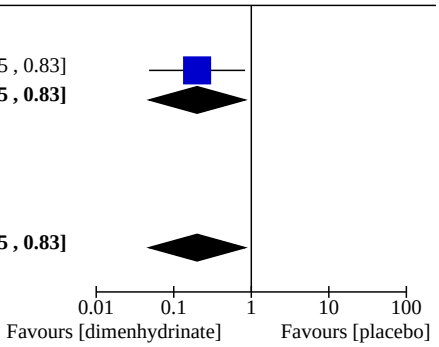


Comparison 4. Dimenhydrinate versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Vomiting within 0 to 24 hours	1	56	Risk Ratio (IV, Random, 95% CI)	0.20 [0.05, 0.83]
4.1.1 NA dose	1	56	Risk Ratio (IV, Random, 95% CI)	0.20 [0.05, 0.83]
4.2 Headache	1	50	Risk Ratio (IV, Random, 95% CI)	0.50 [0.05, 5.17]
4.2.1 NA dose	1	50	Risk Ratio (IV, Random, 95% CI)	0.50 [0.05, 5.17]
4.3 Sedation/drowsiness	1	50	Risk Ratio (IV, Random, 95% CI)	20.00 [2.90, 137.84]
4.3.1 NA dose	1	50	Risk Ratio (IV, Random, 95% CI)	20.00 [2.90, 137.84]

Analysis 4.1. Comparison 4: Dimenhydrinate versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Dimenhydrinate Events	Dimenhydrinate Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
4.1.1 NA dose						
Huseyinoglu 2016	2	28	10	28	100.0%	0.20 [0.05 , 0.83]
Subtotal (95% CI)		**28**		**28**	**100.0%**	**0.20 [0.05 , 0.83]**
Total events:	2		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.21 (P = 0.03)						
Total (95% CI)		**28**		**28**	**100.0%**	**0.20 [0.05 , 0.83]**
Total events:	2		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.21 (P = 0.03)						
Test for subgroup differences: Not applicable						



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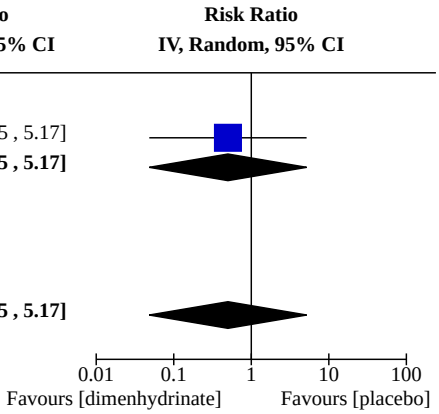
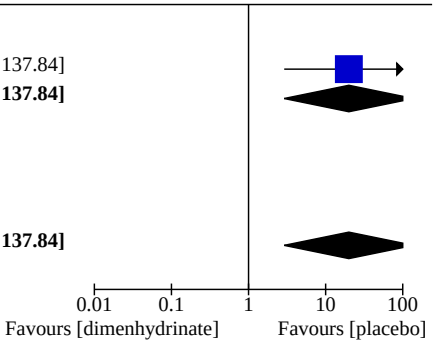
Analysis 4.2. Comparison 4: Dimenhydrinate versus placebo, Outcome 2: Headache

Study or Subgroup	Dimenhydrinate Events	Dimenhydrinate Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
4.2.1 NA dose						
Turhanoglu 1999	1	25	2	25	100.0%	0.50 [0.05 , 5.17]
Subtotal (95% CI)		**25**		**25**	**100.0%**	**0.50 [0.05 , 5.17]**
Total events:	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.58 (P = 0.56)						
Total (95% CI)		**25**		**25**	**100.0%**	**0.50 [0.05 , 5.17]**
Total events:	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.58 (P = 0.56)						
Test for subgroup differences: Not applicable						



Analysis 4.3. Comparison 4: Dimenhydrinate versus placebo, Outcome 3: Sedation/drowsiness

Study or Subgroup	Dimenhydrinate Events	Dimenhydrinate Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
4.3.1 NA dose						
Turhanoglu 1999	20	25	1	25	100.0%	20.00 [2.90 , 137.84]
Subtotal (95% CI)		**25**		**25**	**100.0%**	**20.00 [2.90 , 137.84]**
Total events:	20		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.04 (P = 0.002)						
Total (95% CI)		**25**		**25**	**100.0%**	**20.00 [2.90 , 137.84]**
Total events:	20		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.04 (P = 0.002)						
Test for subgroup differences: Not applicable						



Comparison 5. Dolasetron versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Vomiting within 0 to 24 hours	5	400	Risk Ratio (IV, Random, 95% CI)	0.46 [0.30, 0.70]
5.1.1 Recommended dose	5	368	Risk Ratio (IV, Random, 95% CI)	0.44 [0.27, 0.73]
5.1.2 High dose	1	32	Risk Ratio (IV, Random, 95% CI)	0.45 [0.12, 1.68]
5.2 Serious adverse events	3	1448	Risk Ratio (IV, Random, 95% CI)	0.34 [0.11, 1.04]
5.2.1 Recommended dose	1	81	Risk Ratio (IV, Random, 95% CI)	0.50 [0.03, 7.69]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.2.2 High dose	1	200	Risk Ratio (IV, Random, 95% CI)	0.05 [0.00, 1.28]
5.2.3 NA dose	2	1167	Risk Ratio (IV, Random, 95% CI)	0.43 [0.11, 1.61]
5.3 Any adverse event	1	203	Risk Ratio (IV, Random, 95% CI)	0.86 [0.66, 1.11]
5.3.1 Recommended dose	1	203	Risk Ratio (IV, Random, 95% CI)	0.86 [0.66, 1.11]
5.4 Headache	10	3990	Risk Ratio (IV, Random, 95% CI)	1.11 [0.90, 1.36]
5.4.1 Recommended dose	7	1120	Risk Ratio (IV, Random, 95% CI)	1.04 [0.81, 1.33]
5.4.2 High dose	4	1703	Risk Ratio (IV, Random, 95% CI)	1.17 [0.75, 1.82]
5.4.3 NA dose	2	1167	Risk Ratio (IV, Random, 95% CI)	1.62 [0.82, 3.23]
5.5 Sedation/drowsiness	5	2402	Risk Ratio (IV, Random, 95% CI)	0.80 [0.51, 1.25]
5.5.1 Recommended dose	4	699	Risk Ratio (IV, Random, 95% CI)	0.71 [0.42, 1.19]
5.5.2 High dose	4	1703	Risk Ratio (IV, Random, 95% CI)	1.14 [0.46, 2.80]
5.6 Extrapyramidal symptoms	3	288	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.6.1 Recommended dose	3	288	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.7 Arrhythmia	2	1184	Risk Ratio (IV, Random, 95% CI)	0.72 [0.38, 1.35]
5.7.1 Recommended dose	2	464	Risk Ratio (IV, Random, 95% CI)	0.84 [0.34, 2.10]
5.7.2 High dose	1	720	Risk Ratio (IV, Random, 95% CI)	0.62 [0.26, 1.49]

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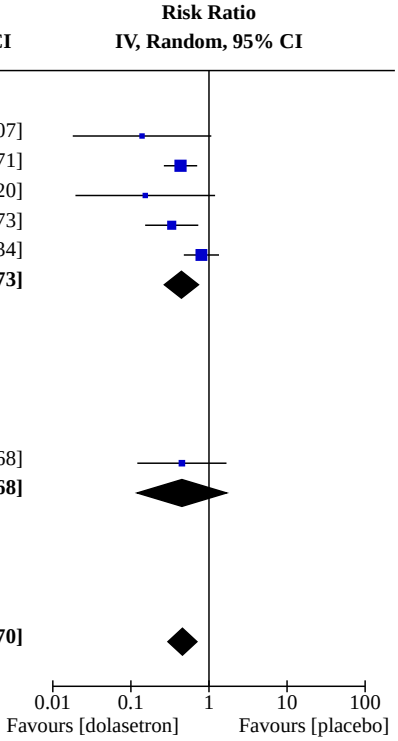
Analysis 5.1. Comparison 5: Dolasetron versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Dolasetron Events	Dolasetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
5.1.1 Recommended dose						
Eberhart 1999b	1	36	7	35	4.0%	0.14 [0.02 , 1.07]
Eberhart 2004	16	76	38	78	32.5%	0.43 [0.26 , 0.71]
Muller 2003	1	18	4	11	4.0%	0.15 [0.02 , 1.20]
Rusch 1999	6	32	18	32	19.5%	0.33 [0.15 , 0.73]
Veneziani 2006	12	25	15	25	31.0%	0.80 [0.48 , 1.34]
Subtotal (95% CI)		**187**		**181**	**91.1%**	**0.44 [0.27 , 0.73]**
Total events:	36		82			
Heterogeneity: Tau² = 0.13; Chi² = 7.30, df = 4 (P = 0.12); I² = 45%						
Test for overall effect: Z = 3.17 (P = 0.002)						
5.1.2 High dose						
Muller 2003	3	20	4	12	8.9%	0.45 [0.12 , 1.68]
Subtotal (95% CI)		**20**		**12**	**8.9%**	**0.45 [0.12 , 1.68]**
Total events:	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.23)						
Total (95% CI)		**207**		**193**	**100.0%**	**0.46 [0.30 , 0.70]**
Total events:	39		86			
Heterogeneity: Tau² = 0.08; Chi² = 7.32, df = 5 (P = 0.20); I² = 32%						
Test for overall effect: Z = 3.60 (P = 0.0003)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.98), I² = 0%						



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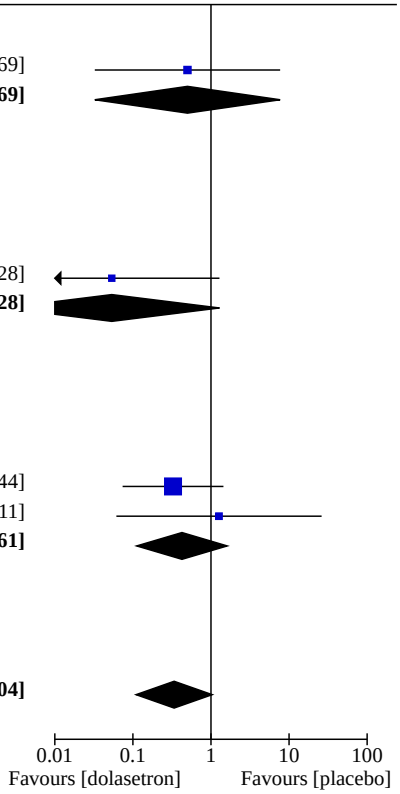
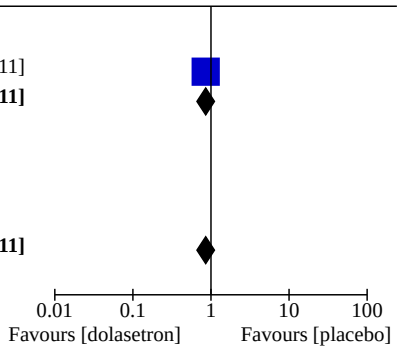
Analysis 5.2. Comparison 5: Dolasetron versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Dolasetron Events	Dolasetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
5.2.1 Recommended dose						
Diemunsch 1997	1	54	1	27	16.8%	0.50 [0.03 , 7.69]
Subtotal (95% CI)		**54**		**27**	**16.8%**	**0.50 [0.03 , 7.69]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						
5.2.2 High dose						
Diemunsch 1997	0	173	1	27	12.5%	0.05 [0.00 , 1.28]
Subtotal (95% CI)		**173**		**27**	**12.5%**	**0.05 [0.00 , 1.28]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.81 (P = 0.07)						
5.2.3 NA dose						
Diemunsch 1998	4	637	3	156	56.9%	0.33 [0.07 , 1.44]
Warriner 1997	2	299	0	75	13.7%	1.27 [0.06 , 26.11]
Subtotal (95% CI)		**936**		**231**	**70.7%**	**0.43 [0.11 , 1.61]**
Total events:	6		3			
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 1.26 (P = 0.21)						
Total (95% CI)		**1163**		**285**	**100.0%**	**0.34 [0.11 , 1.04]**
Total events:	7		5			
Heterogeneity: Tau² = 0.00; Chi² = 2.10, df = 3 (P = 0.55); I² = 0%						
Test for overall effect: Z = 1.90 (P = 0.06)						
Test for subgroup differences: Chi² = 1.48, df = 2 (P = 0.48), I² = 0%						



Analysis 5.3. Comparison 5: Dolasetron versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Dolasetron Events	Dolasetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
5.3.1 Recommended dose						
Joe 2009	50	101	59	102	100.0%	0.86 [0.66 , 1.11]
Subtotal (95% CI)		**101**		**102**	**100.0%**	**0.86 [0.66 , 1.11]**
Total events:	50		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.24)						
Total (95% CI)		**101**		**102**	**100.0%**	**0.86 [0.66 , 1.11]**
Total events:	50		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.24)						
Test for subgroup differences: Not applicable						



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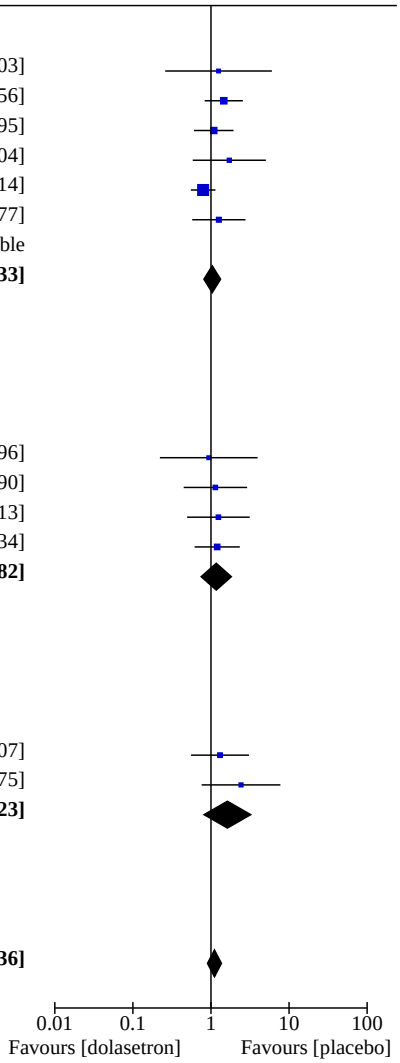
Analysis 5.4. Comparison 5: Dolasetron versus placebo, Outcome 4: Headache

Study or Subgroup	Dolasetron Events	Dolasetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
5.4.1 Recommended dose						
Diemunsch 1997	5	54	2	27	1.7%	1.25 [0.26 , 6.03]
Eberhart 1999b	18	36	12	35	13.3%	1.46 [0.83 , 2.56]
Eberhart 2004	18	76	17	78	12.4%	1.09 [0.61 , 1.95]
Graczyk 1997	14	159	4	78	3.6%	1.72 [0.58 , 5.04]
Joe 2009	33	101	42	102	31.9%	0.79 [0.55 , 1.14]
Philip 2000	20	206	8	104	6.8%	1.26 [0.58 , 2.77]
Rusch 1999	0	32	0	32		Not estimable
Subtotal (95% CI)		**664**		**456**	**69.8%**	**1.04 [0.81 , 1.33]**
Total events:	108		85			
Heterogeneity: Tau² = 0.00; Chi² = 4.65, df = 5 (P = 0.46); I² = 0%						
Test for overall effect: Z = 0.30 (P = 0.77)						
5.4.2 High dose						
Diemunsch 1997	12	173	2	27	2.0%	0.94 [0.22 , 3.96]
Graczyk 1997	23	319	5	79	4.8%	1.14 [0.45 , 2.90]
Korttila 1997	15	257	6	128	5.0%	1.25 [0.49 , 3.13]
Philip 2000	64	616	9	104	9.5%	1.20 [0.62 , 2.34]
Subtotal (95% CI)		**1365**		**338**	**21.3%**	**1.17 [0.75 , 1.82]**
Total events:	114		22			
Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 3 (P = 0.99); I² = 0%						
Test for overall effect: Z = 0.69 (P = 0.49)						
5.4.3 NA dose						
Diemunsch 1998	32	637	6	156	5.8%	1.31 [0.56 , 3.07]
Warriner 1997	29	299	3	75	3.1%	2.42 [0.76 , 7.75]
Subtotal (95% CI)		**936**		**231**	**8.9%**	**1.62 [0.82 , 3.23]**
Total events:	61		9			
Heterogeneity: Tau² = 0.00; Chi² = 0.71, df = 1 (P = 0.40); I² = 0%						
Test for overall effect: Z = 1.38 (P = 0.17)						
Total (95% CI)		**2965**		**1025**	**100.0%**	**1.11 [0.90 , 1.36]**
Total events:	283		116			
Heterogeneity: Tau² = 0.00; Chi² = 6.98, df = 11 (P = 0.80); I² = 0%						
Test for overall effect: Z = 0.98 (P = 0.33)						
Test for subgroup differences: Chi² = 1.51, df = 2 (P = 0.47), I² = 0%						



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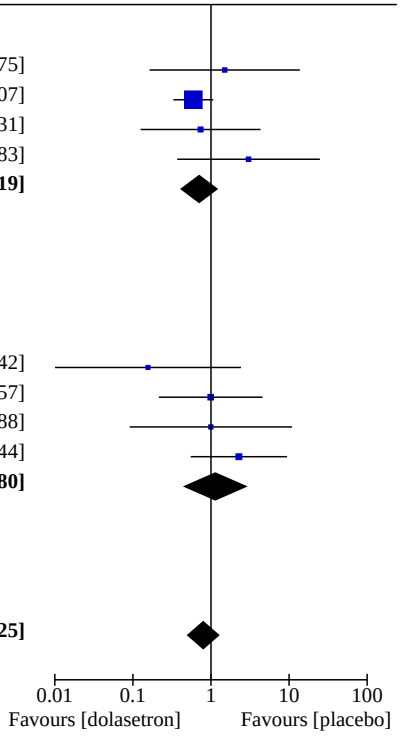
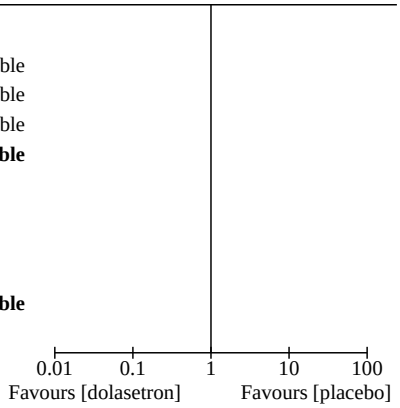
Analysis 5.5. Comparison 5: Dolasetron versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Dolasetron Events	Dolasetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
5.5.1 Recommended dose						
Diemunsch 1997	3	54	1	27	4.2%	1.50 [0.16 , 13.75]
Eberhart 1999b	11	36	18	35	59.3%	0.59 [0.33 , 1.07]
Graczyk 1997	3	159	2	78	6.6%	0.74 [0.13 , 4.31]
Philip 2000	6	206	1	104	4.6%	3.03 [0.37 , 24.83]
Subtotal (95% CI)		**455**		**244**	**74.7%**	**0.71 [0.42 , 1.19]**
Total events:	23		22			
Heterogeneity: Tau² = 0.00; Chi² = 2.62, df = 3 (P = 0.45); I² = 0%						
Test for overall effect: Z = 1.30 (P = 0.19)						
5.5.2 High dose						
Diemunsch 1997	1	173	1	27	2.7%	0.16 [0.01 , 2.42]
Graczyk 1997	8	319	2	79	8.8%	0.99 [0.21 , 4.57]
Korttila 1997	2	257	1	128	3.6%	1.00 [0.09 , 10.88]
Philip 2000	27	616	2	104	10.2%	2.28 [0.55 , 9.44]
Subtotal (95% CI)		**1365**		**338**	**25.3%**	**1.14 [0.46 , 2.80]**
Total events:	38		6			
Heterogeneity: Tau² = 0.00; Chi² = 2.98, df = 3 (P = 0.40); I² = 0%						
Test for overall effect: Z = 0.28 (P = 0.78)						
Total (95% CI)		**1820**		**582**	**100.0%**	**0.80 [0.51 , 1.25]**
Total events:	61		28			
Heterogeneity: Tau² = 0.00; Chi² = 6.39, df = 7 (P = 0.49); I² = 0%						
Test for overall effect: Z = 0.99 (P = 0.32)						
Test for subgroup differences: Chi² = 0.80, df = 1 (P = 0.37), I² = 0%						



Analysis 5.6. Comparison 5: Dolasetron versus placebo, Outcome 6: Extrapyramidal symptoms

Study or Subgroup	Dolasetron Events	Dolasetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
5.6.1 Recommended dose						
Eberhart 1999b	0	35	0	35		Not estimable
Eberhart 2004	0	76	0	78		Not estimable
Rusch 1999	0	32	0	32		Not estimable
Subtotal (95% CI)		**143**		**145**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**143**		**145**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



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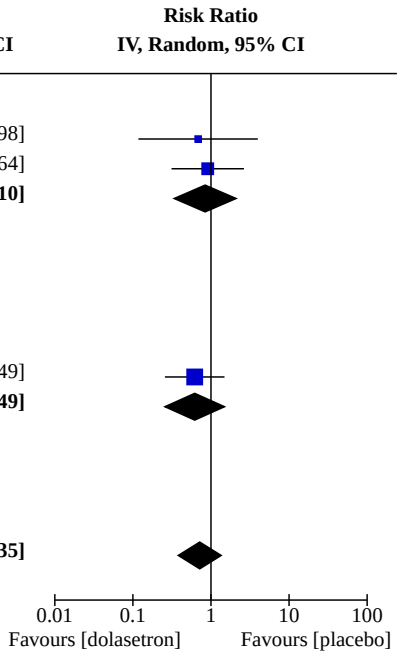
Analysis 5.7. Comparison 5: Dolasetron versus placebo, Outcome 7: Arrhythmia

Study or Subgroup	Dolasetron Events	Dolasetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
5.7.1 Recommended dose						
Eberhart 2004	2	76	3	78	12.9%	0.68 [0.12 , 3.98]
Philip 2000	9	206	5	104	35.2%	0.91 [0.31 , 2.64]
Subtotal (95% CI)		**282**		**182**	**48.1%**	**0.84 [0.34 , 2.10]**
Total events:	11		8			
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.79); I² = 0%						
Test for overall effect: Z = 0.37 (P = 0.71)						
5.7.2 High dose						
Philip 2000	22	616	6	104	51.9%	0.62 [0.26 , 1.49]
Subtotal (95% CI)		**616**		**104**	**51.9%**	**0.62 [0.26 , 1.49]**
Total events:	22		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.28)						
Total (95% CI)		**898**		**286**	**100.0%**	**0.72 [0.38 , 1.35]**
Total events:	33		14			
Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 2 (P = 0.86); I² = 0%						
Test for overall effect: Z = 1.03 (P = 0.30)						
Test for subgroup differences: Chi² = 0.23, df = 1 (P = 0.63), I² = 0%						



Comparison 6. Droperidol versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Vomiting within 0 to 24 hours	41	6156	Risk Ratio (IV, Random, 95% CI)	0.61 [0.53, 0.70]
6.1.1 Low dose	1	54	Risk Ratio (IV, Random, 95% CI)	1.67 [0.07, 39.03]
6.1.2 Recommended dose	28	3579	Risk Ratio (IV, Random, 95% CI)	0.64 [0.54, 0.75]
6.1.3 High dose	14	2331	Risk Ratio (IV, Random, 95% CI)	0.56 [0.43, 0.73]
6.1.4 NA dose	1	192	Risk Ratio (IV, Random, 95% CI)	0.47 [0.16, 1.33]
6.2 Serious adverse events	2	304	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.2.1 Recommended dose	2	304	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.3 Any adverse event	2	1622	Risk Ratio (IV, Random, 95% CI)	0.93 [0.84, 1.03]
6.3.1 Recommended dose	2	1622	Risk Ratio (IV, Random, 95% CI)	0.93 [0.84, 1.03]
6.4 Headache	22	3679	Risk Ratio (IV, Random, 95% CI)	0.76 [0.61, 0.95]
6.4.1 Low dose	2	148	Risk Ratio (IV, Random, 95% CI)	1.05 [0.55, 2.01]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.4.2 Recommended dose	14	2953	Risk Ratio (IV, Random, 95% CI)	0.78 [0.63, 0.95]
6.4.3 High dose	5	475	Risk Ratio (IV, Random, 95% CI)	1.09 [0.17, 6.98]
6.4.4 NA dose	1	103	Risk Ratio (IV, Random, 95% CI)	0.46 [0.23, 0.93]
6.5 Sedation/drowsiness	21	3739	Risk Ratio (IV, Random, 95% CI)	1.07 [0.99, 1.16]
6.5.1 Low dose	3	258	Risk Ratio (IV, Random, 95% CI)	0.85 [0.51, 1.39]
6.5.2 Recommended dose	12	2766	Risk Ratio (IV, Random, 95% CI)	1.01 [0.96, 1.06]
6.5.3 High dose	8	650	Risk Ratio (IV, Random, 95% CI)	1.45 [1.02, 2.06]
6.5.4 NA dose	1	65	Risk Ratio (IV, Random, 95% CI)	1.80 [1.08, 3.02]
6.6 Extrapyramidal symptoms	22	3270	Risk Ratio (IV, Random, 95% CI)	1.43 [0.87, 2.35]
6.6.1 Low dose	1	54	Risk Ratio (IV, Random, 95% CI)	4.34 [0.59, 32.17]
6.6.2 Recommended dose	9	1040	Risk Ratio (IV, Random, 95% CI)	1.40 [0.74, 2.66]
6.6.3 High dose	13	2176	Risk Ratio (IV, Random, 95% CI)	1.35 [0.47, 3.86]
6.7 Arrhythmia	7	659	Risk Ratio (IV, Random, 95% CI)	0.70 [0.12, 4.09]
6.7.1 Recommended dose	5	517	Risk Ratio (IV, Random, 95% CI)	0.70 [0.12, 4.09]
6.7.2 High dose	2	142	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.8 Visual disturbances	5	682	Risk Ratio (IV, Random, 95% CI)	0.70 [0.39, 1.24]
6.8.1 Recommended dose	3	406	Risk Ratio (IV, Random, 95% CI)	1.36 [0.46, 4.02]
6.8.2 High dose	2	276	Risk Ratio (IV, Random, 95% CI)	0.61 [0.19, 1.93]
6.9 QT prolongation	3	303	Risk Ratio (IV, Random, 95% CI)	1.31 [0.71, 2.42]
6.9.1 Recommended dose	3	303	Risk Ratio (IV, Random, 95% CI)	1.31 [0.71, 2.42]

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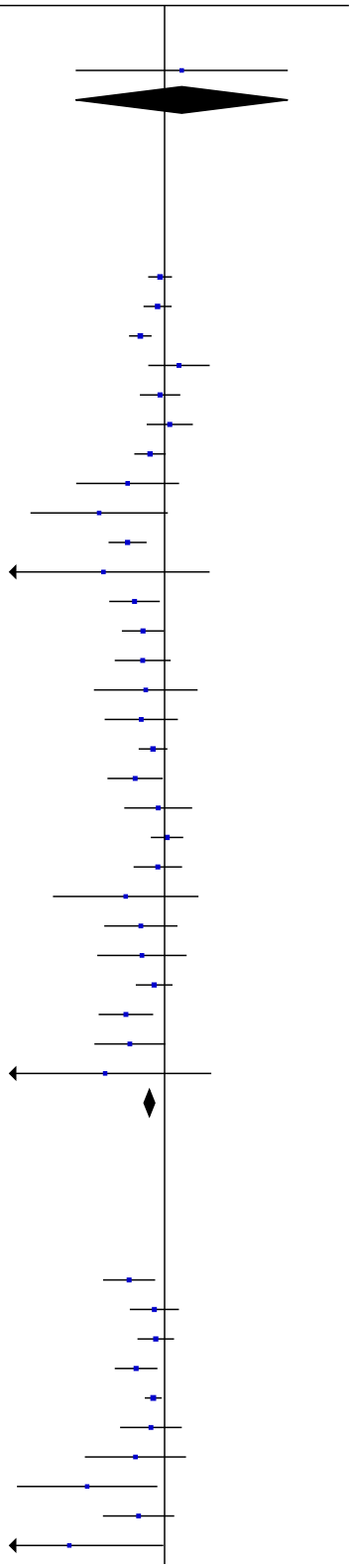
Analysis 6.1. Comparison 6: Droperidol versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.1.1 Low dose						
Foster 1996	1	35	0	19	0.2%	1.67 [0.07 , 39.03]
Subtotal (95% CI)		**35**		**19**	**0.2%**	**1.67 [0.07 , 39.03]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.32 (P = 0.75)						
6.1.2 Recommended dose						
Alkaissi 2004	42	165	48	165	4.8%	0.88 [0.61 , 1.25]
Apfel 2004-1	31	166	40	174	4.3%	0.81 [0.53 , 1.23]
Apfel 2004-2	42	335	89	345	5.0%	0.49 [0.35 , 0.68]
Badaoui 1998	7	19	6	25	1.7%	1.54 [0.62 , 3.82]
Badaoui 1999	14	50	16	50	3.0%	0.88 [0.48 , 1.60]
Beattie 1993	14	26	6	13	2.6%	1.17 [0.59 , 2.32]
Chu 2008	20	77	30	75	3.9%	0.65 [0.41 , 1.04]
Eberhart 1999a	2	35	6	35	0.7%	0.33 [0.07 , 1.54]
Eberhart 1999b	1	35	7	35	0.4%	0.14 [0.02 , 1.10]
Eberhart 2004	12	74	38	78	3.2%	0.33 [0.19 , 0.59]
Foster 1996	0	40	1	19	0.2%	0.16 [0.01 , 3.82]
Gan 1994	7	38	18	40	2.3%	0.41 [0.19 , 0.87]
Helmy 1999	10	40	19	40	2.9%	0.53 [0.28 , 0.99]
Joris 2003	6	50	23	100	2.0%	0.52 [0.23 , 1.20]
Kim 2000	2	21	5	30	0.7%	0.57 [0.12 , 2.67]
Kocamanoglu 2005	4	30	8	30	1.3%	0.50 [0.17 , 1.48]
Koivuranta 1997	51	193	19	51	4.2%	0.71 [0.46 , 1.09]
Korttila 1979	6	36	16	40	2.0%	0.42 [0.18 , 0.95]
Morin 1999	14	93	4	22	1.5%	0.83 [0.30 , 2.27]
Reihner 2000	23	69	22	71	3.8%	1.08 [0.66 , 1.74]
Rudra 2005	9	30	11	30	2.4%	0.82 [0.40 , 1.68]
Satomoto 2017	1	18	3	17	0.4%	0.31 [0.04 , 2.74]
Tzeng 2000	4	36	9	40	1.3%	0.49 [0.17 , 1.47]
Valanne 1985	3	49	6	50	0.9%	0.51 [0.14 , 1.93]
Veneziani 2006	11	25	15	25	3.3%	0.73 [0.42 , 1.27]
Wang 1999b	6	40	18	38	2.0%	0.32 [0.14 , 0.71]
Wang 2008	4	44	12	47	1.4%	0.36 [0.12 , 1.02]
White 2005-1	0	40	1	20	0.2%	0.17 [0.01 , 4.01]
Subtotal (95% CI)		**1874**		**1705**	**62.4%**	**0.64 [0.54 , 0.75]**
Total events:	346		496			
Heterogeneity: Tau² = 0.04; Chi² = 37.27, df = 27 (P = 0.09); I² = 28%						
Test for overall effect: Z = 5.58 (P < 0.00001)						
6.1.3 High dose						
Beattie 1993	9	48	7	13	2.2%	0.35 [0.16 , 0.76]
Bugedo 1999	10	60	14	62	2.4%	0.74 [0.36 , 1.53]
Ekinci 2011	10	20	13	20	3.4%	0.77 [0.45 , 1.32]
Guldogus 1994	6	15	14	15	2.8%	0.43 [0.23 , 0.81]
Hechler 2001	88	665	124	669	5.7%	0.71 [0.56 , 0.92]
Jellish 1995	6	34	9	34	1.7%	0.67 [0.27 , 1.67]
Mitsunari 2007	2	23	6	29	0.7%	0.42 [0.09 , 1.89]
Morin 1999	1	46	5	23	0.4%	0.10 [0.01 , 0.81]
Mortensen 1982	6	78	6	36	1.4%	0.46 [0.16 , 1.33]
Muller 2003	0	23	8	23	0.2%	0.06 [0.00 , 0.96]



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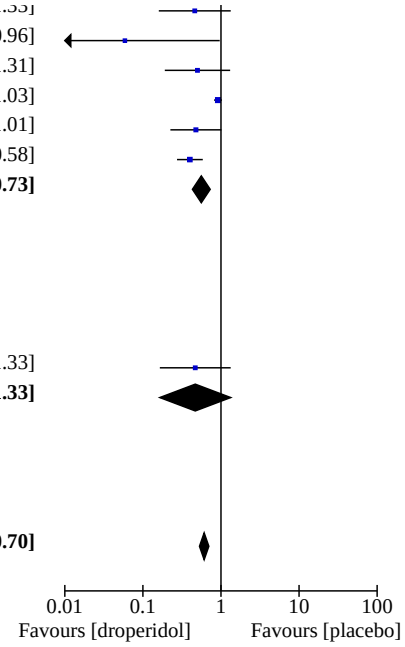
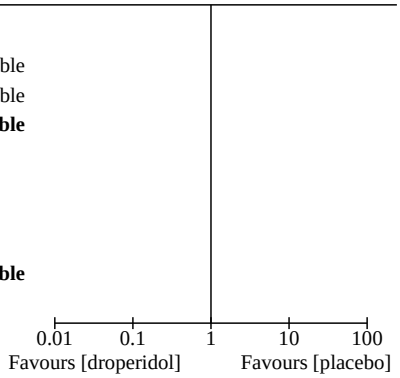
Analysis 6.1. (Continued)

Mortensen 1982	6	78	6	36	1.4%	0.40 [0.16 , 1.33]
Muller 2003	0	23	8	23	0.2%	0.06 [0.00 , 0.96]
Najeeb 2000	4	15	8	15	1.6%	0.50 [0.19 , 1.31]
Paech 1995	74	89	79	87	6.7%	0.92 [0.82 , 1.03]
Rusch 2002	7	33	16	36	2.3%	0.48 [0.22 , 1.01]
Zhu 2010	24	80	30	40	4.6%	0.40 [0.27 , 0.58]
Subtotal (95% CI)		**1229**		**1102**	**36.1%**	**0.56 [0.43 , 0.73]**
Total events:	247		339			
Heterogeneity: Tau² = 0.11; Chi² = 38.61, df = 13 (P = 0.0002); I² = 66%						
Test for overall effect: Z = 4.34 (P < 0.0001)						
6.1.4 NA dose						
Verhasselt 1988	7	137	6	55	1.4%	0.47 [0.16 , 1.33]
Subtotal (95% CI)		**137**		**55**	**1.4%**	**0.47 [0.16 , 1.33]**
Total events:	7		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.42 (P = 0.15)						
Total (95% CI)		**3275**		**2881**	**100.0%**	**0.61 [0.53 , 0.70]**
Total events:	601		841			
Heterogeneity: Tau² = 0.07; Chi² = 82.08, df = 43 (P = 0.0003); I² = 48%						
Test for overall effect: Z = 7.06 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.32, df = 3 (P = 0.73), I² = 0%						



Analysis 6.2. Comparison 6: Droperidol versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.2.1 Recommended dose						
Kocamanoglu 2005	0	30	0	30		Not estimable
Koivuranta 1997	0	193	0	51		Not estimable
Subtotal (95% CI)		**223**		**81**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**223**		**81**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



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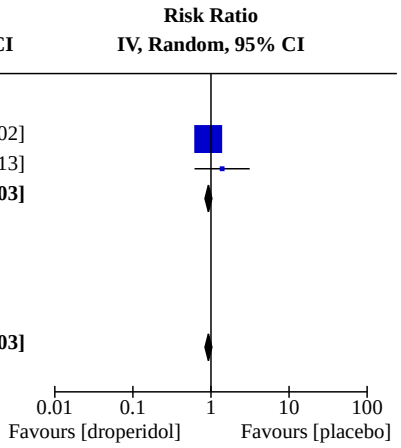
Analysis 6.3. Comparison 6: Droperidol versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.3.1 Recommended dose						
Fortney 1998	505	1028	276	518	98.5%	0.92 [0.83 , 1.02]
Tzeng 2000	10	36	8	40	1.5%	1.39 [0.62 , 3.13]
Subtotal (95% CI)		**1064**		**558**	**100.0%**	**0.93 [0.84 , 1.03]**
Total events:	515		284			
Heterogeneity: Tau² = 0.00; Chi² = 0.96, df = 1 (P = 0.33); I² = 0%						
Test for overall effect: Z = 1.45 (P = 0.15)						
Total (95% CI)		**1064**		**558**	**100.0%**	**0.93 [0.84 , 1.03]**
Total events:	515		284			
Heterogeneity: Tau² = 0.00; Chi² = 0.96, df = 1 (P = 0.33); I² = 0%						
Test for overall effect: Z = 1.45 (P = 0.15)						
Test for subgroup differences: Not applicable						



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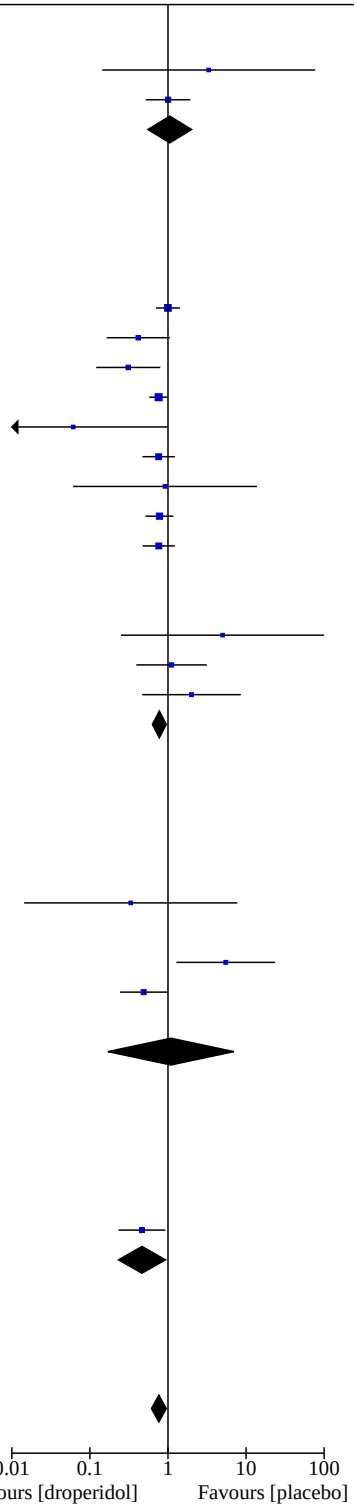
Analysis 6.4. Comparison 6: Droperidol versus placebo, Outcome 4: Headache

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.4.1 Low dose						
Kil 1999	1	18	0	20	0.5%	3.32 [0.14 , 76.60]
Millar 1987	19	72	10	38	7.1%	1.00 [0.52 , 1.93]
Subtotal (95% CI)		**90**		**58**	**7.6%**	**1.05 [0.55 , 2.01]**
Total events:	20		10			
Heterogeneity: Tau² = 0.00; Chi² = 0.53, df = 1 (P = 0.46); I² = 0%						
Test for overall effect: Z = 0.16 (P = 0.87)						
6.4.2 Recommended dose						
Alkaissi 2004	45	165	45	165	13.2%	1.00 [0.70 , 1.42]
Eberhart 1999b	5	35	12	35	4.3%	0.42 [0.16 , 1.06]
Eberhart 2004	5	74	17	78	4.2%	0.31 [0.12 , 0.80]
Fortney 1998	110	1028	73	518	15.2%	0.76 [0.58 , 1.00]
Kim 2000	0	21	11	30	0.6%	0.06 [0.00 , 0.99]
Koivuranta 1997	46	193	16	51	10.2%	0.76 [0.47 , 1.23]
Pertusa 1996	1	24	1	22	0.6%	0.92 [0.06 , 13.79]
Purhonen 1997	21	49	27	49	11.7%	0.78 [0.52 , 1.17]
Reihner 2000	20	69	27	71	10.3%	0.76 [0.47 , 1.22]
Rho 2001-1	0	20	0	20		Not estimable
Rho 2001-2	0	20	0	20		Not estimable
Rudra 2005	2	30	0	30	0.5%	5.00 [0.25 , 99.95]
Tzeng 2000	6	36	6	40	3.6%	1.11 [0.39 , 3.14]
White 2005-1	8	40	2	20	2.0%	2.00 [0.47 , 8.56]
Subtotal (95% CI)		**1804**		**1149**	**76.6%**	**0.78 [0.63 , 0.95]**
Total events:	269		237			
Heterogeneity: Tau² = 0.03; Chi² = 14.13, df = 11 (P = 0.23); I² = 22%						
Test for overall effect: Z = 2.44 (P = 0.01)						
6.4.3 High dose						
Ekinci 2011	0	20	1	20	0.5%	0.33 [0.01 , 7.72]
Jin 2013	0	60	0	30		Not estimable
Mazzarella 1988	11	50	2	50	2.0%	5.50 [1.28 , 23.56]
Paech 1995	10	89	20	87	6.6%	0.49 [0.24 , 0.98]
Rusch 2002	0	33	0	36		Not estimable
Subtotal (95% CI)		**252**		**223**	**9.1%**	**1.09 [0.17 , 6.98]**
Total events:	21		23			
Heterogeneity: Tau² = 1.93; Chi² = 8.90, df = 2 (P = 0.01); I² = 78%						
Test for overall effect: Z = 0.09 (P = 0.93)						
6.4.4 NA dose						
Prescott 1976	9	52	19	51	6.7%	0.46 [0.23 , 0.93]
Subtotal (95% CI)		**52**		**51**	**6.7%**	**0.46 [0.23 , 0.93]**
Total events:	9		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.17 (P = 0.03)						
Total (95% CI)		**2198**		**1481**	**100.0%**	**0.76 [0.61 , 0.95]**
Total events:	319		289			
Heterogeneity: Tau² = 0.06; Chi² = 26.59, df = 17 (P = 0.06); I² = 36%						
Test for overall effect: Z = 2.41 (P = 0.02)						
Test for subgroup differences: Chi² = 3.10, df = 3 (P = 0.38), I² = 3.2%						



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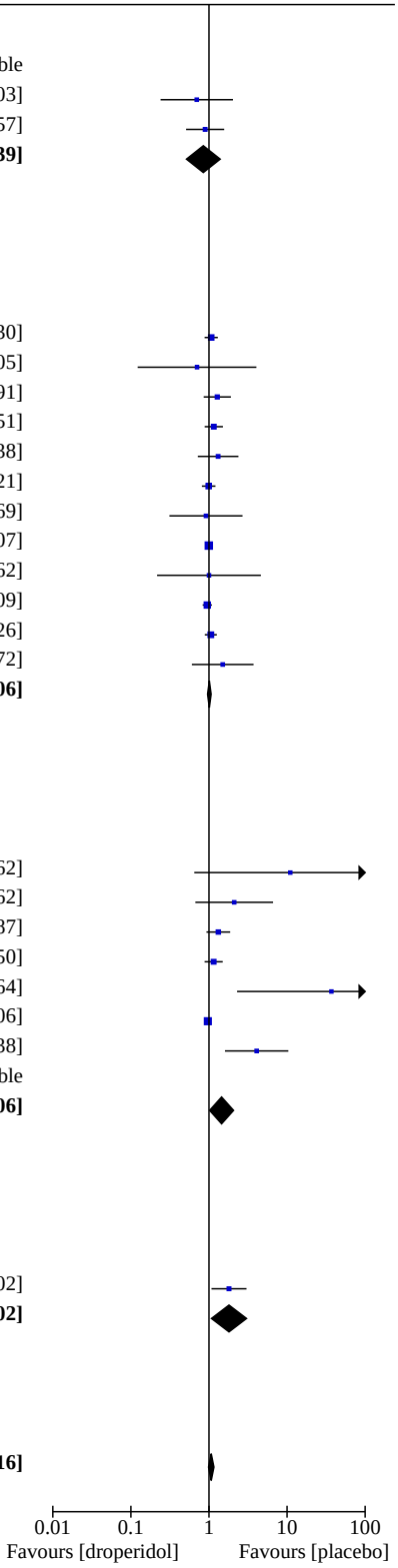
Analysis 6.5. Comparison 6: Droperidol versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.5.1 Low dose						
Kil 1999	0	18	0	20		Not estimable
Lim 1991	10	86	4	24	0.5%	0.70 [0.24 , 2.03]
Millar 1987	22	72	13	38	1.8%	0.89 [0.51 , 1.57]
Subtotal (95% CI)		**176**		**82**	**2.3%**	**0.85 [0.51 , 1.39]**
Total events:	32		17			
Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0%						
Test for overall effect: Z = 0.66 (P = 0.51)						
6.5.2 Recommended dose						
Alkaissi 2004	94	165	88	165	8.9%	1.07 [0.88 , 1.30]
Desilva 1995	2	55	3	58	0.2%	0.70 [0.12 , 4.05]
Eberhart 1999b	23	35	18	35	3.2%	1.28 [0.86 , 1.91]
Fortney 1998	151	1028	66	518	6.0%	1.15 [0.88 , 1.51]
Kim 2000	11	21	12	30	1.6%	1.31 [0.72 , 2.38]
Koivuranta 1997	135	193	36	51	8.6%	0.99 [0.81 , 1.21]
Lim 1991	9	59	4	24	0.5%	0.92 [0.31 , 2.69]
Morin 1999	91	93	22	22	16.7%	1.00 [0.93 , 1.07]
Nesek Adam 2004	3	35	3	35	0.3%	1.00 [0.22 , 4.62]
Rho 2001-1	19	20	20	20	12.2%	0.95 [0.83 , 1.09]
Rho 2001-2	19	20	18	20	9.8%	1.06 [0.88 , 1.26]
Tigerstedt 1988	9	32	6	32	0.7%	1.50 [0.60 , 3.72]
Subtotal (95% CI)		**1756**		**1010**	**68.8%**	**1.01 [0.96 , 1.06]**
Total events:	566		296			
Heterogeneity: Tau² = 0.00; Chi² = 5.41, df = 11 (P = 0.91); I² = 0%						
Test for overall effect: Z = 0.41 (P = 0.68)						
6.5.3 High dose						
Ekinci 2011	5	20	0	20	0.1%	11.00 [0.65 , 186.62]
Lim 1991	14	51	3	23	0.5%	2.10 [0.67 , 6.62]
Madej 1986a	31	48	25	51	4.0%	1.32 [0.93 , 1.87]
Madej 1986b	36	49	32	50	6.0%	1.15 [0.88 , 1.50]
Mazzarella 1988	18	50	0	50	0.1%	37.00 [2.29 , 597.64]
Morin 1999	44	46	23	23	15.4%	0.97 [0.88 , 1.06]
Sharma 2000	17	25	4	24	0.7%	4.08 [1.60 , 10.38]
Zhu 2010	0	80	0	40		Not estimable
Subtotal (95% CI)		**369**		**281**	**26.8%**	**1.45 [1.02 , 2.06]**
Total events:	165		87			
Heterogeneity: Tau² = 0.10; Chi² = 23.29, df = 6 (P = 0.0007); I² = 74%						
Test for overall effect: Z = 2.07 (P = 0.04)						
6.5.4 NA dose						
Rothenberg 1991	21	32	12	33	2.1%	1.80 [1.08 , 3.02]
Subtotal (95% CI)		**32**		**33**	**2.1%**	**1.80 [1.08 , 3.02]**
Total events:	21		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.24 (P = 0.03)						
Total (95% CI)		**2333**		**1406**	**100.0%**	**1.07 [0.99 , 1.16]**
Total events:	784		412			
Heterogeneity: Tau² = 0.01; Chi² = 34.17, df = 21 (P = 0.03); I² = 39%						
Test for overall effect: Z = 1.65 (P = 0.10)						



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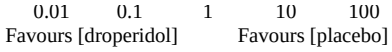
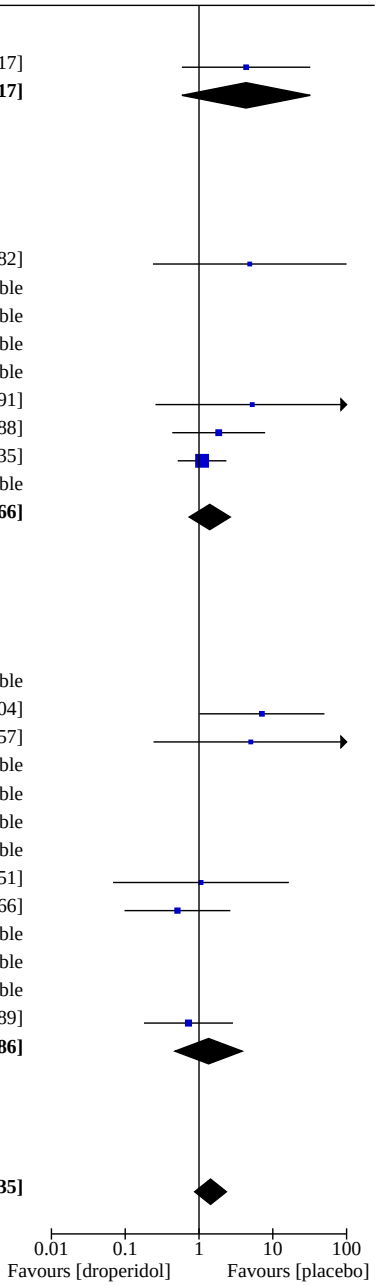
Analysis 6.5. (Continued)

Heterogeneity: Tau² = 0.01; Chi² = 34.17, df = 21 (P = 0.03); I² = 39%
Test for overall effect: Z = 1.65 (P = 0.10)
Test for subgroup differences: Chi² = 9.18, df = 3 (P = 0.03), I² = 67.3%



Analysis 6.6. Comparison 6: Droperidol versus placebo, Outcome 6: Extrapyramidal symptoms

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.6.1 Low dose						
Foster 1996	8	35	1	19	6.1%	4.34 [0.59 , 32.17]
Subtotal (95% CI)		**35**		**19**	**6.1%**	**4.34 [0.59 , 32.17]**
Total events:	8		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.44 (P = 0.15)						
6.6.2 Recommended dose						
Chu 2008	2	77	0	75	2.7%	4.87 [0.24 , 99.82]
Contreras Dominguez 2008	0	25	0	25		Not estimable
Desilva 1995	0	55	0	58		Not estimable
Eberhart 1999a	0	35	0	35		Not estimable
Eberhart 1999b	0	35	0	35		Not estimable
Eberhart 2004	2	74	0	78	2.7%	5.27 [0.26 , 107.91]
Koivuranta 1997	14	193	2	51	11.7%	1.85 [0.43 , 7.88]
Purhonen 1997	11	49	10	49	42.6%	1.10 [0.51 , 2.35]
Wang 2008	0	44	0	47		Not estimable
Subtotal (95% CI)		**587**		**453**	**59.7%**	**1.40 [0.74 , 2.66]**
Total events:	29		12			
Heterogeneity: Tau² = 0.00; Chi² = 1.92, df = 3 (P = 0.59); I² = 0%						
Test for overall effect: Z = 1.02 (P = 0.31)						
6.6.3 High dose						
Ekinci 2011	0	20	0	20		Not estimable
Foster 1996	15	40	1	19	6.5%	7.13 [1.01 , 50.04]
Hechler 2001	2	665	0	669	2.7%	5.03 [0.24 , 104.57]
Heinke 1996-1	0	42	0	43		Not estimable
Heinke 1996-2	0	38	0	39		Not estimable
Jin 2013	0	60	0	30		Not estimable
Lee IH 2007	0	34	0	36		Not estimable
Madej 1986a	1	48	1	51	3.3%	1.06 [0.07 , 16.51]
Madej 1986b	2	49	4	50	9.0%	0.51 [0.10 , 2.66]
Mitsunari 2007	0	23	0	29		Not estimable
Nakata 2002	0	27	0	26		Not estimable
Rusch 2002	0	33	0	36		Not estimable
Sharma 2000	3	25	4	24	12.8%	0.72 [0.18 , 2.89]
Subtotal (95% CI)		**1104**		**1072**	**34.2%**	**1.35 [0.47 , 3.86]**
Total events:	23		10			
Heterogeneity: Tau² = 0.41; Chi² = 5.62, df = 4 (P = 0.23); I² = 29%						
Test for overall effect: Z = 0.56 (P = 0.58)						
Total (95% CI)		**1726**		**1544**	**100.0%**	**1.43 [0.87 , 2.35]**
Total events:	60		23			
Heterogeneity: Tau² = 0.00; Chi² = 8.86, df = 9 (P = 0.45); I² = 0%						
Test for overall effect: Z = 1.42 (P = 0.16)						
Test for subgroup differences: Chi² = 1.17, df = 2 (P = 0.56), I² = 0%						



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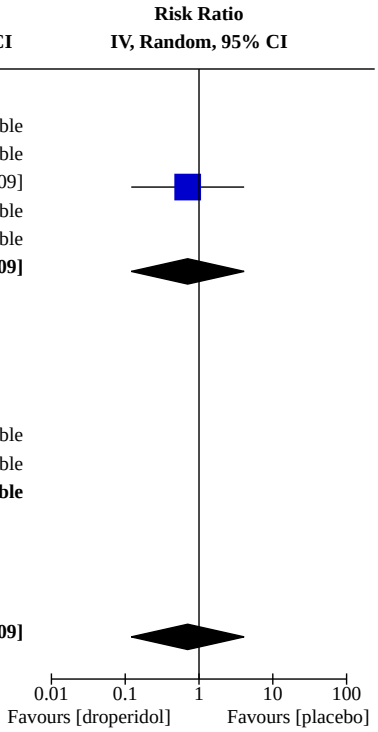
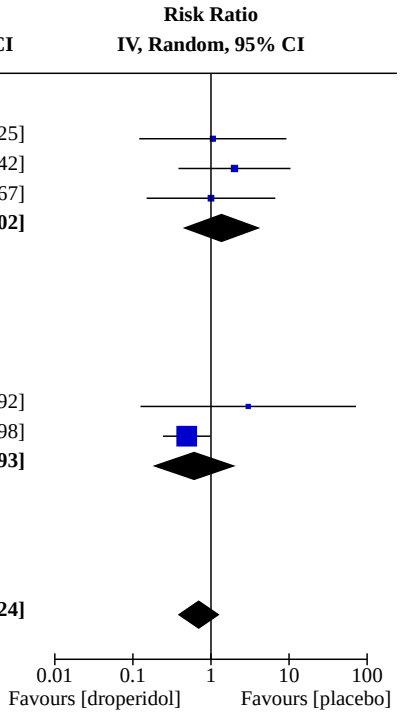
Analysis 6.7. Comparison 6: Droperidol versus placebo, Outcome 7: Arrhythmia

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.7.1 Recommended dose						
Chan 2006	0	98	0	97		Not estimable
Contreras Dominguez 2008	0	25	0	25		Not estimable
Eberhart 2004	2	74	3	78	100.0%	0.70 [0.12 , 4.09]
White 2005-1	0	40	0	20		Not estimable
White 2005-2	0	30	0	30		Not estimable
Subtotal (95% CI)		**267**		**250**	**100.0%**	**0.70 [0.12 , 4.09]**
Total events:	2		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.69)						
6.7.2 High dose						
Lee 2006	0	35	0	37		Not estimable
Lee IH 2007	0	34	0	36		Not estimable
Subtotal (95% CI)		**69**		**73**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**336**		**323**	**100.0%**	**0.70 [0.12 , 4.09]**
Total events:	2		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.69)						
Test for subgroup differences: Not applicable						



Analysis 6.8. Comparison 6: Droperidol versus placebo, Outcome 8: Visual disturbances

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.8.1 Recommended dose						
Koivuranta 1997	4	193	1	51	7.1%	1.06 [0.12 , 9.25]
Purhonen 1997	4	49	2	49	12.2%	2.00 [0.38 , 10.42]
Tigerstedt 1988	2	32	2	32	9.3%	1.00 [0.15 , 6.67]
Subtotal (95% CI)		**274**		**132**	**28.6%**	**1.36 [0.46 , 4.02]**
Total events:	10		5			
Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 2 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.56 (P = 0.57)						
6.8.2 High dose						
Mazzarella 1988	1	50	0	50	3.3%	3.00 [0.13 , 71.92]
Paech 1995	10	89	20	87	68.1%	0.49 [0.24 , 0.98]
Subtotal (95% CI)		**139**		**137**	**71.4%**	**0.61 [0.19 , 1.93]**
Total events:	11		20			
Heterogeneity: Tau² = 0.27; Chi² = 1.20, df = 1 (P = 0.27); I² = 16%						
Test for overall effect: Z = 0.84 (P = 0.40)						
Total (95% CI)		**413**		**269**	**100.0%**	**0.70 [0.39 , 1.24]**
Total events:	21		25			
Heterogeneity: Tau² = 0.00; Chi² = 3.65, df = 4 (P = 0.46); I² = 0%						
Test for overall effect: Z = 1.23 (P = 0.22)						
Test for subgroup differences: Chi² = 1.00, df = 1 (P = 0.32), I² = 0.1%						



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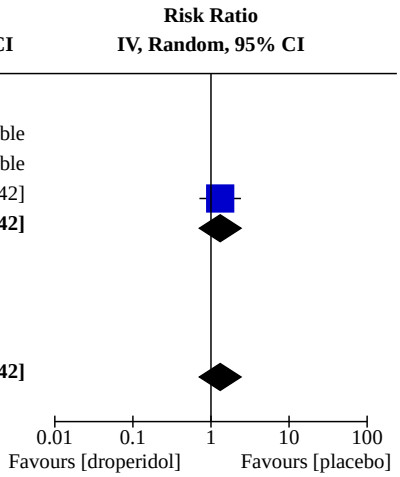
Analysis 6.9. Comparison 6: Droperidol versus placebo, Outcome 9: QT prolongation

Study or Subgroup	Droperidol Events	Droperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
6.9.1 Recommended dose						
Chu 2008	0	77	0	75		Not estimable
Wang 2008	0	44	0	47		Not estimable
White 2005-1	21	40	8	20	100.0%	1.31 [0.71 , 2.42]
Subtotal (95% CI)		**161**		**142**	**100.0%**	**1.31 [0.71 , 2.42]**
Total events:	21		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.87 (P = 0.38)						
Total (95% CI)		**161**		**142**	**100.0%**	**1.31 [0.71 , 2.42]**
Total events:	21		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.87 (P = 0.38)						
Test for subgroup differences: Not applicable						



Comparison 7. Granisetron versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Vomiting within 0 to 24 hours	16	2270	Risk Ratio (IV, Random, 95% CI)	0.49 [0.39, 0.62]
7.1.1 Low dose	3	419	Risk Ratio (IV, Random, 95% CI)	0.82 [0.68, 0.99]
7.1.2 Recommended dose	14	1811	Risk Ratio (IV, Random, 95% CI)	0.44 [0.34, 0.56]
7.1.3 High dose	1	40	Risk Ratio (IV, Random, 95% CI)	0.24 [0.10, 0.58]
7.2 Serious adverse events	2	401	Risk Ratio (IV, Random, 95% CI)	1.57 [0.06, 38.32]
7.2.1 Recommended dose	2	401	Risk Ratio (IV, Random, 95% CI)	1.57 [0.06, 38.32]
7.3 Any adverse event	6	699	Risk Ratio (IV, Random, 95% CI)	0.92 [0.81, 1.06]
7.3.1 Low dose	1	121	Risk Ratio (IV, Random, 95% CI)	0.93 [0.80, 1.08]
7.3.2 Recommended dose	3	478	Risk Ratio (IV, Random, 95% CI)	0.92 [0.66, 1.29]
7.3.3 High dose	1	40	Risk Ratio (IV, Random, 95% CI)	0.80 [0.25, 2.55]
7.3.4 NA dose	1	60	Risk Ratio (IV, Random, 95% CI)	0.83 [0.28, 2.44]
7.4 Headache	15	1639	Risk Ratio (IV, Random, 95% CI)	1.28 [1.03, 1.61]
7.4.1 Low dose	1	121	Risk Ratio (IV, Random, 95% CI)	1.98 [0.63, 6.25]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.4.2 Recommended dose	12	1418	Risk Ratio (IV, Random, 95% CI)	1.23 [0.95, 1.60]
7.4.3 High dose	1	40	Risk Ratio (IV, Random, 95% CI)	0.50 [0.05, 5.08]
7.4.4 NA dose	1	60	Risk Ratio (IV, Random, 95% CI)	0.50 [0.05, 5.22]
7.5 Sedation/drowsiness	9	850	Risk Ratio (IV, Random, 95% CI)	1.08 [0.89, 1.30]
7.5.1 Recommended dose	7	750	Risk Ratio (IV, Random, 95% CI)	1.08 [0.89, 1.30]
7.5.2 High dose	1	40	Risk Ratio (IV, Random, 95% CI)	3.00 [0.13, 69.52]
7.5.3 NA dose	1	60	Risk Ratio (IV, Random, 95% CI)	1.00 [0.07, 15.26]
7.6 Extrapyramidal symptoms	5	330	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.6.1 Recommended dose	5	330	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.7 Constipation	3	230	Risk Ratio (IV, Random, 95% CI)	0.61 [0.20, 1.90]
7.7.1 Recommended dose	3	230	Risk Ratio (IV, Random, 95% CI)	0.61 [0.20, 1.90]
7.8 Arrhythmia	1	50	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.8.1 Recommended dose	1	50	Risk Ratio (IV, Random, 95% CI)	Not estimable

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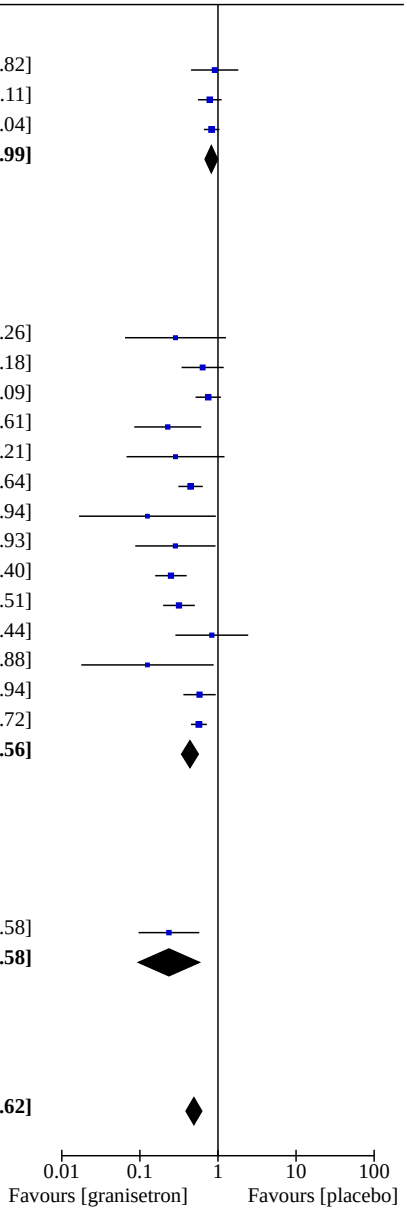
Analysis 7.1. Comparison 7: Granisetron versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Granisetron Events	Granisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
7.1.1 Low dose						
DAngelo 2005	22	91	8	30	5.5%	0.91 [0.45 , 1.82]
Mikawa 1997	44	80	14	20	8.7%	0.79 [0.55 , 1.11]
Wilson 1996	73	132	44	66	9.9%	0.83 [0.66 , 1.04]
Subtotal (95% CI)		**303**		**116**	**24.1%**	**0.82 [0.68 , 0.99]**
Total events:	139		66			
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 2 (P = 0.93); I² = 0%						
Test for overall effect: Z = 2.08 (P = 0.04)						
7.1.2 Recommended dose						
Aghadavoudi 2008	2	30	7	30	2.0%	0.29 [0.06 , 1.26]
Akkaya 2001	7	15	11	15	6.1%	0.64 [0.34 , 1.18]
Alkaissi 2004	36	165	48	165	8.5%	0.75 [0.52 , 1.09]
Choi 1999	5	80	11	40	3.6%	0.23 [0.08 , 0.61]
Erhan 2008	2	20	7	20	2.1%	0.29 [0.07 , 1.21]
Hanaoka 2004	39	208	45	107	8.6%	0.45 [0.31 , 0.64]
Kocamanoglu 2005	1	30	8	30	1.2%	0.13 [0.02 , 0.94]
Lee SY 2002	3	36	12	41	2.8%	0.28 [0.09 , 0.93]
Mikawa 1995	16	80	32	40	7.6%	0.25 [0.16 , 0.40]
Mikawa 1997	19	80	15	20	7.5%	0.32 [0.20 , 0.51]
Moussa 2007	5	30	6	30	3.2%	0.83 [0.28 , 2.44]
Najeeb 2000	1	15	8	15	1.2%	0.13 [0.02 , 0.88]
Tseng 2006	18	70	31	70	7.4%	0.58 [0.36 , 0.94]
Wilson 1996	98	262	44	67	9.8%	0.57 [0.45 , 0.72]
Subtotal (95% CI)		**1121**		**690**	**71.8%**	**0.44 [0.34 , 0.56]**
Total events:	252		285			
Heterogeneity: Tau² = 0.09; Chi² = 28.14, df = 13 (P = 0.009); I² = 54%						
Test for overall effect: Z = 6.60 (P < 0.00001)						
7.1.3 High dose						
Dua 2004	4	20	17	20	4.1%	0.24 [0.10 , 0.58]
Subtotal (95% CI)		**20**		**20**	**4.1%**	**0.24 [0.10 , 0.58]**
Total events:	4		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.17 (P = 0.002)						
Total (95% CI)		**1444**		**826**	**100.0%**	**0.49 [0.39 , 0.62]**
Total events:	395		368			
Heterogeneity: Tau² = 0.13; Chi² = 52.43, df = 17 (P < 0.0001); I² = 68%						
Test for overall effect: Z = 6.03 (P < 0.00001)						
Test for subgroup differences: Chi² = 21.05, df = 2 (P < 0.0001), I² = 90.5%						



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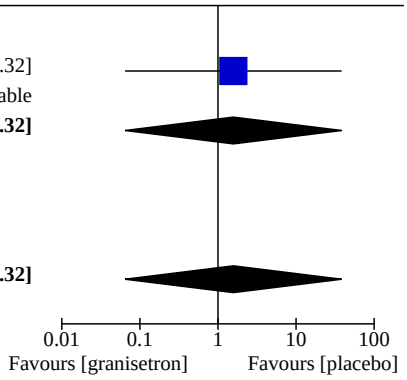
Analysis 7.2. Comparison 7: Granisetron versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Granisetron Events	Granisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
7.2.1 Recommended dose						
Hanaoka 2004	1	224	0	117	100.0%	1.57 [0.06 , 38.32]
Kocamanoglu 2005	0	30	0	30		Not estimable
Subtotal (95% CI)		**254**		**147**	**100.0%**	**1.57 [0.06 , 38.32]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
Total (95% CI)		**254**		**147**	**100.0%**	**1.57 [0.06 , 38.32]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
Test for subgroup differences: Not applicable						



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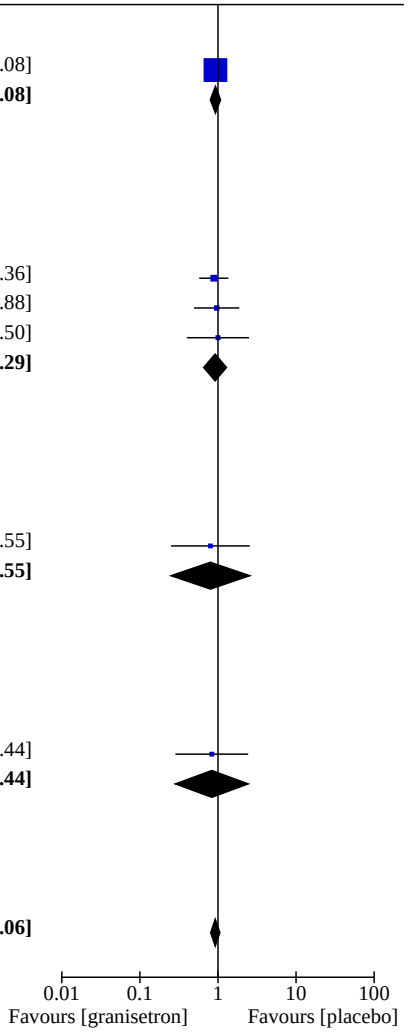
Analysis 7.3. Comparison 7: Granisetron versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Granisetron Events	Granisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
7.3.1 Low dose						
DAngelo 2005	76	91	27	30	80.9%	0.93 [0.80 , 1.08]
Subtotal (95% CI)		**91**		**30**	**80.9%**	**0.93 [0.80 , 1.08]**
Total events:	76		27			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						
7.3.2 Recommended dose						
Hanaoka 2004	44	224	26	117	9.9%	0.88 [0.57 , 1.36]
Lee SY 2001	11	36	13	41	4.1%	0.96 [0.49 , 1.88]
Moussa 2007	7	30	7	30	2.2%	1.00 [0.40 , 2.50]
Subtotal (95% CI)		**290**		**188**	**16.1%**	**0.92 [0.66 , 1.29]**
Total events:	62		46			
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 2 (P = 0.96); I² = 0%						
Test for overall effect: Z = 0.49 (P = 0.62)						
7.3.3 High dose						
Dua 2004	4	20	5	20	1.4%	0.80 [0.25 , 2.55]
Subtotal (95% CI)		**20**		**20**	**1.4%**	**0.80 [0.25 , 2.55]**
Total events:	4		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.71)						
7.3.4 NA dose						
Bhatnagar 2007	5	30	6	30	1.6%	0.83 [0.28 , 2.44]
Subtotal (95% CI)		**30**		**30**	**1.6%**	**0.83 [0.28 , 2.44]**
Total events:	5		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.33 (P = 0.74)						
Total (95% CI)		**431**		**268**	**100.0%**	**0.92 [0.81 , 1.06]**
Total events:	147		84			
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 5 (P = 1.00); I² = 0%						
Test for overall effect: Z = 1.16 (P = 0.25)						
Test for subgroup differences: Chi² = 0.10, df = 3 (P = 0.99), I² = 0%						



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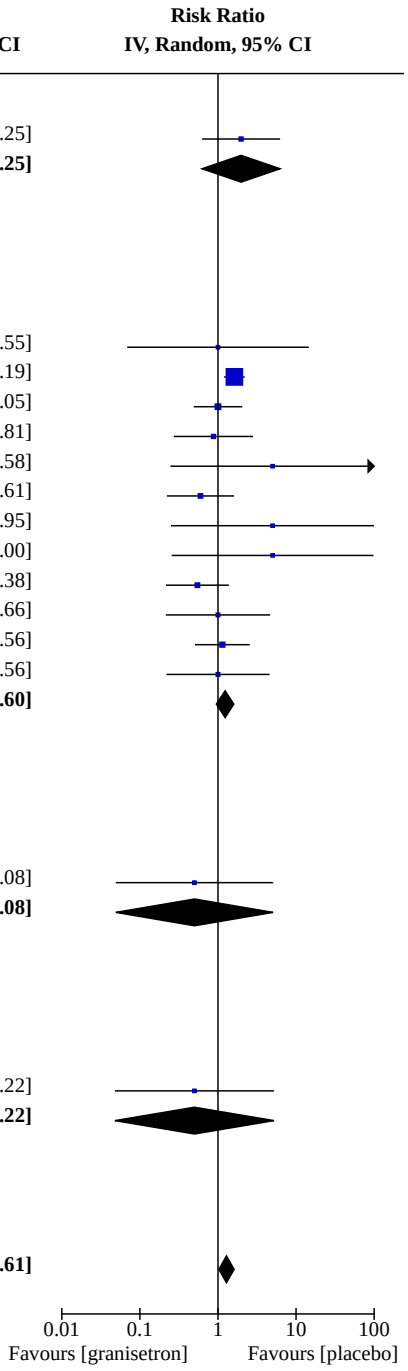
Analysis 7.4. Comparison 7: Granisetron versus placebo, Outcome 4: Headache

Study or Subgroup	Granisetron Events	Granisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
7.4.1 Low dose						
DAngelo 2005	18	91	3	30	3.8%	1.98 [0.63 , 6.25]
Subtotal (95% CI)		**91**		**30**	**3.8%**	**1.98 [0.63 , 6.25]**
Total events:	18		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.25)						
7.4.2 Recommended dose						
Akkaya 2001	1	15	1	15	0.7%	1.00 [0.07 , 14.55]
Alkaissi 2004	73	165	45	165	55.3%	1.62 [1.20 , 2.19]
Bestas 2007	10	30	10	30	9.9%	1.00 [0.49 , 2.05]
Choi 1999	7	80	4	40	3.7%	0.88 [0.27 , 2.81]
Dubey 2003	2	50	0	50	0.6%	5.00 [0.25 , 101.58]
Hanaoka 2004	8	224	7	117	5.2%	0.60 [0.22 , 1.61]
Heidari 2015a	2	30	0	30	0.6%	5.00 [0.25 , 99.95]
Khan 2005	2	20	0	20	0.6%	5.00 [0.26 , 98.00]
Khan 2006	6	60	11	60	5.9%	0.55 [0.22 , 1.38]
Kim JE 2005	3	40	3	40	2.1%	1.00 [0.21 , 4.66]
Lee SY 2002	9	36	9	41	7.7%	1.14 [0.51 , 2.56]
Moussa 2007	3	30	3	30	2.2%	1.00 [0.22 , 4.56]
Subtotal (95% CI)		**780**		**638**	**94.3%**	**1.23 [0.95 , 1.60]**
Total events:	126		93			
Heterogeneity: Tau² = 0.01; Chi² = 11.45, df = 11 (P = 0.41); I² = 4%						
Test for overall effect: Z = 1.60 (P = 0.11)						
7.4.3 High dose						
Dua 2004	1	20	2	20	0.9%	0.50 [0.05 , 5.08]
Subtotal (95% CI)		**20**		**20**	**0.9%**	**0.50 [0.05 , 5.08]**
Total events:	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
7.4.4 NA dose						
Bhatnagar 2007	1	30	2	30	0.9%	0.50 [0.05 , 5.22]
Subtotal (95% CI)		**30**		**30**	**0.9%**	**0.50 [0.05 , 5.22]**
Total events:	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.58 (P = 0.56)						
Total (95% CI)		**921**		**718**	**100.0%**	**1.28 [1.03 , 1.61]**
Total events:	146		100			
Heterogeneity: Tau² = 0.00; Chi² = 13.25, df = 14 (P = 0.51); I² = 0%						
Test for overall effect: Z = 2.19 (P = 0.03)						
Test for subgroup differences: Chi² = 1.80, df = 3 (P = 0.62), I² = 0%						



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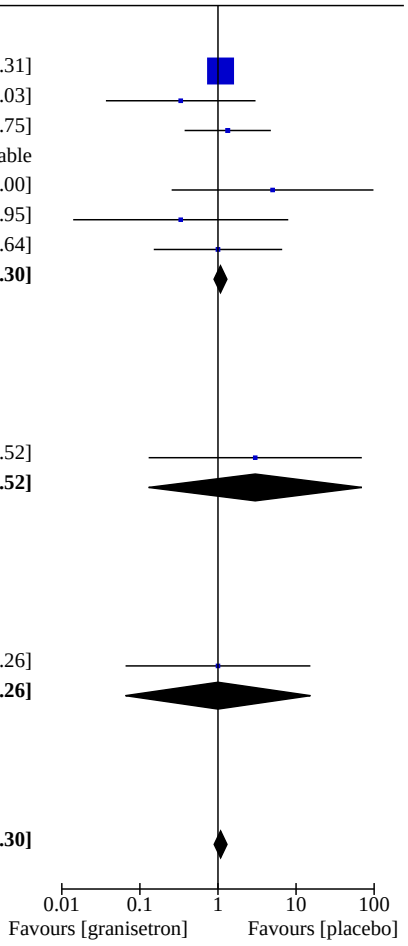
Analysis 7.5. Comparison 7: Granisetron versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Granisetron Events	Granisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
7.5.1 Recommended dose						
Alkaissi 2004	95	165	88	165	94.5%	1.08 [0.89 , 1.31]
Bhatia 2008	1	30	3	30	0.7%	0.33 [0.04 , 3.03]
Choi 1999	8	80	3	40	2.2%	1.33 [0.37 , 4.75]
Heidari 2015a	0	30	0	30		Not estimable
Khan 2005	2	20	0	20	0.4%	5.00 [0.26 , 98.00]
Kim JE 2005	0	40	1	40	0.4%	0.33 [0.01 , 7.95]
Moussa 2007	2	30	2	30	1.0%	1.00 [0.15 , 6.64]
Subtotal (95% CI)		**395**		**355**	**99.2%**	**1.08 [0.89 , 1.30]**
Total events:	108		97			
Heterogeneity: Tau² = 0.00; Chi² = 2.75, df = 5 (P = 0.74); I² = 0%						
Test for overall effect: Z = 0.77 (P = 0.44)						
7.5.2 High dose						
Dua 2004	1	20	0	20	0.4%	3.00 [0.13 , 69.52]
Subtotal (95% CI)		**20**		**20**	**0.4%**	**3.00 [0.13 , 69.52]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
7.5.3 NA dose						
Bhatnagar 2007	1	30	1	30	0.5%	1.00 [0.07 , 15.26]
Subtotal (95% CI)		**30**		**30**	**0.5%**	**1.00 [0.07 , 15.26]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**445**		**405**	**100.0%**	**1.08 [0.89 , 1.30]**
Total events:	110		98			
Heterogeneity: Tau² = 0.00; Chi² = 3.16, df = 7 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.80 (P = 0.42)						
Test for subgroup differences: Chi² = 0.41, df = 2 (P = 0.81), I² = 0%						



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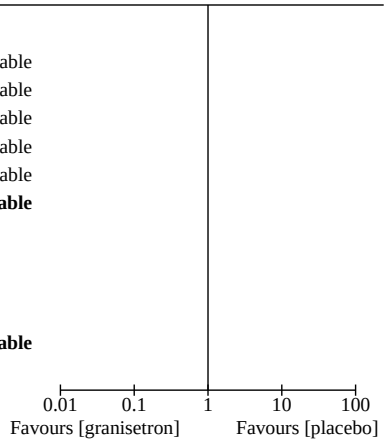
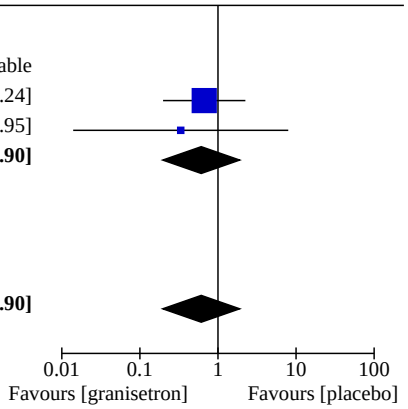
Analysis 7.6. Comparison 7: Granisetron versus placebo, Outcome 6: Extrapyramidal symptoms

Study or Subgroup	Granisetron Events	Granisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
7.6.1 Recommended dose						
Contreras Dominguez 2008	0	25	0	25		Not estimable
Heidari 2015a	0	30	0	30		Not estimable
Khan 2005	0	20	0	20		Not estimable
Khan 2006	0	60	0	60		Not estimable
Moussa 2007	0	30	0	30		Not estimable
Subtotal (95% CI)		**165**		**165**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**165**		**165**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 7.7. Comparison 7: Granisetron versus placebo, Outcome 7: Constipation

Study or Subgroup	Granisetron Events	Granisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
7.7.1 Recommended dose						
Akkaya 2001	0	15	0	15		Not estimable
Khan 2006	4	60	6	60	87.2%	0.67 [0.20 , 2.24]
Kim JE 2005	0	40	1	40	12.8%	0.33 [0.01 , 7.95]
Subtotal (95% CI)		**115**		**115**	**100.0%**	**0.61 [0.20 , 1.90]**
Total events:	4		7			
Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0%						
Test for overall effect: Z = 0.85 (P = 0.39)						
Total (95% CI)		**115**		**115**	**100.0%**	**0.61 [0.20 , 1.90]**
Total events:	4		7			
Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0%						
Test for overall effect: Z = 0.85 (P = 0.39)						
Test for subgroup differences: Not applicable						



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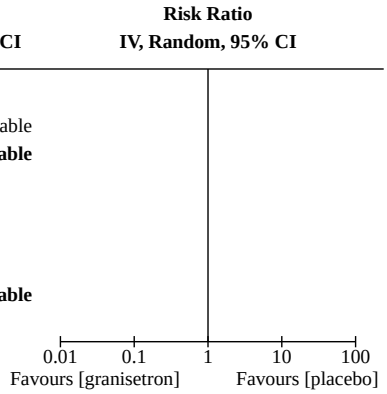
Analysis 7.8. Comparison 7: Granisetron versus placebo, Outcome 8: Arrhythmia

Study or Subgroup	Granisetron Events	Granisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
7.8.1 Recommended dose						
Contreras Dominguez 2008	0	25	0	25		Not estimable
Subtotal (95% CI)		**25**		**25**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**25**		**25**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Comparison 8. Haloperidol versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Vomiting within 0 to 24 hours	4	327	Risk Ratio (IV, Random, 95% CI)	0.58 [0.41, 0.82]
8.1.1 Recommended dose	3	180	Risk Ratio (IV, Random, 95% CI)	0.65 [0.42, 1.01]
8.1.2 High dose	1	147	Risk Ratio (IV, Random, 95% CI)	0.49 [0.28, 0.84]
8.2 Headache	2	99	Risk Ratio (IV, Random, 95% CI)	0.20 [0.01, 3.92]
8.2.1 Recommended dose	1	59	Risk Ratio (IV, Random, 95% CI)	Not estimable
8.2.2 High dose	1	40	Risk Ratio (IV, Random, 95% CI)	0.20 [0.01, 3.92]
8.3 Extrapyramidal symptoms	5	437	Risk Ratio (IV, Random, 95% CI)	3.12 [0.13, 75.44]
8.3.1 Recommended dose	2	151	Risk Ratio (IV, Random, 95% CI)	Not estimable
8.3.2 High dose	3	286	Risk Ratio (IV, Random, 95% CI)	3.12 [0.13, 75.44]
8.4 Arrhythmia	2	99	Risk Ratio (IV, Random, 95% CI)	Not estimable
8.4.1 Recommended dose	1	59	Risk Ratio (IV, Random, 95% CI)	Not estimable
8.4.2 High dose	1	40	Risk Ratio (IV, Random, 95% CI)	Not estimable
8.5 QT prolongation	4	338	Risk Ratio (IV, Random, 95% CI)	Not estimable
8.5.1 Recommended dose	2	151	Risk Ratio (IV, Random, 95% CI)	Not estimable

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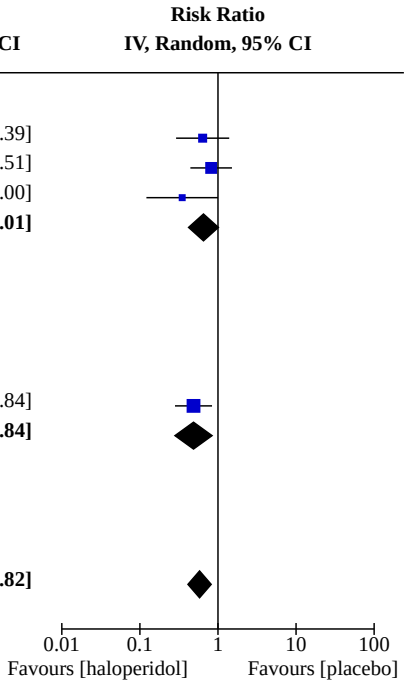
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.5.2 High dose	2	187	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 8.1. Comparison 8: Haloperidol versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Haloperidol Events	Haloperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
8.1.1 Recommended dose						
Aouad 2007	7	27	11	27	19.1%	0.64 [0.29 , 1.39]
Gijzels 2006	8	16	11	18	31.1%	0.82 [0.44 , 1.51]
Wang 2008	4	45	12	47	10.5%	0.35 [0.12 , 1.00]
Subtotal (95% CI)		**88**		**92**	**60.7%**	**0.65 [0.42 , 1.01]**
Total events:	19		34			
Heterogeneity: Tau² = 0.00; Chi² = 1.89, df = 2 (P = 0.39); I² = 0%						
Test for overall effect: Z = 1.91 (P = 0.06)						
8.1.2 High dose						
Chu 2008	14	72	30	75	39.3%	0.49 [0.28 , 0.84]
Subtotal (95% CI)		**72**		**75**	**39.3%**	**0.49 [0.28 , 0.84]**
Total events:	14		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.59 (P = 0.010)						
Total (95% CI)		**160**		**167**	**100.0%**	**0.58 [0.41 , 0.82]**
Total events:	33		64			
Heterogeneity: Tau² = 0.00; Chi² = 2.56, df = 3 (P = 0.46); I² = 0%						
Test for overall effect: Z = 3.11 (P = 0.002)						
Test for subgroup differences: Chi² = 0.68, df = 1 (P = 0.41), I² = 0%						



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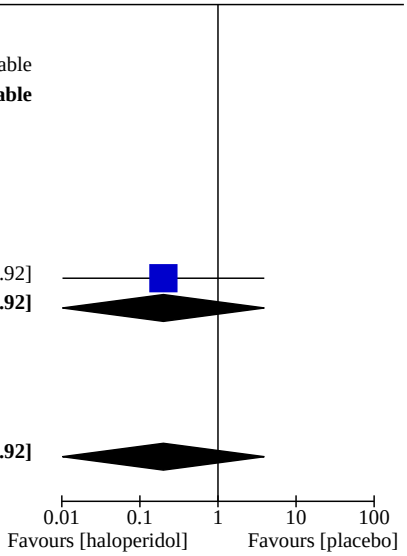
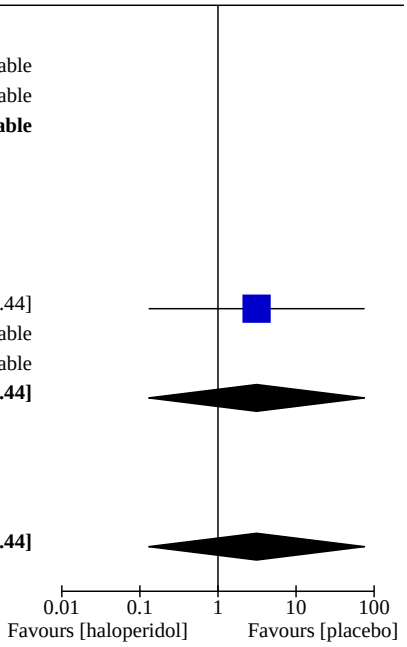
Analysis 8.2. Comparison 8: Haloperidol versus placebo, Outcome 2: Headache

Study or Subgroup	Haloperidol Events	Haloperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
8.2.1 Recommended dose						
Aouad 2007	0	29	0	30		Not estimable
Subtotal (95% CI)		**29**		**30**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
8.2.2 High dose						
Honarmand 2012	0	20	2	20	100.0%	0.20 [0.01 , 3.92]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**0.20 [0.01 , 3.92]**
Total events:	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						
Total (95% CI)		**49**		**50**	**100.0%**	**0.20 [0.01 , 3.92]**
Total events:	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						
Test for subgroup differences: Not applicable						



Analysis 8.3. Comparison 8: Haloperidol versus placebo, Outcome 3: Extrapyramidal symptoms

Study or Subgroup	Haloperidol Events	Haloperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
8.3.1 Recommended dose						
Aouad 2007	0	29	0	30		Not estimable
Wang 2008	0	45	0	47		Not estimable
Subtotal (95% CI)		**74**		**77**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
8.3.2 High dose						
Chu 2008	1	72	0	75	100.0%	3.12 [0.13 , 75.44]
Ebneshahidi 2013	0	49	0	50		Not estimable
Honarmand 2012	0	20	0	20		Not estimable
Subtotal (95% CI)		**141**		**145**	**100.0%**	**3.12 [0.13 , 75.44]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.48)						
Total (95% CI)		**215**		**222**	**100.0%**	**3.12 [0.13 , 75.44]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.48)						
Test for subgroup differences: Not applicable						



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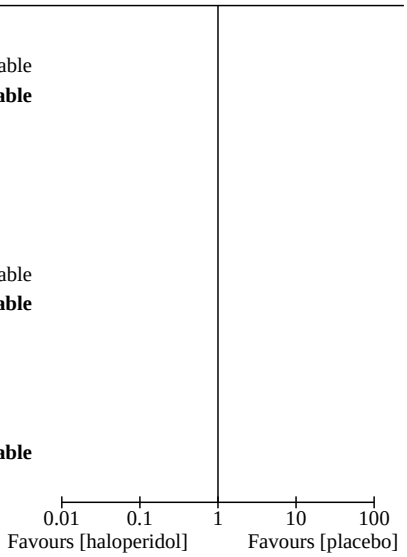
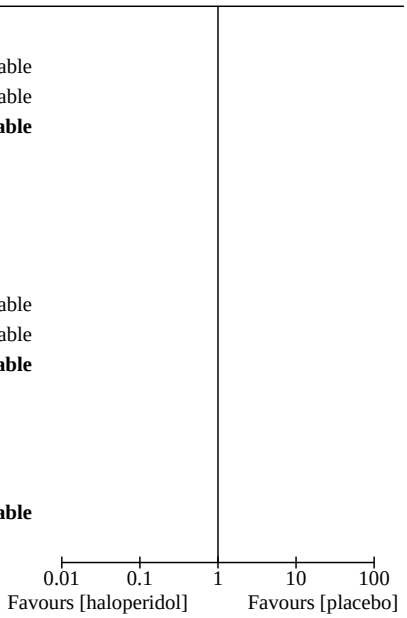
Analysis 8.4. Comparison 8: Haloperidol versus placebo, Outcome 4: Arrhythmia

Study or Subgroup	Haloperidol Events	Haloperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
8.4.1 Recommended dose						
Aouad 2007	0	29	0	30		Not estimable
Subtotal (95% CI)		**29**		**30**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
8.4.2 High dose						
Honarmand 2012	0	20	0	20		Not estimable
Subtotal (95% CI)		**20**		**20**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**49**		**50**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 8.5. Comparison 8: Haloperidol versus placebo, Outcome 5: QT prolongation

Study or Subgroup	Haloperidol Events	Haloperidol Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
8.5.1 Recommended dose						
Aouad 2007	0	29	0	30		Not estimable
Wang 2008	0	45	0	47		Not estimable
Subtotal (95% CI)		**74**		**77**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
8.5.2 High dose						
Chu 2008	0	72	0	75		Not estimable
Honarmand 2012	0	20	0	20		Not estimable
Subtotal (95% CI)		**92**		**95**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**166**		**172**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



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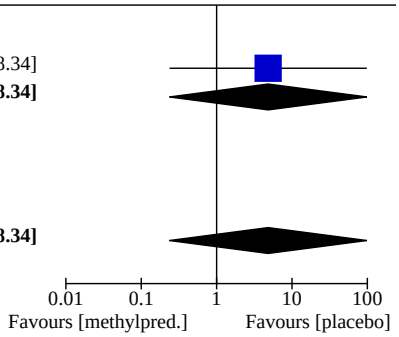
Comparison 9. Methylprednisolone versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Sedation/drowsiness	1	112	Risk Ratio (IV, Random, 95% CI)	4.83 [0.24, 98.34]
9.1.1 High dose	1	112	Risk Ratio (IV, Random, 95% CI)	4.83 [0.24, 98.34]
9.2 Postoperative wound infection	1	40	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.2.1 NA dose	1	40	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.3 Arrhythmia	1	96	Risk Ratio (IV, Random, 95% CI)	0.96 [0.06, 14.90]
9.3.1 High dose	1	96	Risk Ratio (IV, Random, 95% CI)	0.96 [0.06, 14.90]
9.4 Visual disturbances	1	96	Risk Ratio (IV, Random, 95% CI)	0.32 [0.01, 7.66]
9.4.1 High dose	1	96	Risk Ratio (IV, Random, 95% CI)	0.32 [0.01, 7.66]

Analysis 9.1. Comparison 9: Methylprednisolone versus placebo, Outcome 1: Sedation/drowsiness

Study or Subgroup	Methylprednisolone Events	Methylprednisolone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
9.1.1 High dose						
Gautam 2014	2	57	0	55	100.0%	4.83 [0.24 , 98.34]
Subtotal (95% CI)		**57**		**55**	**100.0%**	**4.83 [0.24 , 98.34]**
Total events:	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
Total (95% CI)		**57**		**55**	**100.0%**	**4.83 [0.24 , 98.34]**
Total events:	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
Test for subgroup differences: Not applicable						



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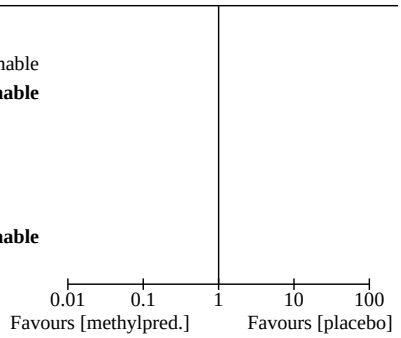
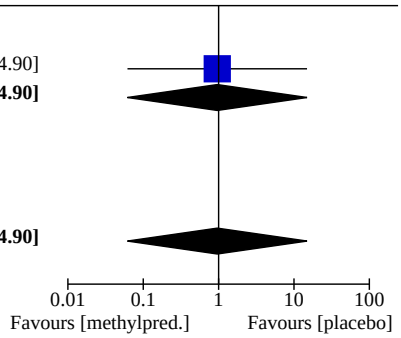
Analysis 9.2. Comparison 9: Methylprednisolone versus placebo, Outcome 2: Postoperative wound infection

Study or Subgroup	Methylprednisolone Events	Methylprednisolone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
9.2.1 NA dose						
Kizilkaya 2004	0	20	0	20		Not estimable
Subtotal (95% CI)		**20**		**20**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**20**		**20**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



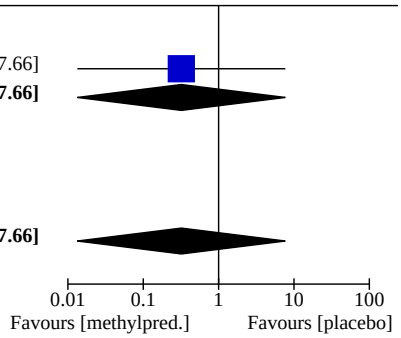
Analysis 9.3. Comparison 9: Methylprednisolone versus placebo, Outcome 3: Arrhythmia

Study or Subgroup	Methylprednisolone Events	Methylprednisolone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
9.3.1 High dose						
Bjerregaard 2018	1	49	1	47	100.0%	0.96 [0.06 , 14.90]
Subtotal (95% CI)		**49**		**47**	**100.0%**	**0.96 [0.06 , 14.90]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.98)						
Total (95% CI)		**49**		**47**	**100.0%**	**0.96 [0.06 , 14.90]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.98)						
Test for subgroup differences: Not applicable						



Analysis 9.4. Comparison 9: Methylprednisolone versus placebo, Outcome 4: Visual disturbances

Study or Subgroup	Methylprednisolone Events	Methylprednisolone Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
9.4.1 High dose						
Bjerregaard 2018	0	49	1	47	100.0%	0.32 [0.01 , 7.66]
Subtotal (95% CI)		**49**		**47**	**100.0%**	**0.32 [0.01 , 7.66]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.48)						
Total (95% CI)		**49**		**47**	**100.0%**	**0.32 [0.01 , 7.66]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.48)						
Test for subgroup differences: Not applicable						



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Comparison 10. Metoclopramide versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Vomiting within 0 to 24 hours	21	2134	Risk Ratio (IV, Random, 95% CI)	0.73 [0.64, 0.83]
10.1.1 Low dose	18	1916	Risk Ratio (IV, Random, 95% CI)	0.74 [0.65, 0.84]
10.1.2 NA dose	3	218	Risk Ratio (IV, Random, 95% CI)	0.64 [0.35, 1.16]
10.2 Any adverse event	3	853	Risk Ratio (IV, Random, 95% CI)	0.90 [0.67, 1.20]
10.2.1 Low dose	2	744	Risk Ratio (IV, Random, 95% CI)	0.82 [0.55, 1.23]
10.2.2 NA dose	1	109	Risk Ratio (IV, Random, 95% CI)	1.13 [0.59, 2.16]
10.3 Headache	12	1313	Risk Ratio (IV, Random, 95% CI)	0.96 [0.56, 1.65]
10.3.1 Low dose	12	1313	Risk Ratio (IV, Random, 95% CI)	0.96 [0.56, 1.65]
10.4 Sedation/drowsiness	15	1178	Risk Ratio (IV, Random, 95% CI)	1.17 [0.91, 1.51]
10.4.1 Low dose	14	1069	Risk Ratio (IV, Random, 95% CI)	1.16 [0.90, 1.51]
10.4.2 NA dose	1	109	Risk Ratio (IV, Random, 95% CI)	4.25 [0.21, 86.51]
10.5 Extrapyramidal symptoms	12	855	Risk Ratio (IV, Random, 95% CI)	0.78 [0.29, 2.07]
10.5.1 Low dose	11	822	Risk Ratio (IV, Random, 95% CI)	0.78 [0.29, 2.07]
10.5.2 NA dose	1	33	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.6 Constipation	1	80	Risk Ratio (IV, Random, 95% CI)	1.00 [0.06, 15.44]
10.6.1 Low dose	1	80	Risk Ratio (IV, Random, 95% CI)	1.00 [0.06, 15.44]
10.7 Postoperative wound infection	1	104	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.7.1 Low dose	1	104	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.8 Arrhythmia	3	150	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.8.1 Low dose	3	150	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.9 Visual disturbances	1	100	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.9.1 Low dose	1	100	Risk Ratio (IV, Random, 95% CI)	Not estimable

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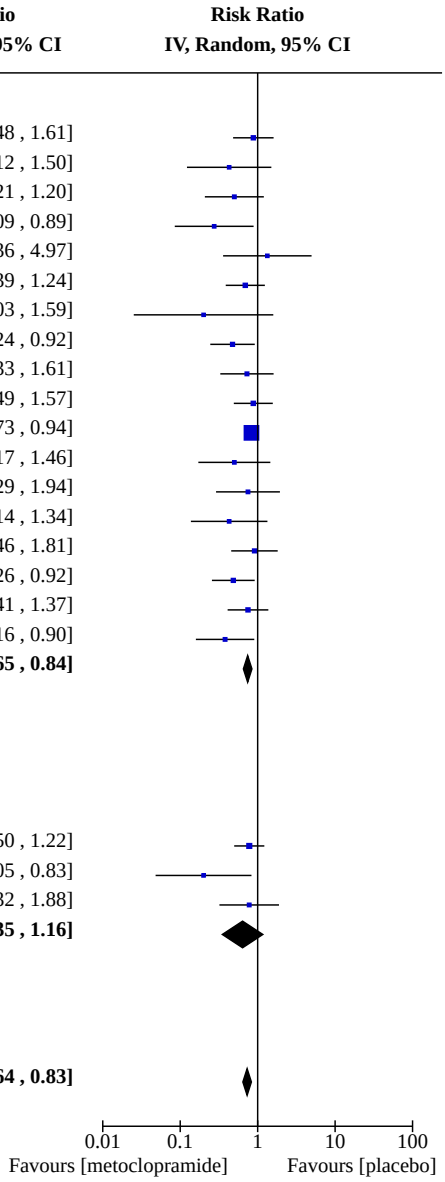
Analysis 10.1. Comparison 10: Metoclopramide versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
10.1.1 Low dose						
Adducci 2002	13	38	14	36	4.2%	0.88 [0.48 , 1.61]
Aghadavoudi 2008	3	30	7	30	1.0%	0.43 [0.12 , 1.50]
Ali Melkkila 1996	6	40	12	40	2.0%	0.50 [0.21 , 1.20]
Ascaso 1997	3	51	18	84	1.1%	0.27 [0.09 , 0.89]
Cekmen 2003	4	15	3	15	0.9%	1.33 [0.36 , 4.97]
Ekinci 2011	9	20	13	20	4.5%	0.69 [0.39 , 1.24]
Entezariasl 2010	1	25	5	25	0.4%	0.20 [0.03 , 1.59]
Helmy 1999	9	40	19	40	3.5%	0.47 [0.24 , 0.92]
Huang 2001	8	38	11	38	2.5%	0.73 [0.33 , 1.61]
Korttila 1979	13	37	16	40	4.5%	0.88 [0.49 , 1.57]
Morris 1998	289	462	88	117	47.8%	0.83 [0.73 , 0.94]
Naghibi 2015	4	26	8	26	1.4%	0.50 [0.17 , 1.46]
Nesek Adam 2004	6	35	8	35	1.7%	0.75 [0.29 , 1.94]
Park 2006	4	84	9	81	1.2%	0.43 [0.14 , 1.34]
Rudra 2005	10	30	11	30	3.2%	0.91 [0.46 , 1.81]
Rusch 1999	9	33	18	32	3.8%	0.48 [0.26 , 0.92]
Rusch 2002	11	33	16	36	4.1%	0.75 [0.41 , 1.37]
Wilson 2001	6	72	18	82	2.1%	0.38 [0.16 , 0.90]
Subtotal (95% CI)		**1109**		**807**	**89.9%**	**0.74 [0.65 , 0.84]**
Total events:	408		294			
Heterogeneity: Tau² = 0.00; Chi² = 17.55, df = 17 (P = 0.42); I² = 3%						
Test for overall effect: Z = 4.61 (P < 0.00001)						
10.1.2 NA dose						
Alexander 1997	18	42	22	40	7.3%	0.78 [0.50 , 1.22]
Huseyinoglu 2016	2	28	10	28	0.8%	0.20 [0.05 , 0.83]
Phillips 1993	7	40	9	40	2.0%	0.78 [0.32 , 1.88]
Subtotal (95% CI)		**110**		**108**	**10.1%**	**0.64 [0.35 , 1.16]**
Total events:	27		41			
Heterogeneity: Tau² = 0.12; Chi² = 3.24, df = 2 (P = 0.20); I² = 38%						
Test for overall effect: Z = 1.46 (P = 0.14)						
Total (95% CI)		**1219**		**915**	**100.0%**	**0.73 [0.64 , 0.83]**
Total events:	435		335			
Heterogeneity: Tau² = 0.00; Chi² = 20.97, df = 20 (P = 0.40); I² = 5%						
Test for overall effect: Z = 4.87 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.23, df = 1 (P = 0.63), I² = 0%						



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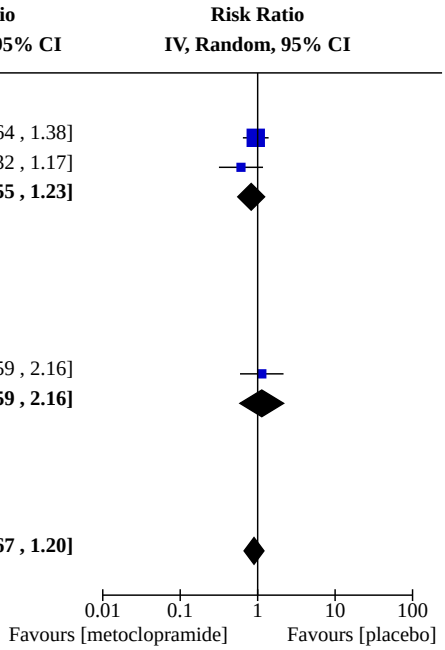
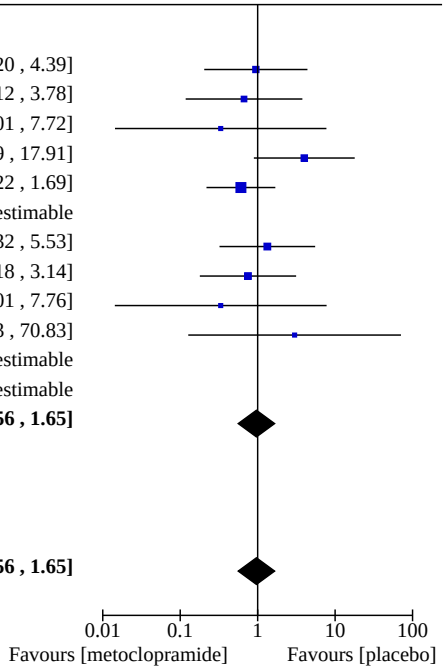
Analysis 10.2. Comparison 10: Metoclopramide versus placebo, Outcome 2: Any adverse event

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
10.2.1 Low dose						
Morris 1998	97	462	26	117	59.2%	0.94 [0.64 , 1.38]
Park 2006	12	84	19	81	20.2%	0.61 [0.32 , 1.17]
Subtotal (95% CI)		**546**		**198**	**79.3%**	**0.82 [0.55 , 1.23]**
Total events:	109		45			
Heterogeneity: Tau² = 0.02; Chi² = 1.29, df = 1 (P = 0.26); I² = 22%						
Test for overall effect: Z = 0.95 (P = 0.34)						
10.2.2 NA dose						
Wagner 1996	16	59	12	50	20.7%	1.13 [0.59 , 2.16]
Subtotal (95% CI)		**59**		**50**	**20.7%**	**1.13 [0.59 , 2.16]**
Total events:	16		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
Total (95% CI)		**605**		**248**	**100.0%**	**0.90 [0.67 , 1.20]**
Total events:	125		57			
Heterogeneity: Tau² = 0.00; Chi² = 1.90, df = 2 (P = 0.39); I² = 0%						
Test for overall effect: Z = 0.72 (P = 0.47)						
Test for subgroup differences: Chi² = 0.66, df = 1 (P = 0.42), I² = 0%						



Analysis 10.3. Comparison 10: Metoclopramide versus placebo, Outcome 3: Headache

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
10.3.1 Low dose						
Adducci 2002	3	38	3	36	12.3%	0.95 [0.20 , 4.39]
Bilgin 2010	2	40	3	40	9.7%	0.67 [0.12 , 3.78]
Ekinci 2011	0	20	1	20	2.9%	0.33 [0.01 , 7.72]
Mazzarella 1988	8	50	2	50	12.9%	4.00 [0.89 , 17.91]
Morris 1998	12	462	5	117	27.7%	0.61 [0.22 , 1.69]
Naghibi 2015	0	26	0	26		Not estimable
Nesek Adam 2004	4	35	3	35	14.4%	1.33 [0.32 , 5.53]
Nesek Adam 2007	3	40	4	40	14.2%	0.75 [0.18 , 3.14]
Pertusa 1996	0	22	1	22	2.9%	0.33 [0.01 , 7.76]
Rudra 2005	1	30	0	30	2.9%	3.00 [0.13 , 70.83]
Rusch 1999	0	33	0	32		Not estimable
Rusch 2002	0	33	0	36		Not estimable
Subtotal (95% CI)		**829**		**484**	**100.0%**	**0.96 [0.56 , 1.65]**
Total events:	33		22			
Heterogeneity: Tau² = 0.00; Chi² = 6.10, df = 8 (P = 0.64); I² = 0%						
Test for overall effect: Z = 0.13 (P = 0.89)						
Total (95% CI)		**829**		**484**	**100.0%**	**0.96 [0.56 , 1.65]**
Total events:	33		22			
Heterogeneity: Tau² = 0.00; Chi² = 6.10, df = 8 (P = 0.64); I² = 0%						
Test for overall effect: Z = 0.13 (P = 0.89)						
Test for subgroup differences: Not applicable						



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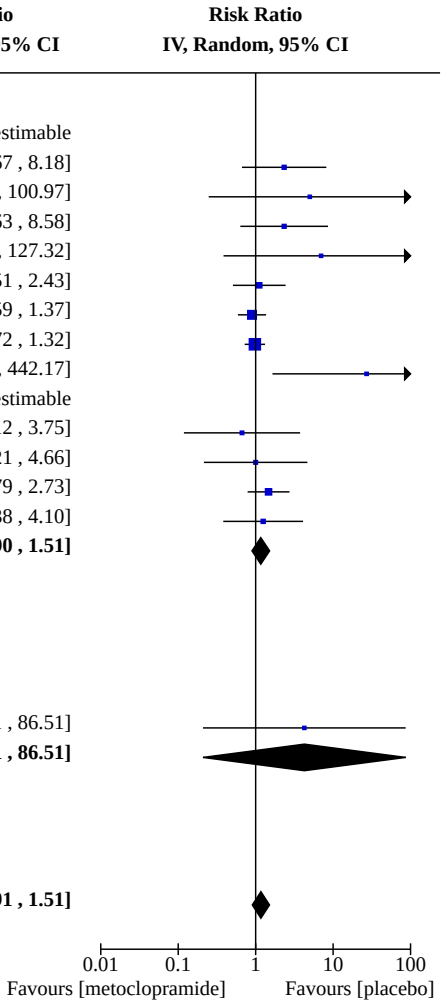
Analysis 10.4. Comparison 10: Metoclopramide versus placebo, Outcome 4: Sedation/drowsiness

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
10.4.1 Low dose						
Adducci 2002	0	38	0	36		Not estimable
Bhatia 2008	7	30	3	30	3.9%	2.33 [0.67 , 8.18]
Bilgin 2010	2	40	0	40	0.7%	5.00 [0.25 , 100.97]
Desilva 1995	7	58	3	58	3.6%	2.33 [0.63 , 8.58]
Ekinci 2011	3	20	0	20	0.8%	7.00 [0.38 , 127.32]
Lim 1991	10	58	11	71	9.1%	1.11 [0.51 , 2.43]
Madej 1986a	22	50	25	51	23.7%	0.90 [0.59 , 1.37]
Madej 1986b	30	48	32	50	34.2%	0.98 [0.72 , 1.32]
Mazzarella 1988	13	50	0	50	0.8%	27.00 [1.65 , 442.17]
Naghibi 2015	0	26	0	26		Not estimable
Nesek Adam 2004	2	35	3	35	2.1%	0.67 [0.12 , 3.75]
Nesek Adam 2007	3	40	3	40	2.6%	1.00 [0.21 , 4.66]
Sandhya 1994	8	10	6	11	13.4%	1.47 [0.79 , 2.73]
Sharma 2000	5	24	4	24	4.3%	1.25 [0.38 , 4.10]
Subtotal (95% CI)		**527**		**542**	**99.3%**	**1.16 [0.90 , 1.51]**
Total events:	112		90			
Heterogeneity: Tau² = 0.03; Chi² = 12.94, df = 11 (P = 0.30); I² = 15%						
Test for overall effect: Z = 1.14 (P = 0.25)						
10.4.2 NA dose						
Wagner 1996	2	59	0	50	0.7%	4.25 [0.21 , 86.51]
Subtotal (95% CI)		**59**		**50**	**0.7%**	**4.25 [0.21 , 86.51]**
Total events:	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (P = 0.35)						
Total (95% CI)		**586**		**592**	**100.0%**	**1.17 [0.91 , 1.51]**
Total events:	114		90			
Heterogeneity: Tau² = 0.03; Chi² = 13.71, df = 12 (P = 0.32); I² = 12%						
Test for overall effect: Z = 1.20 (P = 0.23)						
Test for subgroup differences: Chi² = 0.70, df = 1 (P = 0.40), I² = 0%						



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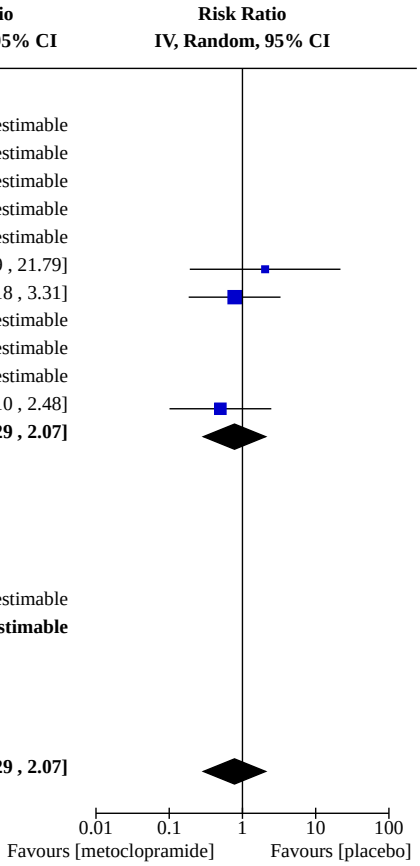
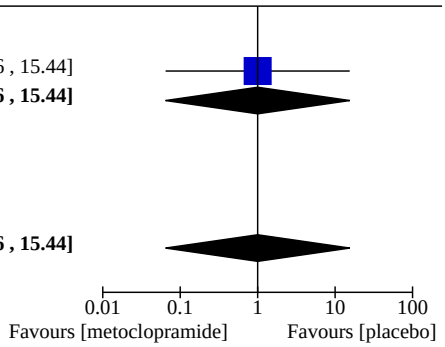
Analysis 10.5. Comparison 10: Metoclopramide versus placebo, Outcome 5: Extrapyramidal symptoms

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
10.5.1 Low dose						
Ascaso 1997	0	51	0	84		Not estimable
Contreras Dominguez 2008	0	25	0	25		Not estimable
Desilva 1995	0	58	0	58		Not estimable
Ekinci 2011	0	20	0	20		Not estimable
Kaya 2000	0	15	0	15		Not estimable
Madej 1986a	2	50	1	51	17.0%	2.04 [0.19 , 21.79]
Madej 1986b	3	48	4	50	45.8%	0.78 [0.18 , 3.31]
Nesek Adam 2004	0	35	0	35		Not estimable
Rusch 1999	0	33	0	32		Not estimable
Rusch 2002	0	33	0	36		Not estimable
Sharma 2000	2	24	4	24	37.2%	0.50 [0.10 , 2.48]
Subtotal (95% CI)		**392**		**430**	**100.0%**	**0.78 [0.29 , 2.07]**
Total events:	7		9			
Heterogeneity: Tau² = 0.00; Chi² = 0.93, df = 2 (P = 0.63); I² = 0%						
Test for overall effect: Z = 0.50 (P = 0.62)						
10.5.2 NA dose						
Mathia 1988	0	18	0	15		Not estimable
Subtotal (95% CI)		**18**		**15**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**410**		**445**	**100.0%**	**0.78 [0.29 , 2.07]**
Total events:	7		9			
Heterogeneity: Tau² = 0.00; Chi² = 0.93, df = 2 (P = 0.63); I² = 0%						
Test for overall effect: Z = 0.50 (P = 0.62)						
Test for subgroup differences: Not applicable						



Analysis 10.6. Comparison 10: Metoclopramide versus placebo, Outcome 6: Constipation

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
10.6.1 Low dose						
Bilgin 2010	1	40	1	40	100.0%	1.00 [0.06 , 15.44]
Subtotal (95% CI)		**40**		**40**	**100.0%**	**1.00 [0.06 , 15.44]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**40**		**40**	**100.0%**	**1.00 [0.06 , 15.44]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Test for subgroup differences: Not applicable						



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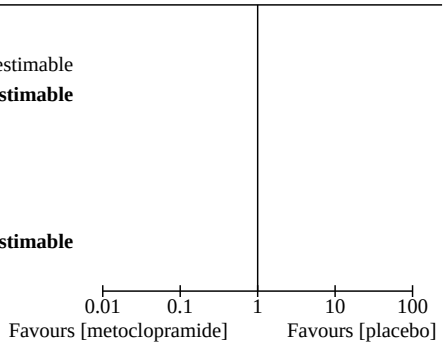
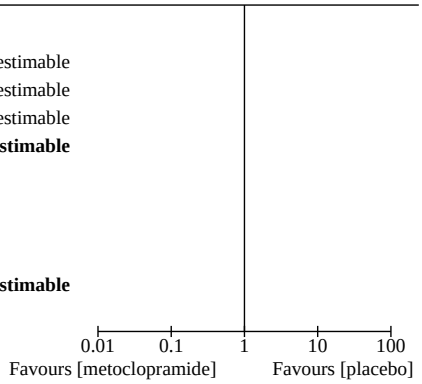
Analysis 10.7. Comparison 10: Metoclopramide versus placebo, Outcome 7: Postoperative wound infection

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
10.7.1 Low dose							
Manaa 2012	0	52	0	52		Not estimable	
Subtotal (95% CI)		**52**		**52**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total (95% CI)		**52**		**52**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



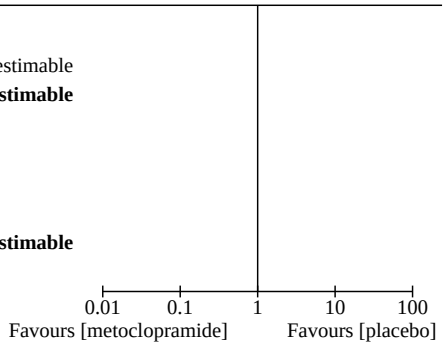
Analysis 10.8. Comparison 10: Metoclopramide versus placebo, Outcome 8: Arrhythmia

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
10.8.1 Low dose							
Cekmen 2003	0	15	0	15		Not estimable	
Contreras Dominguez 2008	0	25	0	25		Not estimable	
Nesek Adam 2004	0	35	0	35		Not estimable	
Subtotal (95% CI)		**75**		**75**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total (95% CI)		**75**		**75**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



Analysis 10.9. Comparison 10: Metoclopramide versus placebo, Outcome 9: Visual disturbances

Study or Subgroup	Metoclopramide Events	Metoclopramide Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
10.9.1 Low dose							
Mazzarella 1988	0	50	0	50		Not estimable	
Subtotal (95% CI)		**50**		**50**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total (95% CI)		**50**		**50**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



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Comparison 11. Ondansetron versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.1 Vomiting within 0 to 24 hours	77	14435	Risk Ratio (IV, Random, 95% CI)	0.58 [0.53, 0.63]
11.1.1 Low dose	7	1843	Risk Ratio (IV, Random, 95% CI)	0.82 [0.75, 0.90]
11.1.2 Recommended dose	60	8288	Risk Ratio (IV, Random, 95% CI)	0.53 [0.46, 0.59]
11.1.3 High dose	27	4304	Risk Ratio (IV, Random, 95% CI)	0.59 [0.51, 0.68]
11.2 Serious adverse events	3	833	Risk Ratio (IV, Random, 95% CI)	17.25 [1.00, 297.39]
11.2.1 Recommended dose	1	546	Risk Ratio (IV, Random, 95% CI)	17.25 [1.00, 297.39]
11.2.2 High dose	2	287	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.3 Any adverse event	12	4892	Risk Ratio (IV, Random, 95% CI)	0.91 [0.82, 1.01]
11.3.1 Low dose	3	594	Risk Ratio (IV, Random, 95% CI)	0.94 [0.73, 1.20]
11.3.2 Recommended dose	7	2851	Risk Ratio (IV, Random, 95% CI)	0.98 [0.90, 1.08]
11.3.3 High dose	5	1447	Risk Ratio (IV, Random, 95% CI)	0.76 [0.58, 1.00]
11.4 Headache	57	12260	Risk Ratio (IV, Random, 95% CI)	1.14 [1.02, 1.27]
11.4.1 Low dose	9	1991	Risk Ratio (IV, Random, 95% CI)	1.41 [1.02, 1.95]
11.4.2 Recommended dose	41	6360	Risk Ratio (IV, Random, 95% CI)	1.14 [0.97, 1.34]
11.4.3 High dose	22	3909	Risk Ratio (IV, Random, 95% CI)	1.06 [0.89, 1.26]
11.5 Sedation/drowsiness	36	6092	Risk Ratio (IV, Random, 95% CI)	0.93 [0.82, 1.06]
11.5.1 Low dose	5	863	Risk Ratio (IV, Random, 95% CI)	1.80 [1.08, 2.99]
11.5.2 Recommended dose	28	3703	Risk Ratio (IV, Random, 95% CI)	1.00 [0.84, 1.19]
11.5.3 High dose	11	1526	Risk Ratio (IV, Random, 95% CI)	0.78 [0.64, 0.94]
11.6 Extrapyramidal symptoms	7	751	Risk Ratio (IV, Random, 95% CI)	0.72 [0.24, 2.18]
11.6.1 Low dose	1	40	Risk Ratio (IV, Random, 95% CI)	Not estimable

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.6.2 Recommended dose	5	465	Risk Ratio (IV, Random, 95% CI)	0.48 [0.10, 2.38]
11.6.3 High dose	1	246	Risk Ratio (IV, Random, 95% CI)	1.05 [0.23, 4.78]
11.7 Constipation	8	1475	Risk Ratio (IV, Random, 95% CI)	1.08 [0.73, 1.59]
11.7.1 Low dose	1	348	Risk Ratio (IV, Random, 95% CI)	1.27 [0.67, 2.38]
11.7.2 Recommended dose	6	507	Risk Ratio (IV, Random, 95% CI)	1.04 [0.45, 2.40]
11.7.3 High dose	2	620	Risk Ratio (IV, Random, 95% CI)	0.95 [0.52, 1.73]
11.8 Arrhythmia	4	1643	Risk Ratio (IV, Random, 95% CI)	0.48 [0.03, 7.37]
11.8.1 Low dose	1	446	Risk Ratio (IV, Random, 95% CI)	0.11 [0.00, 2.64]
11.8.2 Recommended dose	3	704	Risk Ratio (IV, Random, 95% CI)	4.51 [0.60, 33.94]
11.8.3 High dose	2	493	Risk Ratio (IV, Random, 95% CI)	0.11 [0.00, 2.60]
11.9 Visual disturbances	3	506	Risk Ratio (IV, Random, 95% CI)	1.24 [0.77, 1.99]
11.9.1 High dose	3	506	Risk Ratio (IV, Random, 95% CI)	1.24 [0.77, 1.99]
11.10 QT prolongation	1	60	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.10.1 Recommended dose	1	60	Risk Ratio (IV, Random, 95% CI)	Not estimable

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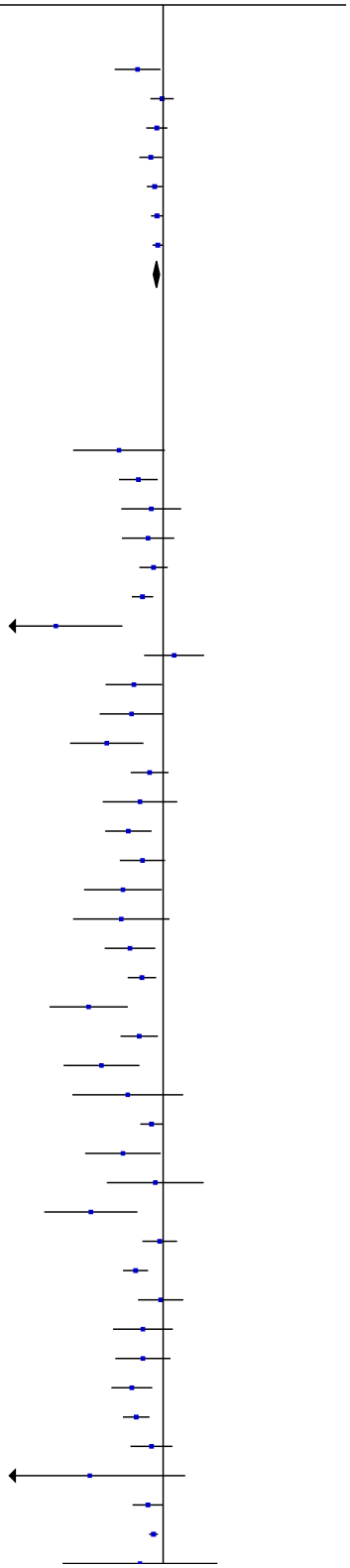
Analysis 11.1. Comparison 11: Ondansetron versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.1.1 Low dose						
Hegde 2014	10	43	11	22	1.0%	0.47 [0.23 , 0.92]
Helmers 1993	65	231	34	117	1.8%	0.97 [0.68 , 1.37]
Khalil 1994	60	131	26	47	1.9%	0.83 [0.60 , 1.14]
McKenzie 1993	50	133	25	46	1.8%	0.69 [0.49 , 0.98]
Pearman 1994	111	264	51	94	2.2%	0.77 [0.61 , 0.98]
Rust 1994	123	201	50	68	2.3%	0.83 [0.70 , 1.00]
Scuderi 2001	195	337	74	109	2.4%	0.85 [0.73 , 1.00]
Subtotal (95% CI)		**1340**		**503**	**13.5%**	**0.82 [0.75 , 0.90]**
Total events:	614		271			
Heterogeneity: Tau² = 0.00; Chi² = 4.92, df = 6 (P = 0.55); I² = 0%						
Test for overall effect: Z = 4.26 (P < 0.0001)						
11.1.2 Recommended dose						
Akcabay 1997	2	20	15	40	0.3%	0.27 [0.07 , 1.05]
Alexander 1997	11	42	22	40	1.2%	0.48 [0.27 , 0.85]
Alghanem 2010	7	60	10	60	0.7%	0.70 [0.29 , 1.72]
Aouad 2007	7	27	11	27	0.8%	0.64 [0.29 , 1.39]
Apfel 2004-1	30	174	40	174	1.6%	0.75 [0.49 , 1.15]
Apfel 2004-2	47	338	89	345	1.9%	0.54 [0.39 , 0.74]
Ascaso 1997	1	116	18	84	0.2%	0.04 [0.01 , 0.30]
Badaoui 1998	8	24	6	25	0.7%	1.39 [0.57 , 3.41]
Badaoui 1999	6	45	16	50	0.7%	0.42 [0.18 , 0.97]
Bugedo 1999	5	57	14	62	0.6%	0.39 [0.15 , 1.01]
Cabrera 1997	3	23	12	17	0.5%	0.18 [0.06 , 0.55]
Campbell 1995	8	16	12	16	1.2%	0.67 [0.38 , 1.17]
Choi 1999	5	40	5	20	0.5%	0.50 [0.16 , 1.53]
Dua 2004	6	20	17	20	1.0%	0.35 [0.18 , 0.71]
Ekinci 2011	7	20	13	20	1.0%	0.54 [0.27 , 1.06]
Elhakim 1995	3	25	10	25	0.4%	0.30 [0.09 , 0.96]
Erhan 2008	2	20	7	20	0.3%	0.29 [0.07 , 1.21]
Gan 1994	7	42	18	40	0.8%	0.37 [0.17 , 0.79]
Gan 2011	23	104	43	103	1.6%	0.53 [0.35 , 0.81]
Grover 2009	3	67	15	36	0.4%	0.11 [0.03 , 0.35]
Hegde 2014	21	86	11	22	1.2%	0.49 [0.28 , 0.85]
Helmy 1999	3	40	19	40	0.5%	0.16 [0.05 , 0.49]
Honkavaara 1996	2	25	3	13	0.2%	0.35 [0.07 , 1.82]
Khalil 1994	52	136	26	48	1.9%	0.71 [0.50 , 0.99]
Kim 1999	3	20	10	20	0.5%	0.30 [0.10 , 0.93]
Kim 2000	3	19	3	15	0.3%	0.79 [0.19 , 3.37]
Kim 2005b	2	39	17	38	0.3%	0.11 [0.03 , 0.46]
Koivuranta 1996	14	31	16	32	1.3%	0.90 [0.54 , 1.52]
Kyokong 1999	31	201	70	199	1.7%	0.44 [0.30 , 0.64]
Lee 2000	13	30	7	15	1.0%	0.93 [0.47 , 1.83]
Lekprasert 1996	6	41	11	41	0.7%	0.55 [0.22 , 1.34]
Lopez Olaondo 1996	6	25	11	25	0.8%	0.55 [0.24 , 1.25]
Martins 1995	9	35	23	35	1.1%	0.39 [0.21 , 0.72]
McKenzie 1993	33	136	25	46	1.7%	0.45 [0.30 , 0.66]
Misra 2005	11	39	16	40	1.1%	0.71 [0.38 , 1.32]
Mitra 1998	0	20	4	20	0.1%	0.11 [0.01 , 1.94]
Moens 1997	22	104	34	102	1.5%	0.63 [0.40 , 1.01]
Morris 1998	262	465	88	117	2.5%	0.75 [0.66 , 0.85]
Ozunlu 2005	1	20	2	20	0.1%	0.50 [0.05 , 5.08]



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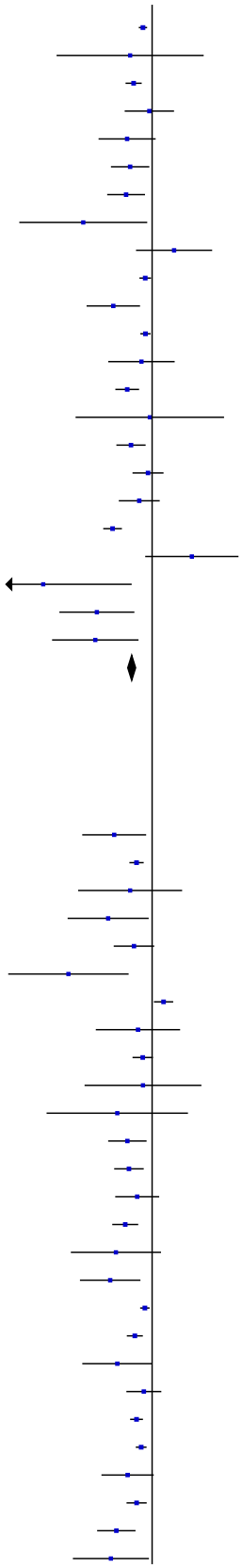
Analysis 11.1. (Continued)

Morris 1998	262	465	88	117	2.5%	0.75 [0.66 , 0.85]
Ozunlu 2005	1	20	2	20	0.1%	0.50 [0.05 , 5.08]
Pearman 1994	84	272	52	94	2.1%	0.56 [0.43 , 0.72]
Principi 1996	11	30	6	15	0.8%	0.92 [0.42 , 2.00]
Pueyo 1996	5	25	11	25	0.7%	0.45 [0.18 , 1.12]
Purhonen 2006a	9	28	18	28	1.1%	0.50 [0.27 , 0.92]
Purhonen 2006b	11	51	24	49	1.1%	0.44 [0.24 , 0.80]
Rodrigo 1994	1	38	9	39	0.2%	0.11 [0.02 , 0.86]
Rodrigo 1996	6	16	3	16	0.4%	2.00 [0.60 , 6.64]
Rust 1994	119	201	50	68	2.3%	0.81 [0.67 , 0.97]
Sadhasivam 1999	5	27	17	27	0.7%	0.29 [0.13 , 0.68]
Scuderi 2001	186	338	74	109	2.4%	0.81 [0.69 , 0.95]
Sinha 2004	5	35	7	35	0.5%	0.71 [0.25 , 2.04]
Suen 1994	26	102	57	102	1.7%	0.46 [0.31 , 0.66]
Sun 1997	2	43	1	20	0.1%	0.93 [0.09 , 9.67]
Tang 1998b	28	112	18	37	1.5%	0.51 [0.32 , 0.81]
Tsui 1999	16	39	21	45	1.4%	0.88 [0.54 , 1.43]
Ulusoy 1996	8	20	12	20	1.0%	0.67 [0.35 , 1.27]
Volpe 1994	48	464	167	464	2.0%	0.29 [0.21 , 0.39]
Wagley 1999	7	25	2	25	0.3%	3.50 [0.80 , 15.23]
Wang 1995	0	50	15	50	0.1%	0.03 [0.00 , 0.52]
Wilson 2001	3	78	18	82	0.4%	0.18 [0.05 , 0.57]
Yuksek 2003	2	20	12	20	0.3%	0.17 [0.04 , 0.65]
Subtotal (95% CI)		**4806**		**3482**	**56.1%**	**0.53 [0.46 , 0.59]**
Total events:	1267		1383			
Heterogeneity: Tau² = 0.10; Chi² = 153.72, df = 59 (P < 0.00001); I² = 62%						
Test for overall effect: Z = 10.23 (P < 0.00001)						
11.1.3 High dose						
Adducci 2002	4	34	14	36	0.6%	0.30 [0.11 , 0.83]
Biedler 1998	69	195	111	192	2.2%	0.61 [0.49 , 0.77]
Chen 2014	2	40	4	40	0.2%	0.50 [0.10 , 2.58]
Choi 1999	3	40	6	20	0.4%	0.25 [0.07 , 0.90]
Goll 2001	12	81	21	80	1.1%	0.56 [0.30 , 1.07]
Guldogus 1994	1	15	14	15	0.2%	0.07 [0.01 , 0.48]
Helmers 1993	189	457	34	118	2.0%	1.44 [1.06 , 1.95]
Honkavaara 1996	4	25	3	12	0.4%	0.64 [0.17 , 2.42]
Khalil 1994	54	129	27	48	1.9%	0.74 [0.54 , 1.03]
Kim 2000	2	20	2	15	0.2%	0.75 [0.12 , 4.73]
Kim 2005a	1	50	3	50	0.1%	0.33 [0.04 , 3.10]
Kim 2009	11	54	24	54	1.1%	0.46 [0.25 , 0.84]
Koivuranta 1997	35	195	19	51	1.5%	0.48 [0.30 , 0.77]
Lee 2000	10	30	8	15	1.0%	0.63 [0.31 , 1.25]
McKenzie 1993	31	136	25	47	1.6%	0.43 [0.28 , 0.65]
Muller 2003	2	18	8	23	0.3%	0.32 [0.08 , 1.32]
Olatosi 2008	4	25	15	25	0.6%	0.27 [0.10 , 0.69]
Paech 1995	60	83	79	87	2.4%	0.80 [0.69 , 0.92]
Pearman 1994	85	265	52	94	2.1%	0.58 [0.45 , 0.75]
Principi 1996	4	30	6	15	0.5%	0.33 [0.11 , 1.00]
Reihner 2000	16	67	22	71	1.2%	0.77 [0.44 , 1.34]
Rust 1994	95	207	51	68	2.3%	0.61 [0.50 , 0.75]
Scuderi 2001	165	343	74	109	2.4%	0.71 [0.60 , 0.84]
Shadangi 2013	6	30	13	30	0.8%	0.46 [0.20 , 1.05]
Sung 1993	33	89	55	91	1.9%	0.61 [0.45 , 0.84]
Zhang 2013-1	11	80	34	80	1.1%	0.32 [0.18 , 0.59]
Zhang 2013-2	3	40	11	40	0.4%	0.27 [0.08 , 0.90]



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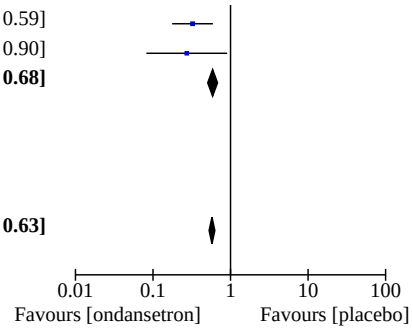
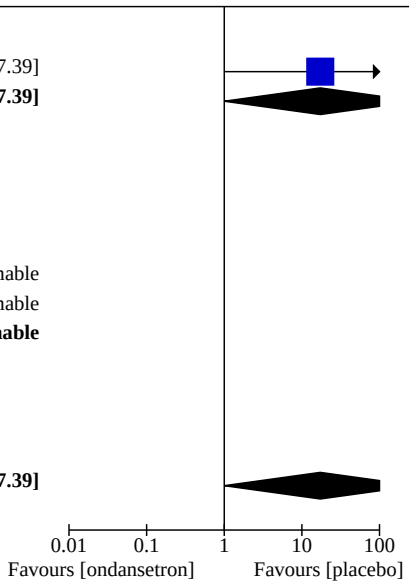
Analysis 11.1. (Continued)

Zhang 2013-1	11	80	34	80	1.1%	0.32 [0.18 , 0.59]
Zhang 2013-2	3	40	11	40	0.4%	0.27 [0.08 , 0.90]
Subtotal (95% CI)		**2778**		**1526**	**30.4%**	**0.59 [0.51 , 0.68]**
Total events:	912		735			
Heterogeneity: Tau² = 0.06; Chi² = 66.84, df = 26 (P < 0.0001); I² = 61%						
Test for overall effect: Z = 7.17 (P < 0.00001)						
Total (95% CI)		**8924**		**5511**	**100.0%**	**0.58 [0.53 , 0.63]**
Total events:	2793		2389			
Heterogeneity: Tau² = 0.07; Chi² = 250.08, df = 93 (P < 0.00001); I² = 63%						
Test for overall effect: Z = 12.73 (P < 0.00001)						
Test for subgroup differences: Chi² = 36.19, df = 2 (P < 0.00001), I² = 94.5%						



Analysis 11.2. Comparison 11: Ondansetron versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.2.1 Recommended dose						
Scholz 1998	8	271	0	275	100.0%	17.25 [1.00 , 297.39]
Subtotal (95% CI)		**271**		**275**	**100.0%**	**17.25 [1.00 , 297.39]**
Total events:	8		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.96 (P = 0.05)						
11.2.2 High dose						
Ibrahim 2013	0	20	0	21		Not estimable
Koivuranta 1997	0	195	0	51		Not estimable
Subtotal (95% CI)		**215**		**72**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**486**		**347**	**100.0%**	**17.25 [1.00 , 297.39]**
Total events:	8		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.96 (P = 0.05)						
Test for subgroup differences: Not applicable						



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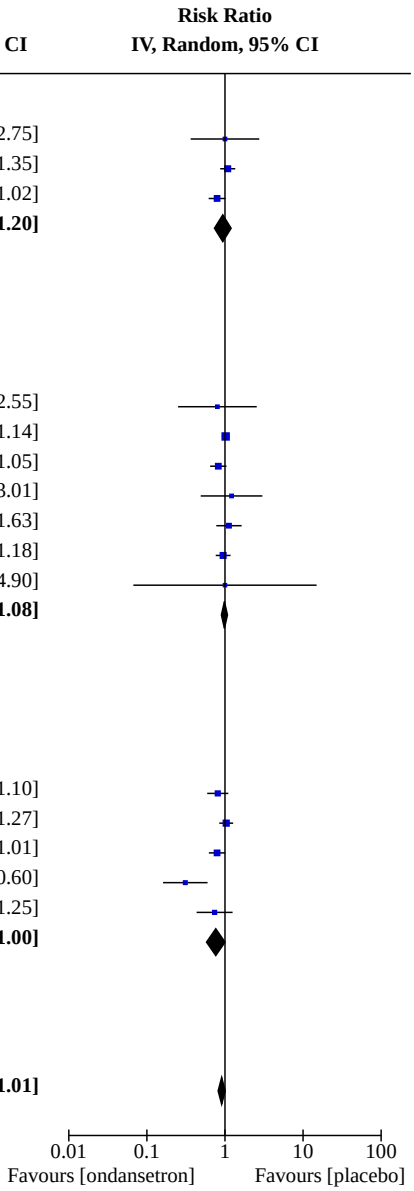
Analysis 11.3. Comparison 11: Ondansetron versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.3.1 Low dose						
Bhatnagar 2007	6	30	6	30	1.0%	1.00 [0.36 , 2.75]
Helmers 1993	122	231	57	117	10.6%	1.08 [0.87 , 1.35]
Kovac 1992	75	139	32	47	9.5%	0.79 [0.62 , 1.02]
Subtotal (95% CI)		**400**		**194**	**21.1%**	**0.94 [0.73 , 1.20]**
Total events:	203		95			
Heterogeneity: Tau² = 0.02; Chi² = 3.40, df = 2 (P = 0.18); I² = 41%						
Test for overall effect: Z = 0.52 (P = 0.61)						
11.3.2 Recommended dose						
Dua 2004	4	20	5	20	0.8%	0.80 [0.25 , 2.55]
Fortney 1998	280	515	276	518	16.7%	1.02 [0.91 , 1.14]
Kovac 1992	85	152	32	47	9.8%	0.82 [0.65 , 1.05]
Kyokong 1999	10	207	8	201	1.2%	1.21 [0.49 , 3.01]
Morris 1998	117	468	26	117	5.6%	1.13 [0.77 , 1.63]
Scholz 1998	98	271	105	275	10.8%	0.95 [0.76 , 1.18]
Yuksek 2003	1	20	1	20	0.1%	1.00 [0.07 , 14.90]
Subtotal (95% CI)		**1653**		**1198**	**45.0%**	**0.98 [0.90 , 1.08]**
Total events:	595		453			
Heterogeneity: Tau² = 0.00; Chi² = 3.49, df = 6 (P = 0.75); I² = 0%						
Test for overall effect: Z = 0.35 (P = 0.72)						
11.3.3 High dose						
Biedler 1998	84	278	37	99	7.2%	0.81 [0.59 , 1.10]
Helmers 1993	233	457	58	118	11.5%	1.04 [0.85 , 1.27]
Kovac 1992	80	147	33	48	9.8%	0.79 [0.62 , 1.01]
Koyuncu 2017	9	60	29	60	2.2%	0.31 [0.16 , 0.60]
Sung 1993	18	89	25	91	3.2%	0.74 [0.43 , 1.25]
Subtotal (95% CI)		**1031**		**416**	**33.9%**	**0.76 [0.58 , 1.00]**
Total events:	424		182			
Heterogeneity: Tau² = 0.06; Chi² = 13.40, df = 4 (P = 0.009); I² = 70%						
Test for overall effect: Z = 1.95 (P = 0.05)						
Total (95% CI)		**3084**		**1808**	**100.0%**	**0.91 [0.82 , 1.01]**
Total events:	1222		730			
Heterogeneity: Tau² = 0.01; Chi² = 23.40, df = 14 (P = 0.05); I² = 40%						
Test for overall effect: Z = 1.85 (P = 0.06)						
Test for subgroup differences: Chi² = 3.07, df = 2 (P = 0.21), I² = 34.9%						



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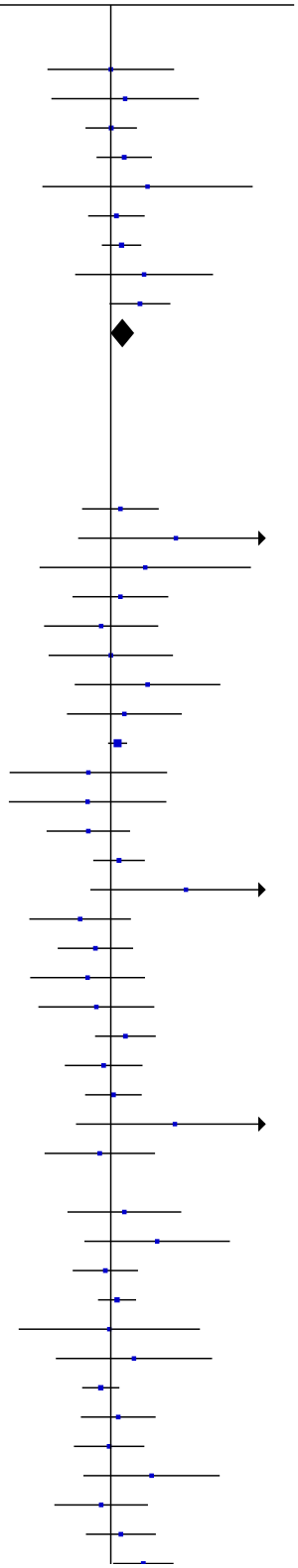
Analysis 11.4. Comparison 11: Ondansetron versus placebo, Outcome 4: Headache

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.4.1 Low dose						
Bhatnagar 2007	2	30	2	30	0.3%	1.00 [0.15 , 6.64]
Hegde 2014	3	43	1	22	0.3%	1.53 [0.17 , 13.91]
Helmers 1993	18	231	9	117	2.1%	1.01 [0.47 , 2.18]
Khalil 1994	26	145	6	50	1.8%	1.49 [0.65 , 3.42]
Khan 2005	1	20	0	20	0.1%	3.00 [0.13 , 69.52]
Kovac 1992	21	139	6	47	1.7%	1.18 [0.51 , 2.75]
Pearman 1994	48	284	12	98	3.5%	1.38 [0.77 , 2.49]
Rust 1994	8	201	1	68	0.3%	2.71 [0.34 , 21.25]
Scuderi 2001	37	337	5	109	1.5%	2.39 [0.96 , 5.94]
Subtotal (95% CI)		**1430**		**561**	**11.7%**	**1.41 [1.02 , 1.95]**
Total events:	164		42			
Heterogeneity: Tau² = 0.00; Chi² = 2.94, df = 8 (P = 0.94); I² = 0%						
Test for overall effect: Z = 2.08 (P = 0.04)						
11.4.2 Recommended dose						
Akcabay 1997	4	20	6	40	0.9%	1.33 [0.42 , 4.19]
Aouad 2007	3	30	0	30	0.1%	7.00 [0.38 , 129.93]
Argiriadou 2002	1	29	0	27	0.1%	2.80 [0.12 , 65.93]
Bilgin 2010	4	40	3	40	0.6%	1.33 [0.32 , 5.58]
Choi 1999	3	40	2	20	0.4%	0.75 [0.14 , 4.13]
Dua 2004	2	20	2	20	0.4%	1.00 [0.16 , 6.42]
Ekinci 2011	3	20	1	20	0.3%	3.00 [0.34 , 26.45]
Elhakim 2002	3	30	2	30	0.4%	1.50 [0.27 , 8.34]
Fortney 1998	89	515	73	518	15.2%	1.23 [0.92 , 1.63]
Hegde 2014	2	86	1	22	0.2%	0.51 [0.05 , 5.39]
Honarmand 2016	1	35	2	35	0.2%	0.50 [0.05 , 5.27]
Joo 2016	3	26	7	31	0.8%	0.51 [0.15 , 1.78]
Khalil 1994	26	148	7	51	2.1%	1.28 [0.59 , 2.77]
Kil 1999	4	19	0	20	0.2%	9.45 [0.54 , 164.49]
Kim 1999	2	20	5	20	0.5%	0.40 [0.09 , 1.83]
Kim 2000	4	19	5	15	1.0%	0.63 [0.20 , 1.95]
Kim 2001	3	60	2	20	0.4%	0.50 [0.09 , 2.78]
Kim 2005b	2	39	3	38	0.4%	0.65 [0.11 , 3.67]
Koivuranta 1996	9	31	6	32	1.5%	1.55 [0.62 , 3.84]
Korttila 1997	5	132	6	128	0.9%	0.81 [0.25 , 2.58]
Kovac 1992	21	152	6	47	1.7%	1.08 [0.46 , 2.52]
Kyokong 1999	3	207	0	201	0.1%	6.80 [0.35 , 130.78]
Lee HS 2004	3	25	2	12	0.5%	0.72 [0.14 , 3.75]
Lekprasert 1996	0	41	0	41		Not estimable
Lopez Olaondo 1996	3	25	2	25	0.4%	1.50 [0.27 , 8.22]
Moens 1997	4	104	1	104	0.3%	4.00 [0.45 , 35.19]
Morris 1998	17	468	5	117	1.3%	0.85 [0.32 , 2.26]
Pearman 1994	48	300	13	98	3.8%	1.21 [0.68 , 2.13]
Pertusa 1996	1	23	1	22	0.2%	0.96 [0.06 , 14.37]
Pueyo 1996	2	25	1	25	0.2%	2.00 [0.19 , 20.67]
Rodrigo 1994	13	38	18	39	4.0%	0.74 [0.43 , 1.29]
Rodrigo 1996	5	16	4	16	1.0%	1.25 [0.41 , 3.82]
Ruiz 1999	6	29	5	23	1.1%	0.95 [0.33 , 2.73]
Rust 1994	10	201	1	68	0.3%	3.38 [0.44 , 25.94]
Sadhasivam 1999	3	27	4	27	0.6%	0.75 [0.19 , 3.04]
Scholz 1998	8	271	6	275	1.1%	1.35 [0.48 , 3.85]
Scuderi 2001	41	338	5	109	1.5%	2.64 [1.07 , 6.52]



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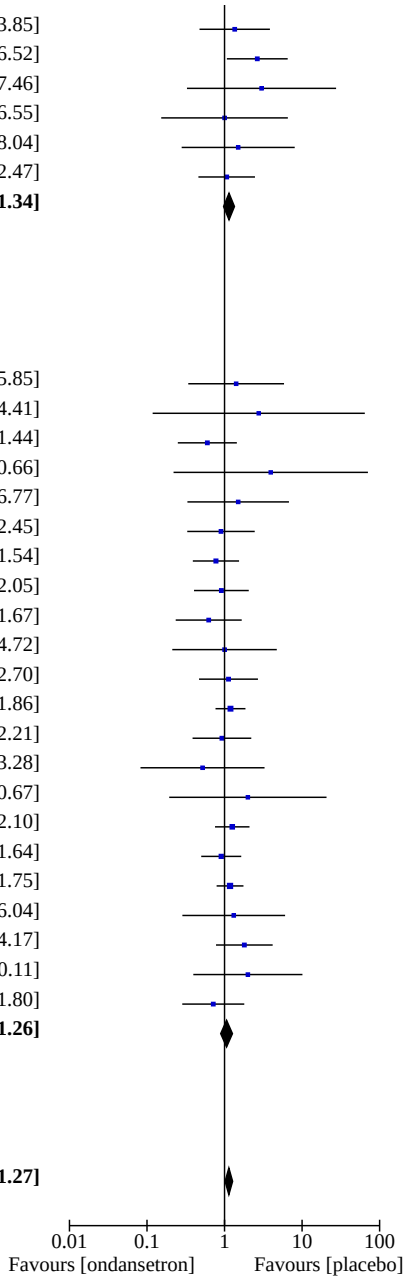
Analysis 11.4. (Continued)

Scholz 1998	8	271	6	275	1.1%	1.35 [0.48 , 3.85]
Scuderi 2001	41	338	5	109	1.5%	2.64 [1.07 , 6.52]
Sinha 2004	3	35	1	35	0.3%	3.00 [0.33 , 27.46]
Turhanoglu 1999	2	25	2	25	0.3%	1.00 [0.15 , 6.55]
Ulusoy 1996	3	20	2	20	0.4%	1.50 [0.28 , 8.04]
Volpe 1994	10	74	9	71	1.7%	1.07 [0.46 , 2.47]
Subtotal (95% CI)		**3803**		**2557**	**47.6%**	**1.14 [0.97 , 1.34]**
Total events:	379		221			
Heterogeneity: Tau² = 0.00; Chi² = 24.83, df = 39 (P = 0.96); I² = 0%						
Test for overall effect: Z = 1.62 (P = 0.10)						
11.4.3 High dose						
Adducci 2002	4	34	3	36	0.6%	1.41 [0.34 , 5.85]
Bacic 1998	1	24	0	22	0.1%	2.76 [0.12 , 64.41]
Bestas 2007	6	30	10	30	1.6%	0.60 [0.25 , 1.44]
Biedler 1998	5	278	0	99	0.1%	3.94 [0.22 , 70.66]
Choi 1999	6	40	2	20	0.5%	1.50 [0.33 , 6.77]
Demiraran 2005	9	60	5	30	1.2%	0.90 [0.33 , 2.45]
Helmers 1993	30	457	10	118	2.6%	0.77 [0.39 , 1.54]
Khalil 1994	18	144	7	51	1.9%	0.91 [0.40 , 2.05]
Kim 2000	5	20	6	15	1.3%	0.63 [0.23 , 1.67]
Kim 2005a	3	50	3	50	0.5%	1.00 [0.21 , 4.72]
Kim 2009	9	54	8	54	1.6%	1.13 [0.47 , 2.70]
Koivuranta 1997	73	195	16	51	6.2%	1.19 [0.76 , 1.86]
Kovac 1992	17	147	6	48	1.6%	0.93 [0.39 , 2.21]
Lee HS 2004	2	25	2	13	0.4%	0.52 [0.08 , 3.28]
Olatosi 2008	2	25	1	25	0.2%	2.00 [0.19 , 20.67]
Paech 1995	24	83	20	87	4.7%	1.26 [0.75 , 2.10]
Pearman 1994	35	291	13	98	3.5%	0.91 [0.50 , 1.64]
Reihner 2000	30	67	27	71	7.8%	1.18 [0.79 , 1.75]
Rust 1994	8	207	2	68	0.5%	1.31 [0.29 , 6.04]
Scuderi 2001	34	343	6	109	1.7%	1.80 [0.78 , 4.17]
Shadangi 2013	4	30	2	30	0.5%	2.00 [0.40 , 10.11]
Sung 1993	7	89	10	91	1.5%	0.72 [0.29 , 1.80]
Subtotal (95% CI)		**2693**		**1216**	**40.7%**	**1.06 [0.89 , 1.26]**
Total events:	332		159			
Heterogeneity: Tau² = 0.00; Chi² = 10.39, df = 21 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.68 (P = 0.50)						
Total (95% CI)		**7926**		**4334**	**100.0%**	**1.14 [1.02 , 1.27]**
Total events:	875		422			
Heterogeneity: Tau² = 0.00; Chi² = 40.45, df = 70 (P = 1.00); I² = 0%						
Test for overall effect: Z = 2.26 (P = 0.02)						
Test for subgroup differences: Chi² = 2.29, df = 2 (P = 0.32), I² = 12.7%						



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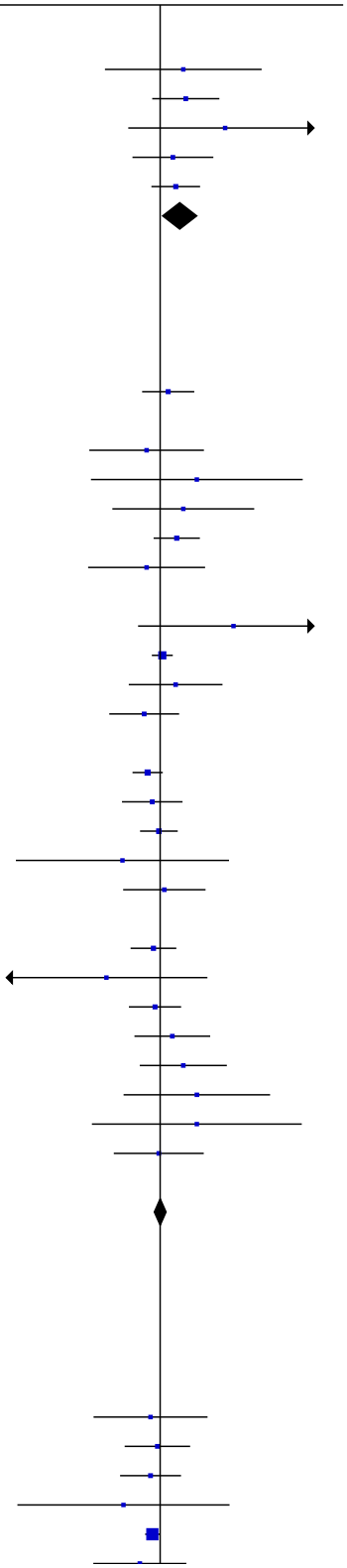
Analysis 11.5. Comparison 11: Ondansetron versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.5.1 Low dose						
Bhatnagar 2007	2	30	1	30	0.3%	2.00 [0.19 , 20.90]
Khalil 1994	25	145	4	50	1.6%	2.16 [0.79 , 5.89]
Khan 2005	3	20	0	20	0.2%	7.00 [0.38 , 127.32]
Kovac 1992	13	139	3	47	1.1%	1.47 [0.44 , 4.92]
Pearman 1994	37	284	8	98	3.0%	1.60 [0.77 , 3.31]
Subtotal (95% CI)		**618**		**245**	**6.1%**	**1.80 [1.08 , 2.99]**
Total events:	80		16			
Heterogeneity: Tau² = 0.00; Chi² = 1.19, df = 4 (P = 0.88); I² = 0%						
Test for overall effect: Z = 2.25 (P = 0.02)						
11.5.2 Recommended dose						
Akcabay 1997	7	20	11	40	2.6%	1.27 [0.58 , 2.78]
Argiriadou 2002	0	29	0	27		Not estimable
Bhatia 2008	2	30	3	30	0.5%	0.67 [0.12 , 3.71]
Bilgin 2010	1	40	0	40	0.2%	3.00 [0.13 , 71.51]
Choi 1999	4	40	1	20	0.3%	2.00 [0.24 , 16.74]
Cholwill 1999	17	60	10	58	3.3%	1.64 [0.82 , 3.29]
Desilva 1995	2	58	3	58	0.5%	0.67 [0.12 , 3.84]
Dua 2004	0	20	0	20		Not estimable
Ekinci 2011	4	20	0	20	0.2%	9.00 [0.52 , 156.91]
Fortney 1998	70	515	66	518	16.0%	1.07 [0.78 , 1.46]
Joo 2016	4	26	3	31	0.8%	1.59 [0.39 , 6.47]
Khalil 1994	9	148	5	51	1.4%	0.62 [0.22 , 1.77]
Kil 1999	0	19	0	20		Not estimable
Kim 1999	11	20	16	20	7.7%	0.69 [0.44 , 1.08]
Kim 2000	6	19	6	15	1.9%	0.79 [0.32 , 1.95]
Kim 2001	26	60	9	20	4.9%	0.96 [0.55 , 1.69]
Korttila 1997	0	132	1	128	0.2%	0.32 [0.01 , 7.86]
Kovac 1992	11	152	3	47	1.0%	1.13 [0.33 , 3.89]
Lekprasert 1996	0	41	0	41		Not estimable
Lopez Olaondo 1996	9	25	11	25	3.4%	0.82 [0.41 , 1.62]
Moens 1997	0	104	2	104	0.2%	0.20 [0.01 , 4.12]
Pearman 1994	21	300	8	98	2.6%	0.86 [0.39 , 1.87]
Sharma 2000	6	25	4	24	1.2%	1.44 [0.46 , 4.48]
Sinha 2004	6	35	3	35	0.9%	2.00 [0.54 , 7.37]
Turhanoglu 1999	3	25	1	25	0.3%	3.00 [0.33 , 26.92]
Ulusoy 1996	1	20	0	20	0.2%	3.00 [0.13 , 69.52]
Volpe 1994	4	74	4	71	0.9%	0.96 [0.25 , 3.69]
Yuksek 2003	0	20	0	20		Not estimable
Subtotal (95% CI)		**2077**		**1626**	**51.1%**	**1.00 [0.84 , 1.19]**
Total events:	224		170			
Heterogeneity: Tau² = 0.00; Chi² = 15.20, df = 22 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.01 (P = 0.99)						
11.5.3 High dose						
Adducci 2002	0	34	0	36		Not estimable
Choi 1999	3	40	2	20	0.5%	0.75 [0.14 , 4.13]
Khalil 1994	13	144	5	51	1.6%	0.92 [0.35 , 2.46]
Kim 2000	6	20	6	15	1.9%	0.75 [0.30 , 1.87]
Kim 2005a	0	50	1	50	0.2%	0.33 [0.01 , 7.99]
Koivuranta 1997	109	195	36	51	33.5%	0.79 [0.64 , 0.98]
Kovac 1992	5	147	3	48	0.8%	0.54 [0.14 , 2.19]



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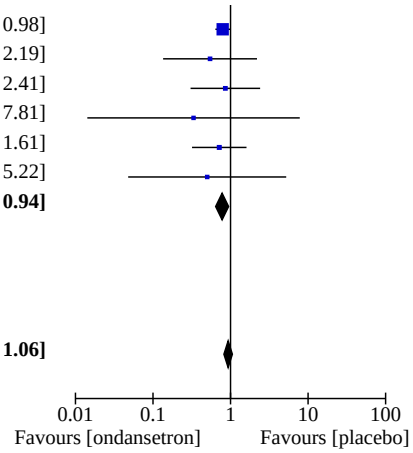
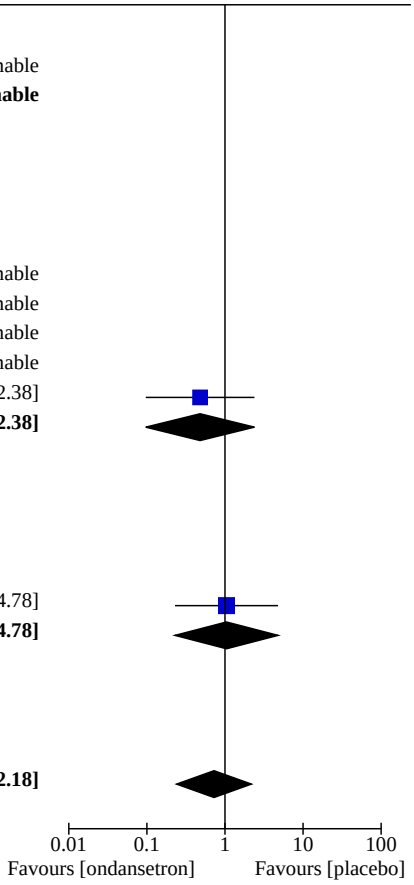
Analysis 11.5. (Continued)

Koivuranta 1997	109	195	36	51	33.5%	0.79 [0.64 , 0.98]
Kovac 1992	5	147	3	48	0.8%	0.54 [0.14 , 2.19]
Murmu 2015	6	63	7	63	1.5%	0.86 [0.31 , 2.41]
Olatosi 2008	0	25	1	25	0.2%	0.33 [0.01 , 7.81]
Pearman 1994	17	291	8	98	2.4%	0.72 [0.32 , 1.61]
Shadangi 2013	1	30	2	30	0.3%	0.50 [0.05 , 5.22]
Subtotal (95% CI)		**1039**		**487**	**42.8%**	**0.78 [0.64 , 0.94]**
Total events:	160		71			
Heterogeneity: Tau² = 0.00; Chi² = 1.16, df = 9 (P = 1.00); I² = 0%						
Test for overall effect: Z = 2.56 (P = 0.01)						
Total (95% CI)		**3734**		**2358**	**100.0%**	**0.93 [0.82 , 1.06]**
Total events:	464		257			
Heterogeneity: Tau² = 0.00; Chi² = 27.94, df = 37 (P = 0.86); I² = 0%						
Test for overall effect: Z = 1.11 (P = 0.27)						
Test for subgroup differences: Chi² = 10.40, df = 2 (P = 0.006), I² = 80.8%						



Analysis 11.6. Comparison 11: Ondansetron versus placebo, Outcome 6: Extrapyramidal symptoms

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.6.1 Low dose						
Khan 2005	0	20	0	20		Not estimable
Subtotal (95% CI)		**20**		**20**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
11.6.2 Recommended dose						
Aouad 2007	0	30	0	30		Not estimable
Ascaso 1997	0	116	0	84		Not estimable
Desilva 1995	0	58	0	58		Not estimable
Ekinci 2011	0	20	0	20		Not estimable
Sharma 2000	2	25	4	24	47.3%	0.48 [0.10 , 2.38]
Subtotal (95% CI)		**249**		**216**	**47.3%**	**0.48 [0.10 , 2.38]**
Total events:	2		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.90 (P = 0.37)						
11.6.3 High dose						
Koivuranta 1997	8	195	2	51	52.7%	1.05 [0.23 , 4.78]
Subtotal (95% CI)		**195**		**51**	**52.7%**	**1.05 [0.23 , 4.78]**
Total events:	8		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.06 (P = 0.95)						
Total (95% CI)		**464**		**287**	**100.0%**	**0.72 [0.24 , 2.18]**
Total events:	10		6			
Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%						
Test for overall effect: Z = 0.58 (P = 0.57)						
Test for subgroup differences: Chi² = 0.48, df = 1 (P = 0.49), I² = 0%						



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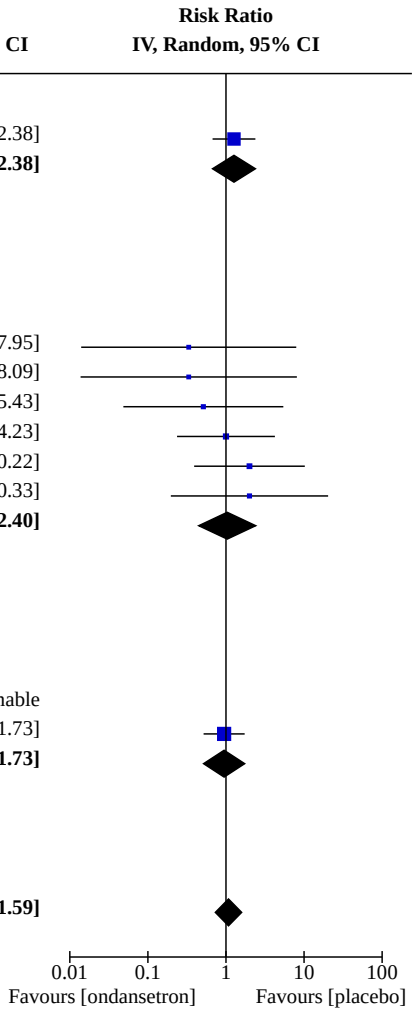
Analysis 11.7. Comparison 11: Ondansetron versus placebo, Outcome 7: Constipation

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.7.1 Low dose						
Helmers 1993	30	231	12	117	37.7%	1.27 [0.67 , 2.38]
Subtotal (95% CI)		**231**		**117**	**37.7%**	**1.27 [0.67 , 2.38]**
Total events:	30		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.73 (P = 0.46)						
11.7.2 Recommended dose						
Bilgin 2010	0	40	1	40	1.5%	0.33 [0.01 , 7.95]
Moens 1997	0	104	1	104	1.5%	0.33 [0.01 , 8.09]
Rodrigo 1994	1	38	2	39	2.7%	0.51 [0.05 , 5.43]
Rodrigo 1996	3	16	3	16	7.2%	1.00 [0.24 , 4.23]
Sinha 2004	4	35	2	35	5.6%	2.00 [0.39 , 10.22]
Ulusoy 1996	2	20	1	20	2.8%	2.00 [0.20 , 20.33]
Subtotal (95% CI)		**253**		**254**	**21.3%**	**1.04 [0.45 , 2.40]**
Total events:	10		10			
Heterogeneity: Tau² = 0.00; Chi² = 2.25, df = 5 (P = 0.81); I² = 0%						
Test for overall effect: Z = 0.09 (P = 0.93)						
11.7.3 High dose						
Bacic 1998	0	21	0	24		Not estimable
Helmers 1993	44	457	12	118	41.0%	0.95 [0.52 , 1.73]
Subtotal (95% CI)		**478**		**142**	**41.0%**	**0.95 [0.52 , 1.73]**
Total events:	44		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.18 (P = 0.86)						
Total (95% CI)		**962**		**513**	**100.0%**	**1.08 [0.73 , 1.59]**
Total events:	84		34			
Heterogeneity: Tau² = 0.00; Chi² = 2.69, df = 7 (P = 0.91); I² = 0%						
Test for overall effect: Z = 0.38 (P = 0.71)						
Test for subgroup differences: Chi² = 0.43, df = 2 (P = 0.80), I² = 0%						



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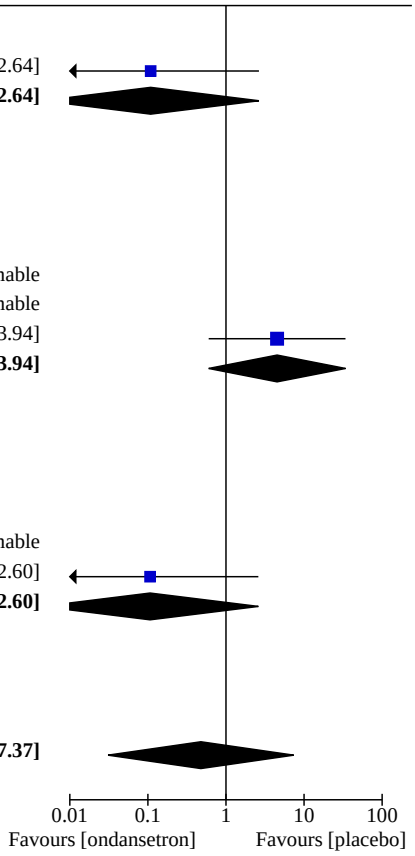
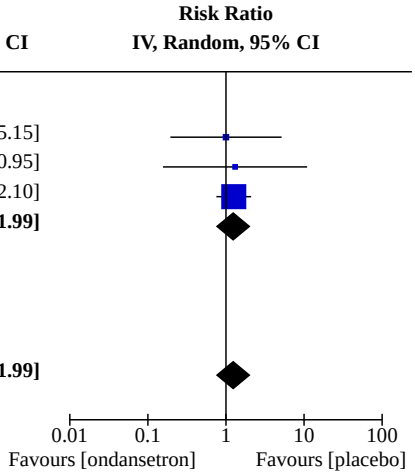
Analysis 11.8. Comparison 11: Ondansetron versus placebo, Outcome 8: Arrhythmia

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.8.1 Low dose						
Scuderi 2001	0	337	1	109	30.1%	0.11 [0.00 , 2.64]
Subtotal (95% CI)		**337**		**109**	**30.1%**	**0.11 [0.00 , 2.64]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.36 (P = 0.17)						
11.8.2 Recommended dose						
Aouad 2007	0	30	0	30		Not estimable
Chan 2006	0	100	0	97		Not estimable
Scuderi 2001	14	338	1	109	39.9%	4.51 [0.60 , 33.94]
Subtotal (95% CI)		**468**		**236**	**39.9%**	**4.51 [0.60 , 33.94]**
Total events:	14		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.46 (P = 0.14)						
11.8.3 High dose						
Ibrahim 2013	0	20	0	21		Not estimable
Scuderi 2001	0	343	1	109	30.1%	0.11 [0.00 , 2.60]
Subtotal (95% CI)		**363**		**130**	**30.1%**	**0.11 [0.00 , 2.60]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.37 (P = 0.17)						
Total (95% CI)		**1168**		**475**	**100.0%**	**0.48 [0.03 , 7.37]**
Total events:	14		3			
Heterogeneity: Tau² = 3.83; Chi² = 5.85, df = 2 (P = 0.05); I² = 66%						
Test for overall effect: Z = 0.53 (P = 0.60)						
Test for subgroup differences: Chi² = 5.85, df = 2 (P = 0.05), I² = 65.8%						



Analysis 11.9. Comparison 11: Ondansetron versus placebo, Outcome 9: Visual disturbances

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.9.1 High dose						
Demiraran 2005	4	60	2	30	8.4%	1.00 [0.19 , 5.15]
Koivuranta 1997	5	195	1	51	5.0%	1.31 [0.16 , 10.95]
Paech 1995	24	83	20	87	86.6%	1.26 [0.75 , 2.10]
Subtotal (95% CI)		**338**		**168**	**100.0%**	**1.24 [0.77 , 1.99]**
Total events:	33		23			
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 2 (P = 0.96); I² = 0%						
Test for overall effect: Z = 0.87 (P = 0.38)						
Total (95% CI)		**338**		**168**	**100.0%**	**1.24 [0.77 , 1.99]**
Total events:	33		23			
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 2 (P = 0.96); I² = 0%						
Test for overall effect: Z = 0.87 (P = 0.38)						
Test for subgroup differences: Not applicable						



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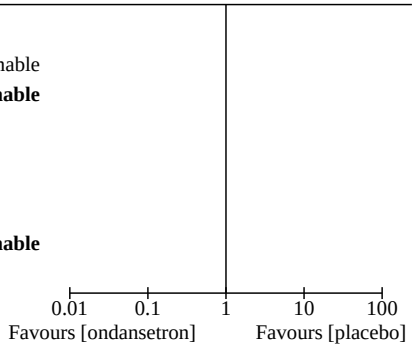
Analysis 11.10. Comparison 11: Ondansetron versus placebo, Outcome 10: QT prolongation

Study or Subgroup	Ondansetron Events	Ondansetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
11.10.1 Recommended dose						
Aouad 2007	0	30	0	30		Not estimable
Subtotal (95% CI)		**30**		**30**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**30**		**30**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Comparison 12. Palonosetron versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 Vomiting within 0 to 24 hours	6	1111	Risk Ratio (IV, Random, 95% CI)	0.69 [0.58, 0.81]
12.1.1 Low dose	3	624	Risk Ratio (IV, Random, 95% CI)	0.71 [0.59, 0.86]
12.1.2 Recommended dose	4	396	Risk Ratio (IV, Random, 95% CI)	0.64 [0.41, 0.99]
12.1.3 High dose	1	91	Risk Ratio (IV, Random, 95% CI)	0.56 [0.29, 1.09]
12.2 Serious adverse events	3	1319	Risk Ratio (IV, Random, 95% CI)	0.67 [0.29, 1.51]
12.2.1 Low dose	2	761	Risk Ratio (IV, Random, 95% CI)	0.93 [0.32, 2.74]
12.2.2 Recommended dose	3	558	Risk Ratio (IV, Random, 95% CI)	0.42 [0.12, 1.47]
12.3 Any adverse event	2	946	Risk Ratio (IV, Random, 95% CI)	0.95 [0.87, 1.04]
12.3.1 Low dose	2	694	Risk Ratio (IV, Random, 95% CI)	0.95 [0.85, 1.07]
12.3.2 Recommended dose	1	252	Risk Ratio (IV, Random, 95% CI)	0.95 [0.83, 1.08]
12.4 Headache	7	1259	Risk Ratio (IV, Random, 95% CI)	1.28 [0.86, 1.91]
12.4.1 Low dose	2	420	Risk Ratio (IV, Random, 95% CI)	2.12 [0.59, 7.68]
12.4.2 Recommended dose	7	748	Risk Ratio (IV, Random, 95% CI)	1.18 [0.77, 1.82]
12.4.3 High dose	1	91	Risk Ratio (IV, Random, 95% CI)	2.13 [0.31, 14.74]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.5 Sedation/drowsiness	2	278	Risk Ratio (IV, Random, 95% CI)	0.37 [0.08, 1.68]
12.5.1 Low dose	1	80	Risk Ratio (IV, Random, 95% CI)	1.32 [0.07, 24.05]
12.5.2 Recommended dose	2	107	Risk Ratio (IV, Random, 95% CI)	0.45 [0.05, 3.91]
12.5.3 High dose	1	91	Risk Ratio (IV, Random, 95% CI)	0.05 [0.00, 1.26]
12.6 Extrapyramidal symptoms	1	60	Risk Ratio (IV, Random, 95% CI)	Not estimable
12.6.1 Recommended dose	1	60	Risk Ratio (IV, Random, 95% CI)	Not estimable
12.7 Constipation	3	1437	Risk Ratio (IV, Random, 95% CI)	1.02 [0.76, 1.38]
12.7.1 Low dose	3	841	Risk Ratio (IV, Random, 95% CI)	1.20 [0.76, 1.89]
12.7.2 Recommended dose	3	505	Risk Ratio (IV, Random, 95% CI)	1.02 [0.64, 1.62]
12.7.3 High dose	1	91	Risk Ratio (IV, Random, 95% CI)	0.67 [0.31, 1.43]
12.8 QT prolongation	1	546	Risk Ratio (IV, Random, 95% CI)	0.17 [0.01, 4.01]
12.8.1 Low dose	1	340	Risk Ratio (IV, Random, 95% CI)	Not estimable
12.8.2 Recommended dose	1	206	Risk Ratio (IV, Random, 95% CI)	0.17 [0.01, 4.01]

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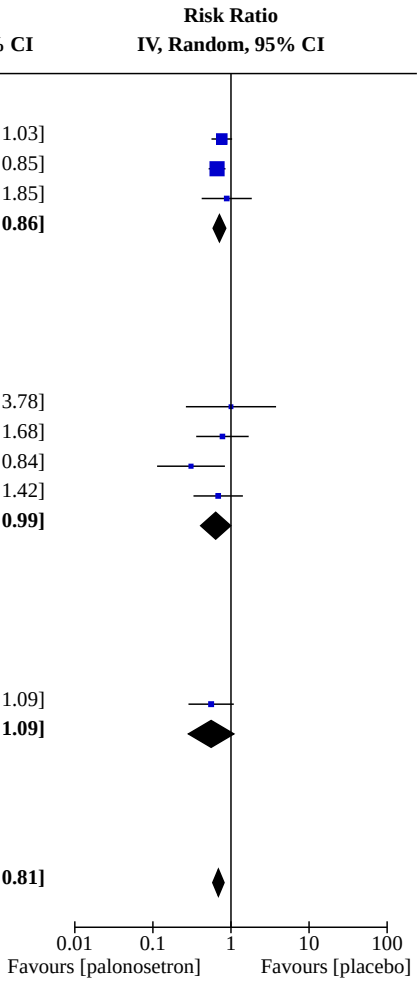
Analysis 12.1. Comparison 12: Palonosetron versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Palonosetron Events	Palonosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
12.1.1 Low dose						
Candiotti 2008	46	138	59	135	29.8%	0.76 [0.56 , 1.03]
Kovac 2008	54	135	82	136	44.9%	0.66 [0.52 , 0.85]
Tang 1998a	25	68	5	12	5.0%	0.88 [0.42 , 1.85]
Subtotal (95% CI)		**341**		**283**	**79.7%**	**0.71 [0.59 , 0.86]**
Total events:	125		146			
Heterogeneity: Tau² = 0.00; Chi² = 0.83, df = 2 (P = 0.66); I² = 0%						
Test for overall effect: Z = 3.59 (P = 0.0003)						
12.1.2 Recommended dose						
Bang 2016	4	50	4	50	1.6%	1.00 [0.26 , 3.78]
Chun 2014	10	94	13	95	4.6%	0.78 [0.36 , 1.68]
Shadangi 2013	4	30	13	30	2.8%	0.31 [0.11 , 0.84]
Tang 1998a	12	35	6	12	5.2%	0.69 [0.33 , 1.42]
Subtotal (95% CI)		**209**		**187**	**14.1%**	**0.64 [0.41 , 0.99]**
Total events:	30		36			
Heterogeneity: Tau² = 0.00; Chi² = 2.77, df = 3 (P = 0.43); I² = 0%						
Test for overall effect: Z = 2.00 (P = 0.05)						
12.1.3 High dose						
Tang 1998a	22	79	6	12	6.2%	0.56 [0.29 , 1.09]
Subtotal (95% CI)		**79**		**12**	**6.2%**	**0.56 [0.29 , 1.09]**
Total events:	22		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.72 (P = 0.09)						
Total (95% CI)		**629**		**482**	**100.0%**	**0.69 [0.58 , 0.81]**
Total events:	177		188			
Heterogeneity: Tau² = 0.00; Chi² = 4.23, df = 7 (P = 0.75); I² = 0%						
Test for overall effect: Z = 4.38 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.63, df = 2 (P = 0.73), I² = 0%						



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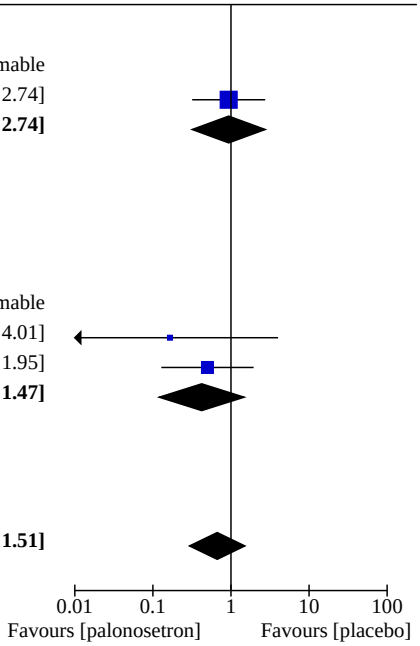
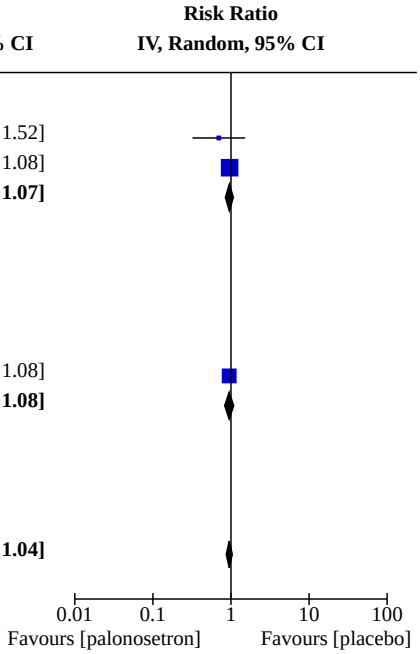
Analysis 12.2. Comparison 12: Palonosetron versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Palonosetron Events	Palonosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
12.2.1 Low dose						
Candiotti 2008	0	273	0	67		Not estimable
PALO-04-07	15	337	4	84	57.5%	0.93 [0.32 , 2.74]
Subtotal (95% CI)		**610**		**151**	**57.5%**	**0.93 [0.32 , 2.74]**
Total events:	15		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.90)						
12.2.2 Recommended dose						
Bang 2016	0	50	0	50		Not estimable
Candiotti 2008	0	138	1	68	6.6%	0.17 [0.01 , 4.01]
PALO-04-07	4	168	4	84	36.0%	0.50 [0.13 , 1.95]
Subtotal (95% CI)		**356**		**202**	**42.5%**	**0.42 [0.12 , 1.47]**
Total events:	4		5			
Heterogeneity: Tau² = 0.00; Chi² = 0.39, df = 1 (P = 0.53); I² = 0%						
Test for overall effect: Z = 1.35 (P = 0.18)						
Total (95% CI)		**966**		**353**	**100.0%**	**0.67 [0.29 , 1.51]**
Total events:	19		9			
Heterogeneity: Tau² = 0.00; Chi² = 1.28, df = 2 (P = 0.53); I² = 0%						
Test for overall effect: Z = 0.98 (P = 0.33)						
Test for subgroup differences: Chi² = 0.89, df = 1 (P = 0.34), I² = 0%						



Analysis 12.3. Comparison 12: Palonosetron versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Palonosetron Events	Palonosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
12.3.1 Low dose						
Candiotti 2008	10	138	14	135	1.3%	0.70 [0.32 , 1.52]
PALO-04-07	262	337	68	84	55.0%	0.96 [0.85 , 1.08]
Subtotal (95% CI)		**475**		**219**	**56.3%**	**0.95 [0.85 , 1.07]**
Total events:	272		82			
Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 0.80 (P = 0.42)						
12.3.2 Recommended dose						
PALO-04-07	129	168	68	84	43.7%	0.95 [0.83 , 1.08]
Subtotal (95% CI)		**168**		**84**	**43.7%**	**0.95 [0.83 , 1.08]**
Total events:	129		68			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.44)						
Total (95% CI)		**643**		**303**	**100.0%**	**0.95 [0.87 , 1.04]**
Total events:	401		150			
Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 2 (P = 0.73); I² = 0%						
Test for overall effect: Z = 1.11 (P = 0.27)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%						



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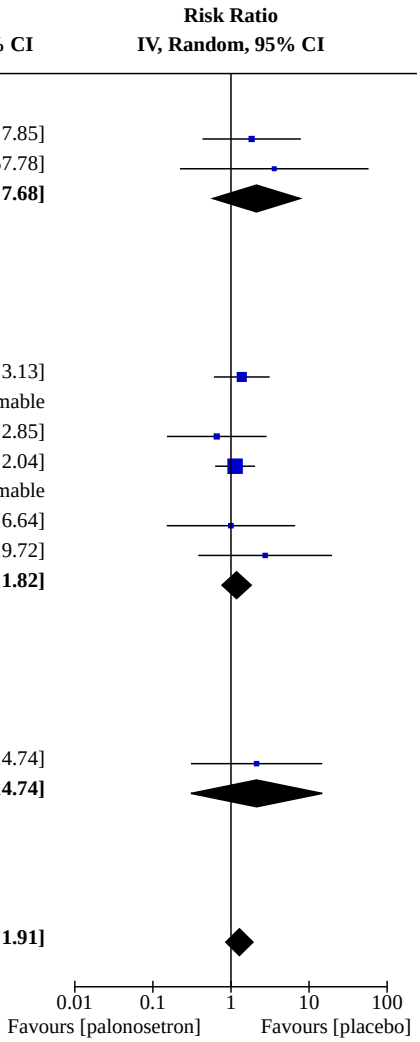
Analysis 12.4. Comparison 12: Palonosetron versus placebo, Outcome 4: Headache

Study or Subgroup	Palonosetron Events	Palonosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
12.4.1 Low dose						
Candiotti 2008	15	273	2	67	7.6%	1.84 [0.43 , 7.85]
Tang 1998a	9	68	0	12	2.1%	3.58 [0.22 , 57.78]
Subtotal (95% CI)		**341**		**79**	**9.7%**	**2.12 [0.59 , 7.68]**
Total events:	24		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.17, df = 1 (P = 0.68); I² = 0%						
Test for overall effect: Z = 1.15 (P = 0.25)						
12.4.2 Recommended dose						
Bang 2016	11	50	8	50	23.7%	1.38 [0.60 , 3.13]
Bang 2017	0	29	0	29		Not estimable
Candiotti 2008	4	138	3	68	7.4%	0.66 [0.15 , 2.85]
Chun 2014	19	94	17	95	46.3%	1.13 [0.63 , 2.04]
Kim 2015	0	44	0	44		Not estimable
Shadangi 2013	2	30	2	30	4.5%	1.00 [0.15 , 6.64]
Tang 1998a	8	35	1	12	4.1%	2.74 [0.38 , 19.72]
Subtotal (95% CI)		**420**		**328**	**86.0%**	**1.18 [0.77 , 1.82]**
Total events:	44		31			
Heterogeneity: Tau² = 0.00; Chi² = 1.50, df = 4 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.75 (P = 0.45)						
12.4.3 High dose						
Tang 1998a	14	79	1	12	4.3%	2.13 [0.31 , 14.74]
Subtotal (95% CI)		**79**		**12**	**4.3%**	**2.13 [0.31 , 14.74]**
Total events:	14		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.76 (P = 0.44)						
Total (95% CI)		**840**		**419**	**100.0%**	**1.28 [0.86 , 1.91]**
Total events:	82		34			
Heterogeneity: Tau² = 0.00; Chi² = 2.66, df = 7 (P = 0.91); I² = 0%						
Test for overall effect: Z = 1.21 (P = 0.23)						
Test for subgroup differences: Chi² = 0.99, df = 2 (P = 0.61), I² = 0%						



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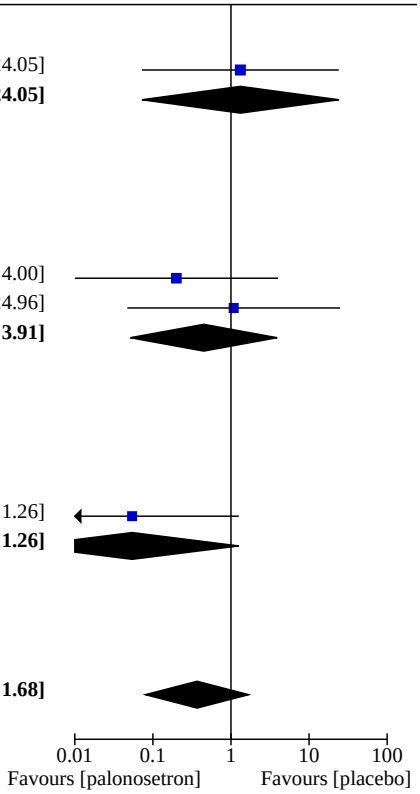
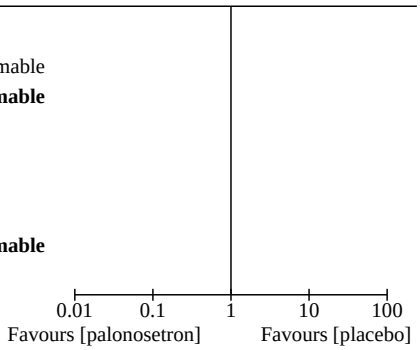
Analysis 12.5. Comparison 12: Palonosetron versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Palonosetron Events	Palonosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
12.5.1 Low dose						
Tang 1998a	3	68	0	12	27.4%	1.32 [0.07 , 24.05]
Subtotal (95% CI)		**68**		**12**	**27.4%**	**1.32 [0.07 , 24.05]**
Total events:	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.19 (P = 0.85)						
12.5.2 Recommended dose						
Shadangi 2013	0	30	2	30	25.8%	0.20 [0.01 , 4.00]
Tang 1998a	1	35	0	12	23.5%	1.08 [0.05 , 24.96]
Subtotal (95% CI)		**65**		**42**	**49.2%**	**0.45 [0.05 , 3.91]**
Total events:	1		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.58, df = 1 (P = 0.45); I² = 0%						
Test for overall effect: Z = 0.73 (P = 0.47)						
12.5.3 High dose						
Tang 1998a	0	79	1	12	23.3%	0.05 [0.00 , 1.26]
Subtotal (95% CI)		**79**		**12**	**23.3%**	**0.05 [0.00 , 1.26]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.82 (P = 0.07)						
Total (95% CI)		**212**		**66**	**100.0%**	**0.37 [0.08 , 1.68]**
Total events:	4		3			
Heterogeneity: Tau² = 0.00; Chi² = 2.78, df = 3 (P = 0.43); I² = 0%						
Test for overall effect: Z = 1.29 (P = 0.20)						
Test for subgroup differences: Chi² = 2.20, df = 2 (P = 0.33), I² = 9.0%						



Analysis 12.6. Comparison 12: Palonosetron versus placebo, Outcome 6: Extrapyramidal symptoms

Study or Subgroup	Palonosetron Events	Palonosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
12.6.1 Recommended dose						
Lee 2014	0	30	0	30		Not estimable
Subtotal (95% CI)		**30**		**30**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**30**		**30**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



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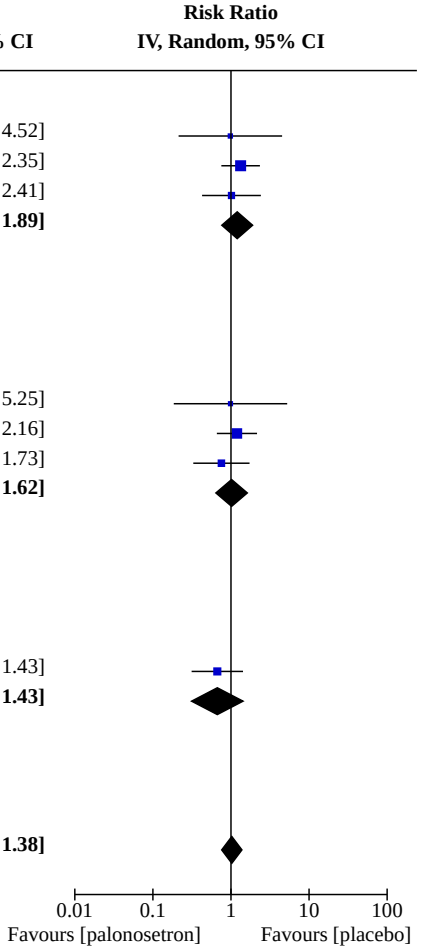
Analysis 12.7. Comparison 12: Palonosetron versus placebo, Outcome 7: Constipation

Study or Subgroup	Palonosetron Events	Palonosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
12.7.1 Low dose						
Candiotti 2008	8	273	2	67	3.8%	0.98 [0.21 , 4.52]
PALO-04-07	64	337	12	84	27.5%	1.33 [0.75 , 2.35]
Tang 1998a	23	68	4	12	11.8%	1.01 [0.43 , 2.41]
Subtotal (95% CI)		**678**		**163**	**43.1%**	**1.20 [0.76 , 1.89]**
Total events:	95		18			
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 2 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.79 (P = 0.43)						
12.7.2 Recommended dose						
Candiotti 2008	4	138	2	68	3.2%	0.99 [0.19 , 5.25]
PALO-04-07	31	168	13	84	25.3%	1.19 [0.66 , 2.16]
Tang 1998a	11	35	5	12	12.9%	0.75 [0.33 , 1.73]
Subtotal (95% CI)		**341**		**164**	**41.4%**	**1.02 [0.64 , 1.62]**
Total events:	46		20			
Heterogeneity: Tau² = 0.00; Chi² = 0.78, df = 2 (P = 0.68); I² = 0%						
Test for overall effect: Z = 0.08 (P = 0.94)						
12.7.3 High dose						
Tang 1998a	22	79	5	12	15.5%	0.67 [0.31 , 1.43]
Subtotal (95% CI)		**79**		**12**	**15.5%**	**0.67 [0.31 , 1.43]**
Total events:	22		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.04 (P = 0.30)						
Total (95% CI)		**1098**		**339**	**100.0%**	**1.02 [0.76 , 1.38]**
Total events:	163		43			
Heterogeneity: Tau² = 0.00; Chi² = 2.81, df = 6 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.16 (P = 0.87)						
Test for subgroup differences: Chi² = 1.70, df = 2 (P = 0.43), I² = 0%						



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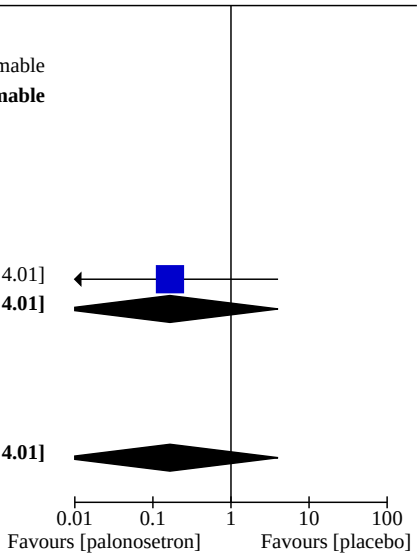
Analysis 12.8. Comparison 12: Palonosetron versus placebo, Outcome 8: QT prolongation

Study or Subgroup	Palonosetron Events	Palonosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
12.8.1 Low dose						
Candiotti 2008	0	273	0	67		Not estimable
Subtotal (95% CI)		**273**		**67**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
12.8.2 Recommended dose						
Candiotti 2008	0	138	1	68	100.0%	0.17 [0.01 , 4.01]
Subtotal (95% CI)		**138**		**68**	**100.0%**	**0.17 [0.01 , 4.01]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
Total (95% CI)		**411**		**135**	**100.0%**	**0.17 [0.01 , 4.01]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
Test for subgroup differences: Not applicable						



Comparison 13. Perphenazine versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.1 Sedation/drowsiness	1	115	Risk Ratio (IV, Random, 95% CI)	0.34 [0.04, 3.17]
13.1.1 Recommended dose	1	115	Risk Ratio (IV, Random, 95% CI)	0.34 [0.04, 3.17]
13.2 Extrapyramidal symptoms	1	115	Risk Ratio (IV, Random, 95% CI)	Not estimable
13.2.1 Recommended dose	1	115	Risk Ratio (IV, Random, 95% CI)	Not estimable

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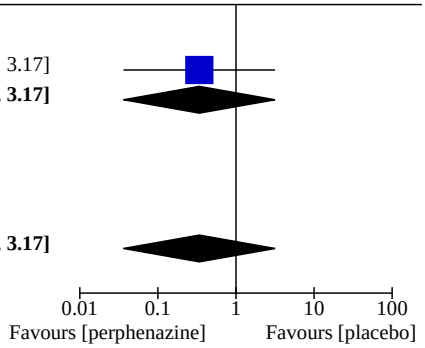
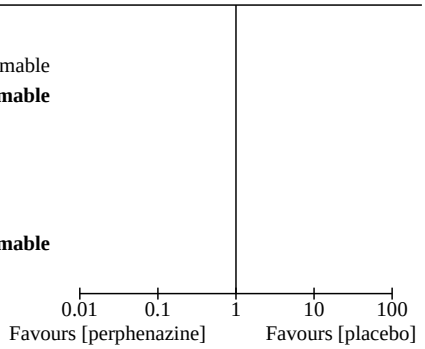
Analysis 13.1. Comparison 13: Perphenazine versus placebo, Outcome 1: Sedation/drowsiness

Study or Subgroup	Perphenazine Events	Perphenazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
13.1.1 Recommended dose						
Desilva 1995	1	57	3	58	100.0%	0.34 [0.04 , 3.17]
Subtotal (95% CI)		**57**		**58**	**100.0%**	**0.34 [0.04 , 3.17]**
Total events:	1		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
Total (95% CI)		**57**		**58**	**100.0%**	**0.34 [0.04 , 3.17]**
Total events:	1		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
Test for subgroup differences: Not applicable						



Analysis 13.2. Comparison 13: Perphenazine versus placebo, Outcome 2: Extrapyramidal symptoms

Study or Subgroup	Perphenazine Events	Perphenazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
13.2.1 Recommended dose						
Desilva 1995	0	57	0	58		Not estimable
Subtotal (95% CI)		**57**		**58**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**57**		**58**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Comparison 14. Promethazine versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 Vomiting within 0 to 24 hours	3	210	Risk Ratio (IV, Random, 95% CI)	0.38 [0.15, 0.93]
14.1.1 Low dose	1	90	Risk Ratio (IV, Random, 95% CI)	0.26 [0.10, 0.70]
14.1.2 High dose	1	50	Risk Ratio (IV, Random, 95% CI)	0.20 [0.07, 0.61]
14.1.3 NA dose	1	70	Risk Ratio (IV, Random, 95% CI)	0.74 [0.49, 1.12]
14.2 Headache	1	50	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.81]
14.2.1 High dose	1	50	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.81]

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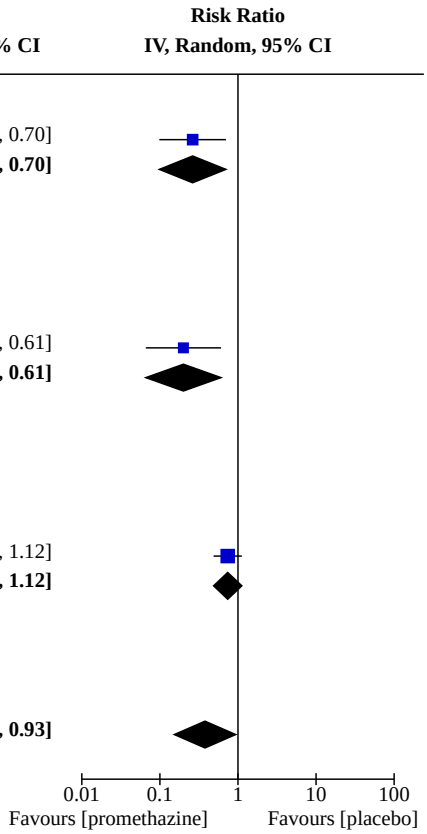
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.3 Sedation/drowsiness	3	162	Risk Ratio (IV, Random, 95% CI)	1.77 [0.53, 5.86]
14.3.1 Low dose	1	90	Risk Ratio (IV, Random, 95% CI)	1.84 [0.41, 8.33]
14.3.2 High dose	2	72	Risk Ratio (IV, Random, 95% CI)	2.13 [0.24, 18.98]

Analysis 14.1. Comparison 14: Promethazine versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Promethazine Events	Promethazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
14.1.1 Low dose						
Chia 2004	5	59	10	31	30.1%	0.26 [0.10 , 0.70]
Subtotal (95% CI)		**59**		**31**	**30.1%**	**0.26 [0.10 , 0.70]**
Total events:	5		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.67 (P = 0.008)						
14.1.2 High dose						
Olatosi 2008	3	25	15	25	27.4%	0.20 [0.07 , 0.61]
Subtotal (95% CI)		**25**		**25**	**27.4%**	**0.20 [0.07 , 0.61]**
Total events:	3		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.85 (P = 0.004)						
14.1.3 NA dose						
Martins 1995	17	35	23	35	42.5%	0.74 [0.49 , 1.12]
Subtotal (95% CI)		**35**		**35**	**42.5%**	**0.74 [0.49 , 1.12]**
Total events:	17		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.42 (P = 0.15)						
Total (95% CI)		**119**		**91**	**100.0%**	**0.38 [0.15 , 0.93]**
Total events:	25		48			
Heterogeneity: Tau² = 0.46; Chi² = 7.30, df = 2 (P = 0.03); I² = 73%						
Test for overall effect: Z = 2.11 (P = 0.04)						
Test for subgroup differences: Chi² = 7.30, df = 2 (P = 0.03), I² = 72.6%						



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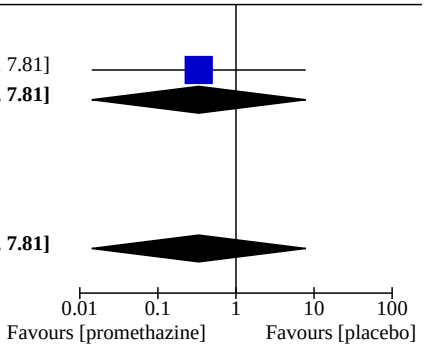
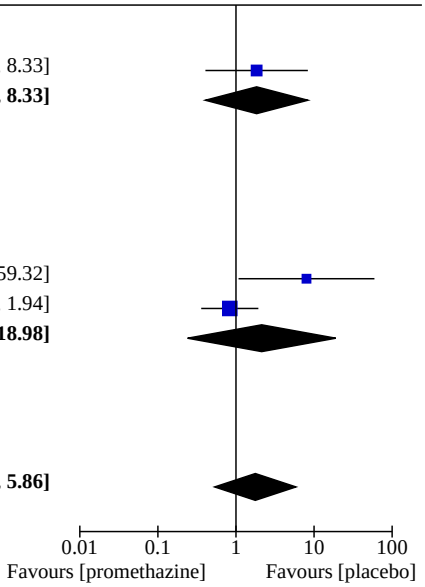
Analysis 14.2. Comparison 14: Promethazine versus placebo, Outcome 2: Headache

Study or Subgroup	Promethazine Events	Promethazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
14.2.1 High dose						
Olatosi 2008	0	25	1	25	100.0%	0.33 [0.01 , 7.81]
Subtotal (95% CI)		**25**		**25**	**100.0%**	**0.33 [0.01 , 7.81]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
Total (95% CI)		**25**		**25**	**100.0%**	**0.33 [0.01 , 7.81]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
Test for subgroup differences: Not applicable						



Analysis 14.3. Comparison 14: Promethazine versus placebo, Outcome 3: Sedation/drowsiness

Study or Subgroup	Promethazine Events	Promethazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
14.3.1 Low dose						
Chia 2004	7	59	2	31	30.9%	1.84 [0.41 , 8.33]
Subtotal (95% CI)		**59**		**31**	**30.9%**	**1.84 [0.41 , 8.33]**
Total events:	7		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
14.3.2 High dose						
Olatosi 2008	8	25	1	25	22.5%	8.00 [1.08 , 59.32]
Sandhya 1994	5	11	6	11	46.6%	0.83 [0.36 , 1.94]
Subtotal (95% CI)		**36**		**36**	**69.1%**	**2.13 [0.24 , 18.98]**
Total events:	13		7			
Heterogeneity: Tau² = 1.94; Chi² = 4.16, df = 1 (P = 0.04); I² = 76%						
Test for overall effect: Z = 0.68 (P = 0.50)						
Total (95% CI)		**95**		**67**	**100.0%**	**1.77 [0.53 , 5.86]**
Total events:	20		9			
Heterogeneity: Tau² = 0.62; Chi² = 4.43, df = 2 (P = 0.11); I² = 55%						
Test for overall effect: Z = 0.93 (P = 0.35)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.91), I² = 0%						



Comparison 15. Ramosetron versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.1 Vomiting within 0 to 24 hours	6	618	Risk Ratio (IV, Random, 95% CI)	0.51 [0.36, 0.72]
15.1.1 Low dose	2	143	Risk Ratio (IV, Random, 95% CI)	0.58 [0.27, 1.26]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.1.2 Recommended dose	4	408	Risk Ratio (IV, Random, 95% CI)	0.45 [0.24, 0.84]
15.1.3 High dose	1	67	Risk Ratio (IV, Random, 95% CI)	0.45 [0.11, 1.82]
15.2 Serious adverse events	1	236	Risk Ratio (IV, Random, 95% CI)	Not estimable
15.2.1 NA dose	1	236	Risk Ratio (IV, Random, 95% CI)	Not estimable
15.3 Any adverse event	2	173	Risk Ratio (IV, Random, 95% CI)	0.59 [0.08, 4.36]
15.3.1 Low dose	2	173	Risk Ratio (IV, Random, 95% CI)	0.59 [0.08, 4.36]
15.4 Headache	14	1529	Risk Ratio (IV, Random, 95% CI)	1.14 [0.89, 1.46]
15.4.1 Low dose	4	475	Risk Ratio (IV, Random, 95% CI)	1.40 [0.78, 2.52]
15.4.2 Recommended dose	11	927	Risk Ratio (IV, Random, 95% CI)	1.10 [0.83, 1.45]
15.4.3 High dose	1	67	Risk Ratio (IV, Random, 95% CI)	0.34 [0.02, 5.14]
15.4.4 NA dose	1	60	Risk Ratio (IV, Random, 95% CI)	Not estimable
15.5 Sedation/drowsiness	5	581	Risk Ratio (IV, Random, 95% CI)	1.24 [0.70, 2.17]
15.5.1 Low dose	1	236	Risk Ratio (IV, Random, 95% CI)	1.94 [0.56, 6.66]
15.5.2 Recommended dose	4	345	Risk Ratio (IV, Random, 95% CI)	1.10 [0.58, 2.07]
15.6 Constipation	2	280	Risk Ratio (IV, Random, 95% CI)	0.67 [0.13, 3.49]
15.6.1 Low dose	1	66	Risk Ratio (IV, Random, 95% CI)	1.00 [0.04, 23.41]
15.6.2 Recommended dose	2	147	Risk Ratio (IV, Random, 95% CI)	1.00 [0.06, 15.44]
15.6.3 High dose	1	67	Risk Ratio (IV, Random, 95% CI)	0.34 [0.02, 5.14]
15.7 Arrhythmia	1	140	Risk Ratio (IV, Random, 95% CI)	1.30 [0.80, 2.10]
15.7.1 Recommended dose	1	140	Risk Ratio (IV, Random, 95% CI)	1.30 [0.80, 2.10]

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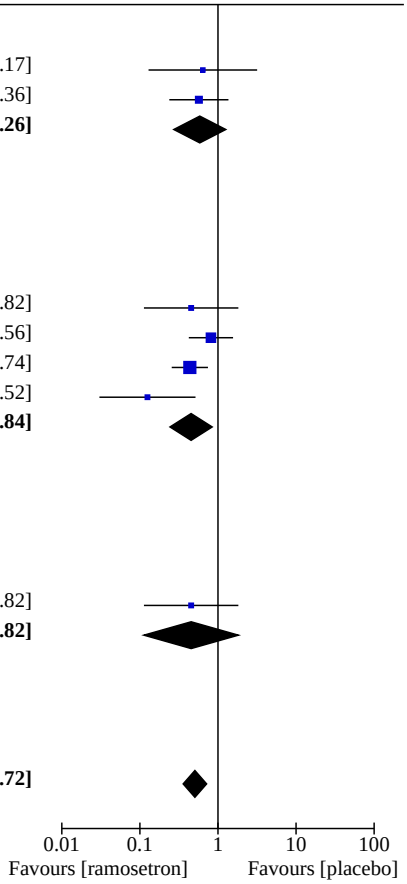
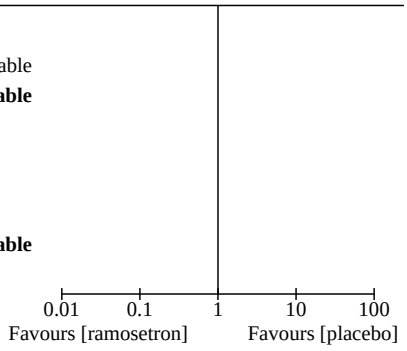
Analysis 15.1. Comparison 15: Ramosetron versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Ramosetron Events	Ramosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
15.1.1 Low dose						
Choi 2008	4	50	2	16	4.6%	0.64 [0.13 , 3.17]
Lee SY 2002	6	36	12	41	14.9%	0.57 [0.24 , 1.36]
Subtotal (95% CI)		**86**		**57**	**19.5%**	**0.58 [0.27 , 1.26]**
Total events:	10		14			
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%						
Test for overall effect: Z = 1.37 (P = 0.17)						
15.1.2 Recommended dose						
Choi 2010	4	50	3	17	6.0%	0.45 [0.11 , 1.82]
Doo 2016	13	70	16	70	25.7%	0.81 [0.42 , 1.56]
Kim 2007	13	53	27	48	36.9%	0.44 [0.26 , 0.74]
Kim 2009	2	50	16	50	5.8%	0.13 [0.03 , 0.52]
Subtotal (95% CI)		**223**		**185**	**74.4%**	**0.45 [0.24 , 0.84]**
Total events:	32		62			
Heterogeneity: Tau² = 0.19; Chi² = 6.07, df = 3 (P = 0.11); I² = 51%						
Test for overall effect: Z = 2.50 (P = 0.01)						
15.1.3 High dose						
Choi 2008	4	50	3	17	6.0%	0.45 [0.11 , 1.82]
Subtotal (95% CI)		**50**		**17**	**6.0%**	**0.45 [0.11 , 1.82]**
Total events:	4		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
Total (95% CI)		**359**		**259**	**100.0%**	**0.51 [0.36 , 0.72]**
Total events:	46		79			
Heterogeneity: Tau² = 0.01; Chi² = 6.26, df = 6 (P = 0.39); I² = 4%						
Test for overall effect: Z = 3.86 (P = 0.0001)						
Test for subgroup differences: Chi² = 0.28, df = 2 (P = 0.87), I² = 0%						



Analysis 15.2. Comparison 15: Ramosetron versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Ramosetron Events	Ramosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
15.2.1 NA dose						
Lee 2008a	0	159	0	77		Not estimable
Subtotal (95% CI)		**159**		**77**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**159**		**77**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



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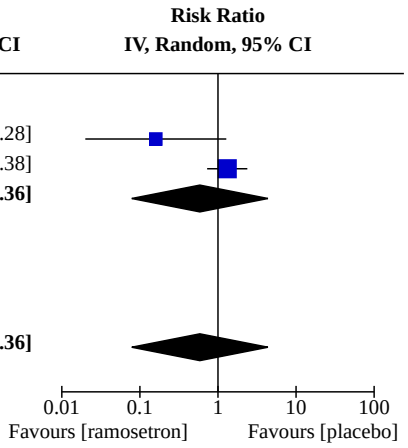
Analysis 15.3. Comparison 15: Ramosetron versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Ramosetron Events	Ramosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
15.3.1 Low dose						
Lee 2008b	1	49	6	47	38.4%	0.16 [0.02 , 1.28]
Lee SY 2002	15	36	13	41	61.6%	1.31 [0.73 , 2.38]
Subtotal (95% CI)		**85**		**88**	**100.0%**	**0.59 [0.08 , 4.36]**
Total events:	16		19			
Heterogeneity: Tau² = 1.61; Chi² = 3.65, df = 1 (P = 0.06); I² = 73%						
Test for overall effect: Z = 0.52 (P = 0.60)						
Total (95% CI)		**85**		**88**	**100.0%**	**0.59 [0.08 , 4.36]**
Total events:	16		19			
Heterogeneity: Tau² = 1.61; Chi² = 3.65, df = 1 (P = 0.06); I² = 73%						
Test for overall effect: Z = 0.52 (P = 0.60)						
Test for subgroup differences: Not applicable						



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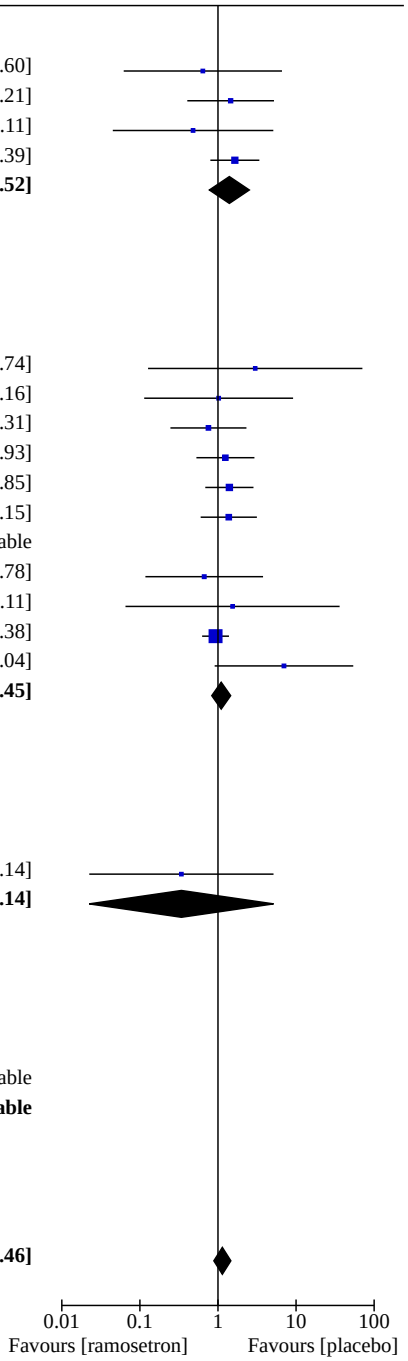
Analysis 15.4. Comparison 15: Ramosetron versus placebo, Outcome 4: Headache

Study or Subgroup	Ramosetron Events	Ramosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
15.4.1 Low dose						
Choi 2008	2	50	1	16	1.1%	0.64 [0.06 , 6.60]
Lee 2008a	9	159	3	77	3.8%	1.45 [0.40 , 5.21]
Lee 2008b	1	49	2	47	1.1%	0.48 [0.04 , 5.11]
Lee SY 2002	13	36	9	41	12.0%	1.65 [0.80 , 3.39]
Subtotal (95% CI)		**294**		**181**	**18.1%**	**1.40 [0.78 , 2.52]**
Total events:	25		15			
Heterogeneity: Tau² = 0.00; Chi² = 1.41, df = 3 (P = 0.70); I² = 0%						
Test for overall effect: Z = 1.12 (P = 0.26)						
15.4.2 Recommended dose						
Bang 2017	1	29	0	29	0.6%	3.00 [0.13 , 70.74]
Choi 2008	3	50	1	17	1.3%	1.02 [0.11 , 9.16]
Doo 2016	5	53	6	48	5.0%	0.75 [0.25 , 2.31]
Joo 2016	9	32	7	31	8.5%	1.25 [0.53 , 2.93]
Kim 2007	14	50	10	50	12.4%	1.40 [0.69 , 2.85]
Kim 2009	11	54	8	54	9.1%	1.38 [0.60 , 3.15]
Kim 2015	0	44	0	44		Not estimable
Kim JE 2005	2	40	3	40	2.1%	0.67 [0.12 , 3.78]
Lee D 2009	1	40	0	20	0.6%	1.54 [0.07 , 36.11]
Lee DC 2011	27	65	29	65	39.9%	0.93 [0.63 , 1.38]
Lee MJ 2015	7	36	1	36	1.5%	7.00 [0.91 , 54.04]
Subtotal (95% CI)		**493**		**434**	**81.1%**	**1.10 [0.83 , 1.45]**
Total events:	80		65			
Heterogeneity: Tau² = 0.00; Chi² = 5.82, df = 9 (P = 0.76); I² = 0%						
Test for overall effect: Z = 0.67 (P = 0.50)						
15.4.3 High dose						
Choi 2008	1	50	1	17	0.8%	0.34 [0.02 , 5.14]
Subtotal (95% CI)		**50**		**17**	**0.8%**	**0.34 [0.02 , 5.14]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.44)						
15.4.4 NA dose						
Lee D 2009	0	40	0	20		Not estimable
Subtotal (95% CI)		**40**		**20**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**877**		**652**	**100.0%**	**1.14 [0.89 , 1.46]**
Total events:	106		81			
Heterogeneity: Tau² = 0.00; Chi² = 8.53, df = 14 (P = 0.86); I² = 0%						
Test for overall effect: Z = 1.01 (P = 0.31)						
Test for subgroup differences: Chi² = 1.29, df = 2 (P = 0.53), I² = 0%						



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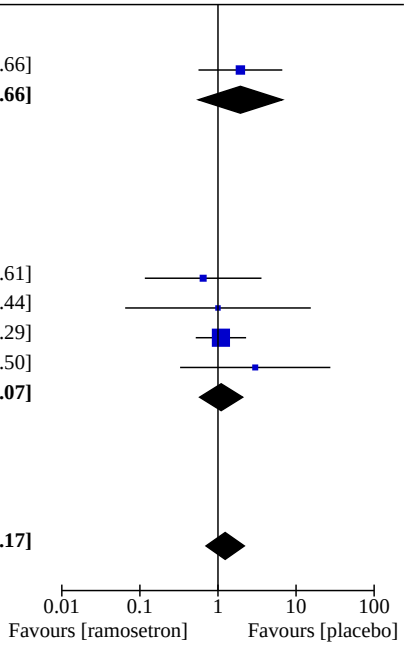
Analysis 15.5. Comparison 15: Ramosetron versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Ramosetron Events	Ramosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
15.5.1 Low dose						
Lee 2008a	12	159	3	77	20.8%	1.94 [0.56 , 6.66]
Subtotal (95% CI)		**159**		**77**	**20.8%**	**1.94 [0.56 , 6.66]**
Total events:	12		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.05 (P = 0.29)						
15.5.2 Recommended dose						
Joo 2016	2	32	3	31	10.8%	0.65 [0.12 , 3.61]
Kim JE 2005	1	40	1	40	4.2%	1.00 [0.06 , 15.44]
Lee DC 2011	12	65	11	65	57.7%	1.09 [0.52 , 2.29]
Lee MJ 2015	3	36	1	36	6.5%	3.00 [0.33 , 27.50]
Subtotal (95% CI)		**173**		**172**	**79.2%**	**1.10 [0.58 , 2.07]**
Total events:	18		16			
Heterogeneity: Tau² = 0.00; Chi² = 1.16, df = 3 (P = 0.76); I² = 0%						
Test for overall effect: Z = 0.29 (P = 0.77)						
Total (95% CI)		**332**		**249**	**100.0%**	**1.24 [0.70 , 2.17]**
Total events:	30		19			
Heterogeneity: Tau² = 0.00; Chi² = 1.80, df = 4 (P = 0.77); I² = 0%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Test for subgroup differences: Chi² = 0.64, df = 1 (P = 0.42), I² = 0%						



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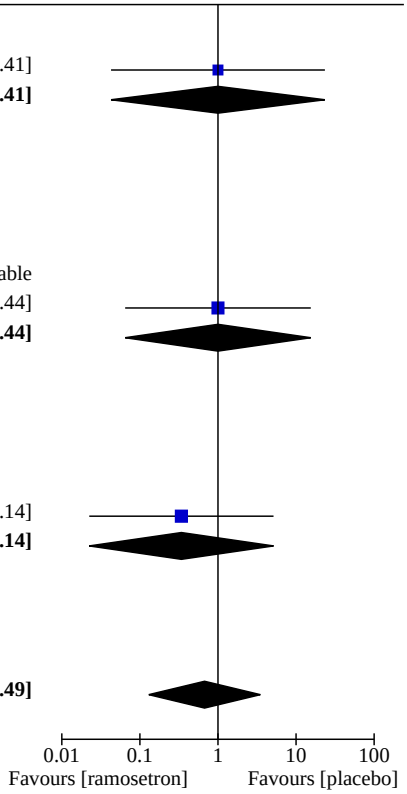
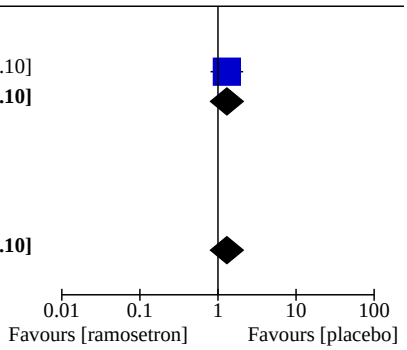
Analysis 15.6. Comparison 15: Ramosetron versus placebo, Outcome 6: Constipation

Study or Subgroup	Ramosetron Events	Ramosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
15.6.1 Low dose						
Choi 2008	1	50	0	16	27.2%	1.00 [0.04 , 23.41]
Subtotal (95% CI)		**50**		**16**	**27.2%**	**1.00 [0.04 , 23.41]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
15.6.2 Recommended dose						
Choi 2008	0	50	0	17		Not estimable
Kim JE 2005	1	40	1	40	36.1%	1.00 [0.06 , 15.44]
Subtotal (95% CI)		**90**		**57**	**36.1%**	**1.00 [0.06 , 15.44]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
15.6.3 High dose						
Choi 2008	1	50	1	17	36.7%	0.34 [0.02 , 5.14]
Subtotal (95% CI)		**50**		**17**	**36.7%**	**0.34 [0.02 , 5.14]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.44)						
Total (95% CI)		**190**		**90**	**100.0%**	**0.67 [0.13 , 3.49]**
Total events:	3		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.38, df = 2 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.47 (P = 0.64)						
Test for subgroup differences: Chi² = 0.38, df = 2 (P = 0.83), I² = 0%						



Analysis 15.7. Comparison 15: Ramosetron versus placebo, Outcome 7: Arrhythmia

Study or Subgroup	Ramosetron Events	Ramosetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
15.7.1 Recommended dose						
Choi 2010	26	70	20	70	100.0%	1.30 [0.80 , 2.10]
Subtotal (95% CI)		**70**		**70**	**100.0%**	**1.30 [0.80 , 2.10]**
Total events:	26		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.28)						
Total (95% CI)		**70**		**70**	**100.0%**	**1.30 [0.80 , 2.10]**
Total events:	26		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.28)						
Test for subgroup differences: Not applicable						



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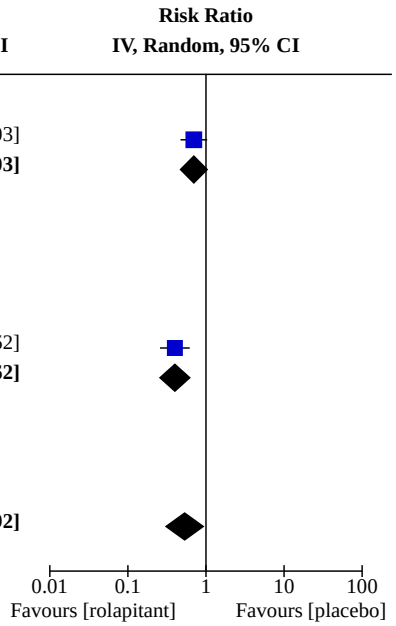
Comparison 16. Rolapitant versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16.1 Vomiting within 0 to 24 hours	1	515	Risk Ratio (IV, Random, 95% CI)	0.53 [0.31, 0.92]
16.1.1 Low dose	1	256	Risk Ratio (IV, Random, 95% CI)	0.70 [0.47, 1.03]
16.1.2 Recommended dose	1	259	Risk Ratio (IV, Random, 95% CI)	0.40 [0.26, 0.62]

Analysis 16.1. Comparison 16: Rolapitant versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Rolapitant Events	Rolapitant Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
16.1.1 Low dose						
Gan 2011	59	205	21	51	51.6%	0.70 [0.47 , 1.03]
Subtotal (95% CI)		**205**		**51**	**51.6%**	**0.70 [0.47 , 1.03]**
Total events:	59		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.79 (P = 0.07)						
16.1.2 Recommended dose						
Gan 2011	35	207	22	52	48.4%	0.40 [0.26 , 0.62]
Subtotal (95% CI)		**207**		**52**	**48.4%**	**0.40 [0.26 , 0.62]**
Total events:	35		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.10 (P < 0.0001)						
Total (95% CI)		**412**		**103**	**100.0%**	**0.53 [0.31 , 0.92]**
Total events:	94		43			
Heterogeneity: Tau² = 0.11; Chi² = 3.47, df = 1 (P = 0.06); I² = 71%						
Test for overall effect: Z = 2.25 (P = 0.02)						
Test for subgroup differences: Chi² = 3.47, df = 1 (P = 0.06), I² = 71.2%						



Comparison 17. Scopalamine versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17.1 Vomiting within 0 to 24 hours	6	549	Risk Ratio (IV, Random, 95% CI)	0.61 [0.44, 0.84]
17.1.1 NA dose	6	549	Risk Ratio (IV, Random, 95% CI)	0.61 [0.44, 0.84]
17.2 Serious adverse events	1	174	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.2.1 NA dose	1	174	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.3 Any adverse event	3	273	Risk Ratio (IV, Random, 95% CI)	2.12 [1.70, 2.65]

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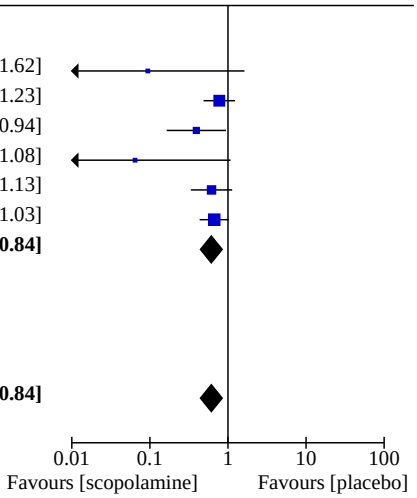
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17.3.1 NA dose	3	273	Risk Ratio (IV, Random, 95% CI)	2.12 [1.70, 2.65]
17.4 Headache	4	447	Risk Ratio (IV, Random, 95% CI)	0.95 [0.33, 2.78]
17.4.1 NA dose	4	447	Risk Ratio (IV, Random, 95% CI)	0.95 [0.33, 2.78]
17.5 Sedation/drowsiness	4	204	Risk Ratio (IV, Random, 95% CI)	2.20 [0.70, 6.91]
17.5.1 NA dose	4	204	Risk Ratio (IV, Random, 95% CI)	2.20 [0.70, 6.91]
17.6 Visual disturbances	8	683	Risk Ratio (IV, Random, 95% CI)	2.12 [1.12, 4.01]
17.6.1 NA dose	8	683	Risk Ratio (IV, Random, 95% CI)	2.12 [1.12, 4.01]

Analysis 17.1. Comparison 17: Scopalamine versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Scopalamine Events	Scopalamine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
17.1.1 NA dose						
Kim 1992	0	27	5	28	1.2%	0.09 [0.01 , 1.62]
Sohi 1994	17	43	24	47	30.9%	0.77 [0.49 , 1.23]
Stromberg 1991	6	59	15	58	11.6%	0.39 [0.16 , 0.94]
Tolksdorf 1986	0	30	7	29	1.3%	0.06 [0.00 , 1.08]
Uppington 1986	8	19	13	19	21.0%	0.62 [0.33 , 1.13]
Wilkinson 1989	24	95	36	95	33.9%	0.67 [0.43 , 1.03]
Subtotal (95% CI)		**273**		**276**	**100.0%**	**0.61 [0.44 , 0.84]**
Total events:	55		100			
Heterogeneity: Tau² = 0.03; Chi² = 6.17, df = 5 (P = 0.29); I² = 19%						
Test for overall effect: Z = 3.01 (P = 0.003)						
Total (95% CI)		**273**		**276**	**100.0%**	**0.61 [0.44 , 0.84]**
Total events:	55		100			
Heterogeneity: Tau² = 0.03; Chi² = 6.17, df = 5 (P = 0.29); I² = 19%						
Test for overall effect: Z = 3.01 (P = 0.003)						
Test for subgroup differences: Not applicable						



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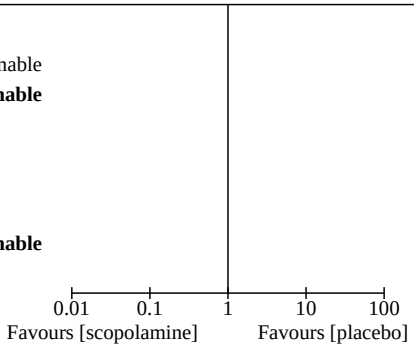
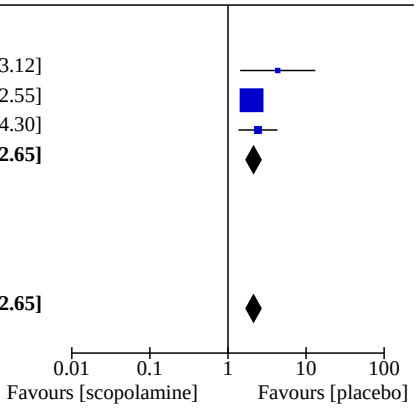
Analysis 17.2. Comparison 17: Scopalamine versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Scopalamine Events	Scopalamine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
17.2.1 NA dose						
Bailey 1990	0	88	0	86		Not estimable
Subtotal (95% CI)		**88**		**86**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**88**		**86**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 17.3. Comparison 17: Scopalamine versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Scopalamine Events	Scopalamine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
17.3.1 NA dose						
Ahn 2002	13	22	3	22	4.0%	4.33 [1.43 , 13.12]
Bailey 1990	80	88	39	86	81.4%	2.00 [1.57 , 2.55]
Kim 1992	21	27	9	28	14.7%	2.42 [1.36 , 4.30]
Subtotal (95% CI)		**137**		**136**	**100.0%**	**2.12 [1.70 , 2.65]**
Total events:	114		51			
Heterogeneity: Tau² = 0.00; Chi² = 2.01, df = 2 (P = 0.37); I² = 1%						
Test for overall effect: Z = 6.70 (P < 0.00001)						
Total (95% CI)		**137**		**136**	**100.0%**	**2.12 [1.70 , 2.65]**
Total events:	114		51			
Heterogeneity: Tau² = 0.00; Chi² = 2.01, df = 2 (P = 0.37); I² = 1%						
Test for overall effect: Z = 6.70 (P < 0.00001)						
Test for subgroup differences: Not applicable						



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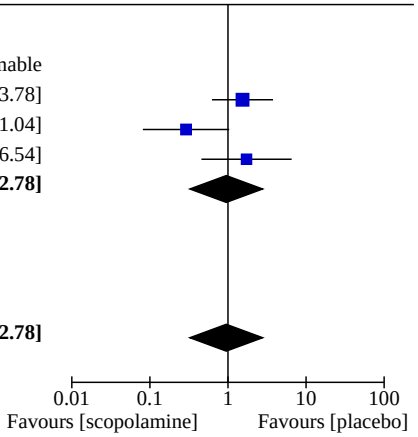
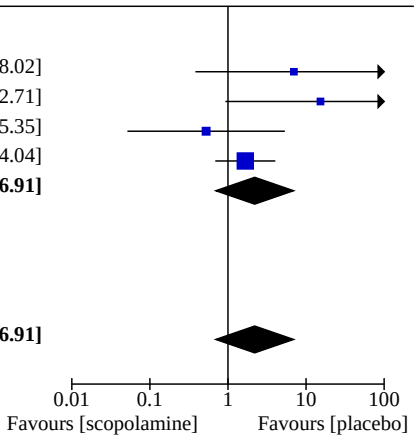
Analysis 17.4. Comparison 17: Scopalamine versus placebo, Outcome 4: Headache

Study or Subgroup	Scopalamine Events	Scopalamine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
17.4.1 NA dose						
Ahn 2002	0	22	0	22		Not estimable
Bailey 1990	11	88	7	86	39.5%	1.54 [0.62 , 3.78]
Jespersen 1989	3	93	9	81	30.9%	0.29 [0.08 , 1.04]
Kim 1992	5	27	3	28	29.7%	1.73 [0.46 , 6.54]
Subtotal (95% CI)		**230**		**217**	**100.0%**	**0.95 [0.33 , 2.78]**
Total events:	19		19			
Heterogeneity: Tau² = 0.55; Chi² = 5.14, df = 2 (P = 0.08); I² = 61%						
Test for overall effect: Z = 0.09 (P = 0.93)						
Total (95% CI)		**230**		**217**	**100.0%**	**0.95 [0.33 , 2.78]**
Total events:	19		19			
Heterogeneity: Tau² = 0.55; Chi² = 5.14, df = 2 (P = 0.08); I² = 61%						
Test for overall effect: Z = 0.09 (P = 0.93)						
Test for subgroup differences: Not applicable						



Analysis 17.5. Comparison 17: Scopalamine versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Scopalamine Events	Scopalamine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
17.5.1 NA dose						
Ahn 2002	3	22	0	22	13.0%	7.00 [0.38 , 128.02]
Larsson 1988	8	29	0	26	13.8%	15.30 [0.93 , 252.71]
Simpson 1988	1	20	2	21	18.7%	0.53 [0.05 , 5.35]
Tigerstedt 1988	10	32	6	32	54.5%	1.67 [0.69 , 4.04]
Subtotal (95% CI)		**103**		**101**	**100.0%**	**2.20 [0.70 , 6.91]**
Total events:	22		8			
Heterogeneity: Tau² = 0.42; Chi² = 4.16, df = 3 (P = 0.24); I² = 28%						
Test for overall effect: Z = 1.35 (P = 0.18)						
Total (95% CI)		**103**		**101**	**100.0%**	**2.20 [0.70 , 6.91]**
Total events:	22		8			
Heterogeneity: Tau² = 0.42; Chi² = 4.16, df = 3 (P = 0.24); I² = 28%						
Test for overall effect: Z = 1.35 (P = 0.18)						
Test for subgroup differences: Not applicable						



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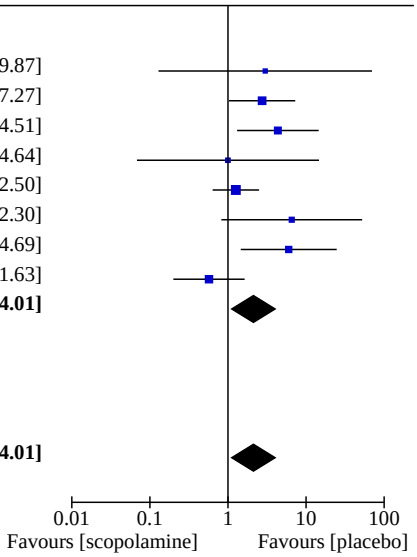
Analysis 17.6. Comparison 17: Scopalamine versus placebo, Outcome 6: Visual disturbances

Study or Subgroup	Scopalamine Events	Scopalamine Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
17.6.1 NA dose						
Ahn 2002	1	22	0	22	3.6%	3.00 [0.13 , 69.87]
Bailey 1990	14	88	5	86	17.9%	2.74 [1.03 , 7.27]
Jespersen 1989	15	93	3	81	14.7%	4.35 [1.31 , 14.51]
Reinhart 1994	1	16	1	16	4.8%	1.00 [0.07 , 14.64]
Semple 1992	14	37	9	30	22.7%	1.26 [0.64 , 2.50]
Sohi 1994	6	43	1	47	7.2%	6.56 [0.82 , 52.30]
Tigerstedt 1988	12	32	2	32	12.3%	6.00 [1.46 , 24.69]
Uppington 1986	4	19	7	19	16.8%	0.57 [0.20 , 1.63]
Subtotal (95% CI)		**350**		**333**	**100.0%**	**2.12 [1.12 , 4.01]**
Total events:	67		28			
Heterogeneity: Tau² = 0.34; Chi² = 12.94, df = 7 (P = 0.07); I² = 46%						
Test for overall effect: Z = 2.30 (P = 0.02)						
Total (95% CI)		**350**		**333**	**100.0%**	**2.12 [1.12 , 4.01]**
Total events:	67		28			
Heterogeneity: Tau² = 0.34; Chi² = 12.94, df = 7 (P = 0.07); I² = 46%						
Test for overall effect: Z = 2.30 (P = 0.02)						
Test for subgroup differences: Not applicable						



Comparison 18. Tropisetron versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
18.1 Vomiting within 0 to 24 hours	13	1275	Risk Ratio (IV, Random, 95% CI)	0.61 [0.51, 0.72]
18.1.1 Low dose	2	180	Risk Ratio (IV, Random, 95% CI)	0.80 [0.53, 1.21]
18.1.2 Recommended dose	3	281	Risk Ratio (IV, Random, 95% CI)	0.63 [0.42, 0.94]
18.1.3 High dose	8	590	Risk Ratio (IV, Random, 95% CI)	0.53 [0.41, 0.68]
18.1.4 NA dose	2	224	Risk Ratio (IV, Random, 95% CI)	0.70 [0.42, 1.16]
18.2 Serious adverse events	2	727	Risk Ratio (IV, Random, 95% CI)	1.13 [0.04, 35.93]
18.2.1 Recommended dose	1	571	Risk Ratio (IV, Random, 95% CI)	6.51 [0.34, 125.37]
18.2.2 NA dose	1	156	Risk Ratio (IV, Random, 95% CI)	0.19 [0.01, 3.90]
18.3 Any adverse event	3	1007	Risk Ratio (IV, Random, 95% CI)	1.01 [0.83, 1.22]
18.3.1 Low dose	2	180	Risk Ratio (IV, Random, 95% CI)	1.32 [0.69, 2.54]
18.3.2 Recommended dose	2	698	Risk Ratio (IV, Random, 95% CI)	0.98 [0.80, 1.20]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
18.3.3 High dose	1	129	Risk Ratio (IV, Random, 95% CI)	1.03 [0.36, 2.98]
18.4 Headache	10	1656	Risk Ratio (IV, Random, 95% CI)	1.12 [0.83, 1.52]
18.4.1 Low dose	2	180	Risk Ratio (IV, Random, 95% CI)	3.13 [0.82, 12.00]
18.4.2 Recommended dose	3	772	Risk Ratio (IV, Random, 95% CI)	1.44 [0.57, 3.62]
18.4.3 High dose	7	548	Risk Ratio (IV, Random, 95% CI)	1.01 [0.71, 1.42]
18.4.4 NA dose	1	156	Risk Ratio (IV, Random, 95% CI)	1.19 [0.33, 4.26]
18.5 Sedation/drowsiness	2	98	Risk Ratio (IV, Random, 95% CI)	5.81 [0.71, 47.88]
18.5.1 High dose	2	98	Risk Ratio (IV, Random, 95% CI)	5.81 [0.71, 47.88]
18.6 Extrapyramidal symptoms	3	187	Risk Ratio (IV, Random, 95% CI)	0.82 [0.35, 1.89]
18.6.1 High dose	3	187	Risk Ratio (IV, Random, 95% CI)	0.82 [0.35, 1.89]
18.7 Constipation	2	226	Risk Ratio (IV, Random, 95% CI)	1.42 [0.24, 8.29]
18.7.1 High dose	1	70	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.7.2 NA dose	1	156	Risk Ratio (IV, Random, 95% CI)	1.42 [0.24, 8.29]
18.8 Postoperative wound infection	1	156	Risk Ratio (IV, Random, 95% CI)	0.32 [0.01, 7.66]
18.8.1 NA dose	1	156	Risk Ratio (IV, Random, 95% CI)	0.32 [0.01, 7.66]
18.9 Arrhythmia	1	50	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.9.1 High dose	1	50	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.10 Visual disturbances	1	97	Risk Ratio (IV, Random, 95% CI)	2.55 [0.52, 12.52]
18.10.1 High dose	1	97	Risk Ratio (IV, Random, 95% CI)	2.55 [0.52, 12.52]
18.11 QT prolongation	1	385	Risk Ratio (IV, Random, 95% CI)	1.01 [0.04, 24.20]
18.11.1 Low dose	1	129	Risk Ratio (IV, Random, 95% CI)	1.01 [0.04, 24.20]
18.11.2 Recommended dose	1	127	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.11.3 High dose	1	129	Risk Ratio (IV, Random, 95% CI)	Not estimable

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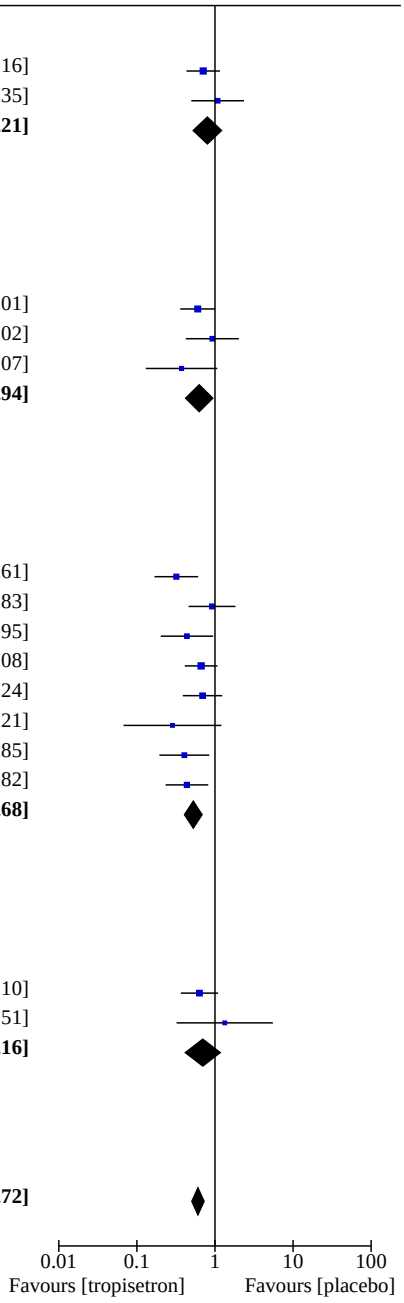
Analysis 18.1. Comparison 18: Tropisetron versus placebo, Outcome 1: Vomiting within 0 to 24 hours

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.1.1 Low dose						
Capouet 1996	30	97	14	32	11.6%	0.71 [0.43 , 1.16]
Lee SY 2001	8	23	9	28	5.0%	1.08 [0.50 , 2.35]
Subtotal (95% CI)		**120**		**60**	**16.6%**	**0.80 [0.53 , 1.21]**
Total events:	38		23			
Heterogeneity: Tau² = 0.00; Chi² = 0.82, df = 1 (P = 0.36); I² = 0%						
Test for overall effect: Z = 1.06 (P = 0.29)						
18.1.2 Recommended dose						
Capouet 1996	25	95	14	32	10.6%	0.60 [0.36 , 1.01]
Wang 2002a	9	38	10	39	5.0%	0.92 [0.42 , 2.02]
Wang 2002b	4	38	11	39	2.8%	0.37 [0.13 , 1.07]
Subtotal (95% CI)		**171**		**110**	**18.4%**	**0.63 [0.42 , 0.94]**
Total events:	38		35			
Heterogeneity: Tau² = 0.00; Chi² = 1.90, df = 2 (P = 0.39); I² = 0%						
Test for overall effect: Z = 2.28 (P = 0.02)						
18.1.3 High dose						
Akin 2006	8	35	25	35	7.2%	0.32 [0.17 , 0.61]
Ali Melkkila 1996	11	40	12	40	6.3%	0.92 [0.46 , 1.83]
Alon 1996	7	40	16	40	5.1%	0.44 [0.20 , 0.95]
Capouet 1996	29	96	15	33	12.1%	0.66 [0.41 , 1.08]
Ekinci 2011	9	20	13	20	8.6%	0.69 [0.39 , 1.24]
Stefani 1995	2	20	7	20	1.5%	0.29 [0.07 , 1.21]
Tsui 1999	7	37	21	45	5.6%	0.41 [0.19 , 0.85]
Zomers 1993	9	35	20	34	7.5%	0.44 [0.23 , 0.82]
Subtotal (95% CI)		**323**		**267**	**53.8%**	**0.53 [0.41 , 0.68]**
Total events:	82		129			
Heterogeneity: Tau² = 0.02; Chi² = 8.24, df = 7 (P = 0.31); I² = 15%						
Test for overall effect: Z = 4.87 (P < 0.00001)						
18.1.4 NA dose						
Eberhart 2006	16	80	24	76	9.6%	0.63 [0.37 , 1.10]
Jakobsson 1999	4	34	3	34	1.6%	1.33 [0.32 , 5.51]
Subtotal (95% CI)		**114**		**110**	**11.1%**	**0.70 [0.42 , 1.16]**
Total events:	20		27			
Heterogeneity: Tau² = 0.00; Chi² = 0.92, df = 1 (P = 0.34); I² = 0%						
Test for overall effect: Z = 1.38 (P = 0.17)						
Total (95% CI)		**728**		**547**	**100.0%**	**0.61 [0.51 , 0.72]**
Total events:	178		214			
Heterogeneity: Tau² = 0.01; Chi² = 15.06, df = 14 (P = 0.37); I² = 7%						
Test for overall effect: Z = 5.50 (P < 0.00001)						
Test for subgroup differences: Chi² = 3.13, df = 3 (P = 0.37), I² = 4.1%						



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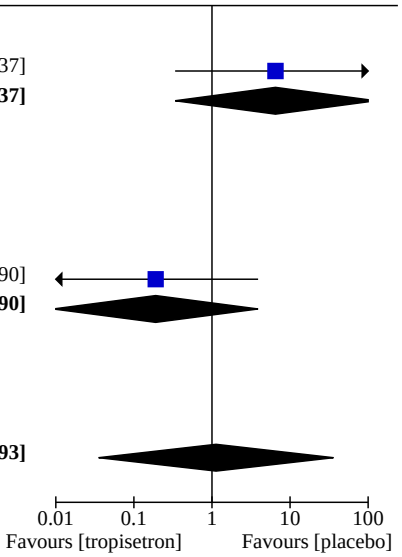
Analysis 18.2. Comparison 18: Tropisetron versus placebo, Outcome 2: Serious adverse events

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.2.1 Recommended dose						
Scholz 1998	3	296	0	275	50.4%	6.51 [0.34 , 125.37]
Subtotal (95% CI)		**296**		**275**	**50.4%**	**6.51 [0.34 , 125.37]**
Total events:	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.24 (P = 0.21)						
18.2.2 NA dose						
Eberhart 2006	0	80	2	76	49.6%	0.19 [0.01 , 3.90]
Subtotal (95% CI)		**80**		**76**	**49.6%**	**0.19 [0.01 , 3.90]**
Total events:	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.08 (P = 0.28)						
Total (95% CI)		**376**		**351**	**100.0%**	**1.13 [0.04 , 35.93]**
Total events:	3		2			
Heterogeneity: Tau² = 3.91; Chi² = 2.68, df = 1 (P = 0.10); I² = 63%						
Test for overall effect: Z = 0.07 (P = 0.95)						
Test for subgroup differences: Chi² = 2.68, df = 1 (P = 0.10), I² = 62.7%						



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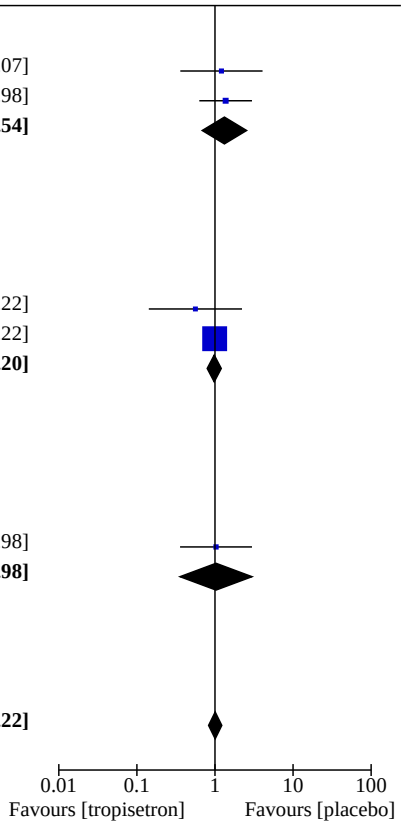
Analysis 18.3. Comparison 18: Tropisetron versus placebo, Outcome 3: Any adverse event

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.3.1 Low dose						
Capouet 1996	11	97	3	32	2.6%	1.21 [0.36 , 4.07]
Lee SY 2001	9	23	8	28	6.3%	1.37 [0.63 , 2.98]
Subtotal (95% CI)		**120**		**60**	**8.8%**	**1.32 [0.69 , 2.54]**
Total events:	20		11			
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.83 (P = 0.40)						
18.3.2 Recommended dose						
Capouet 1996	5	95	3	32	2.0%	0.56 [0.14 , 2.22]
Scholz 1998	112	296	105	275	85.8%	0.99 [0.80 , 1.22]
Subtotal (95% CI)		**391**		**307**	**87.8%**	**0.98 [0.80 , 1.20]**
Total events:	117		108			
Heterogeneity: Tau² = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%						
Test for overall effect: Z = 0.21 (P = 0.84)						
18.3.3 High dose						
Capouet 1996	12	96	4	33	3.4%	1.03 [0.36 , 2.98]
Subtotal (95% CI)		**96**		**33**	**3.4%**	**1.03 [0.36 , 2.98]**
Total events:	12		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.06 (P = 0.95)						
Total (95% CI)		**607**		**400**	**100.0%**	**1.01 [0.83 , 1.22]**
Total events:	149		123			
Heterogeneity: Tau² = 0.00; Chi² = 1.41, df = 4 (P = 0.84); I² = 0%						
Test for overall effect: Z = 0.06 (P = 0.95)						
Test for subgroup differences: Chi² = 0.74, df = 2 (P = 0.69), I² = 0%						



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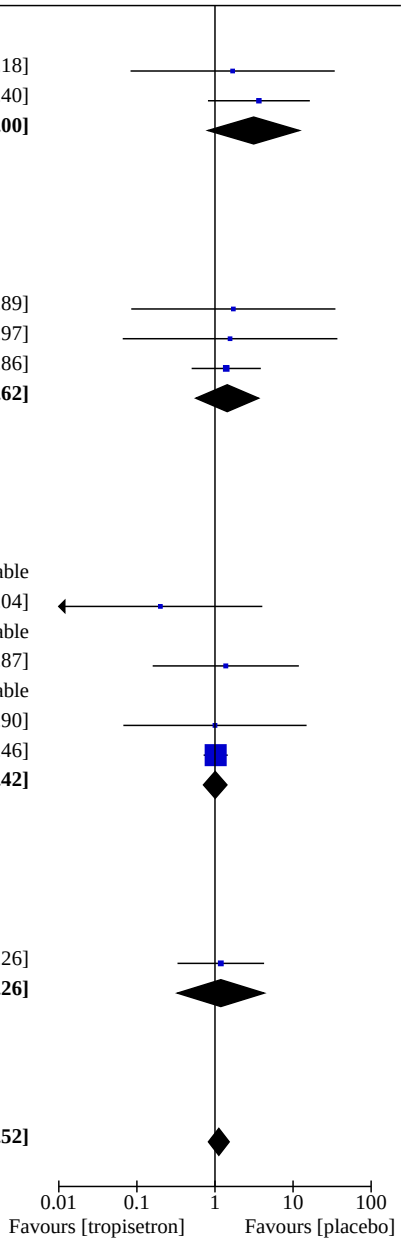
Analysis 18.4. Comparison 18: Tropisetron versus placebo, Outcome 4: Headache

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.4.1 Low dose						
Capouet 1996	2	97	0	32	1.0%	1.68 [0.08 , 34.18]
Lee SY 2001	6	23	2	28	4.1%	3.65 [0.81 , 16.40]
Subtotal (95% CI)		**120**		**60**	**5.2%**	**3.13 [0.82 , 12.00]**
Total events:	8		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 1 (P = 0.65); I² = 0%						
Test for overall effect: Z = 1.66 (P = 0.10)						
18.4.2 Recommended dose						
Capouet 1996	2	95	0	32	1.0%	1.72 [0.08 , 34.89]
Chan 1998	1	49	0	25	0.9%	1.56 [0.07 , 36.97]
Scholz 1998	9	296	6	275	9.0%	1.39 [0.50 , 3.86]
Subtotal (95% CI)		**440**		**332**	**10.9%**	**1.44 [0.57 , 3.62]**
Total events:	12		6			
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 2 (P = 0.99); I² = 0%						
Test for overall effect: Z = 0.77 (P = 0.44)						
18.4.3 High dose						
Akin 2005	0	35	0	35		Not estimable
Alon 1996	0	40	2	40	1.0%	0.20 [0.01 , 4.04]
Argiriadou 2002	0	31	0	27		Not estimable
Capouet 1996	4	96	1	33	2.0%	1.38 [0.16 , 11.87]
Chan 1998	0	49	0	25		Not estimable
Ekinci 2011	1	20	1	20	1.3%	1.00 [0.07 , 14.90]
Purhonen 1997	27	48	27	49	73.9%	1.02 [0.72 , 1.46]
Subtotal (95% CI)		**319**		**229**	**78.2%**	**1.01 [0.71 , 1.42]**
Total events:	32		31			
Heterogeneity: Tau² = 0.00; Chi² = 1.20, df = 3 (P = 0.75); I² = 0%						
Test for overall effect: Z = 0.04 (P = 0.97)						
18.4.4 NA dose						
Eberhart 2006	5	80	4	76	5.7%	1.19 [0.33 , 4.26]
Subtotal (95% CI)		**80**		**76**	**5.7%**	**1.19 [0.33 , 4.26]**
Total events:	5		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.79)						
Total (95% CI)		**959**		**697**	**100.0%**	**1.12 [0.83 , 1.52]**
Total events:	57		43			
Heterogeneity: Tau² = 0.00; Chi² = 4.32, df = 9 (P = 0.89); I² = 0%						
Test for overall effect: Z = 0.73 (P = 0.47)						
Test for subgroup differences: Chi² = 2.90, df = 3 (P = 0.41), I² = 0%						



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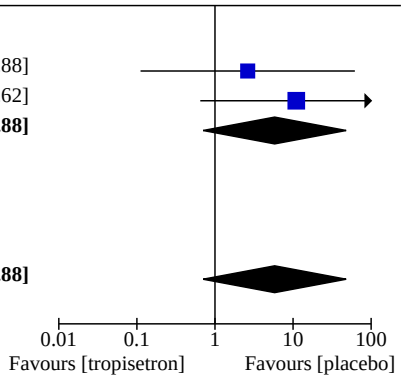
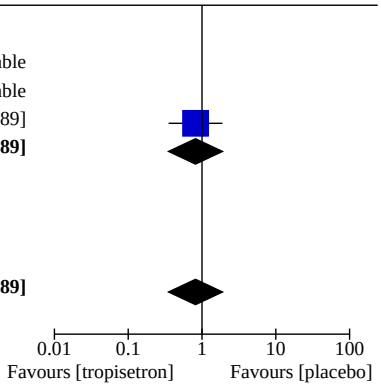
Analysis 18.5. Comparison 18: Tropisetron versus placebo, Outcome 5: Sedation/drowsiness

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.5.1 High dose						
Argiriadou 2002	1	31	0	27	44.5%	2.63 [0.11 , 61.88]
Ekinci 2011	5	20	0	20	55.5%	11.00 [0.65 , 186.62]
Subtotal (95% CI)		**51**		**47**	**100.0%**	**5.81 [0.71 , 47.88]**
Total events:	6		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.44, df = 1 (P = 0.51); I² = 0%						
Test for overall effect: Z = 1.64 (P = 0.10)						
Total (95% CI)		**51**		**47**	**100.0%**	**5.81 [0.71 , 47.88]**
Total events:	6		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.44, df = 1 (P = 0.51); I² = 0%						
Test for overall effect: Z = 1.64 (P = 0.10)						
Test for subgroup differences: Not applicable						



Analysis 18.6. Comparison 18: Tropisetron versus placebo, Outcome 6: Extrapyramidal symptoms

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.6.1 High dose						
Contreras Dominguez 2008	0	25	0	25		Not estimable
Ekinci 2011	0	20	0	20		Not estimable
Purhonen 1997	8	48	10	49	100.0%	0.82 [0.35 , 1.89]
Subtotal (95% CI)		**93**		**94**	**100.0%**	**0.82 [0.35 , 1.89]**
Total events:	8		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						
Total (95% CI)		**93**		**94**	**100.0%**	**0.82 [0.35 , 1.89]**
Total events:	8		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						
Test for subgroup differences: Not applicable						



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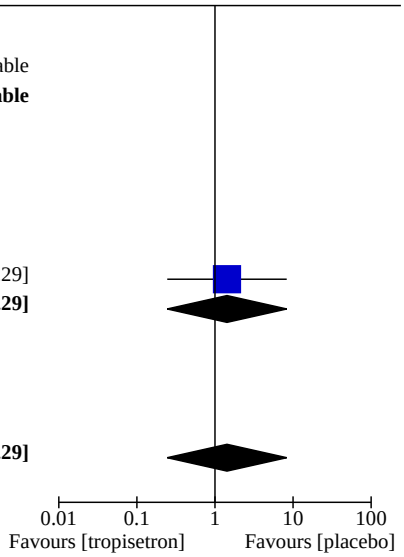
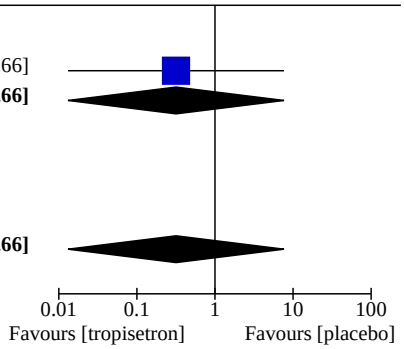
Analysis 18.7. Comparison 18: Tropisetron versus placebo, Outcome 7: Constipation

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.7.1 High dose						
Akin 2005	0	35	0	35		Not estimable
Subtotal (95% CI)		**35**		**35**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
18.7.2 NA dose						
Eberhart 2006	3	80	2	76	100.0%	1.43 [0.24 , 8.29]
Subtotal (95% CI)		**80**		**76**	**100.0%**	**1.43 [0.24 , 8.29]**
Total events:	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.69)						
Total (95% CI)		**115**		**111**	**100.0%**	**1.43 [0.24 , 8.29]**
Total events:	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.69)						
Test for subgroup differences: Not applicable						



Analysis 18.8. Comparison 18: Tropisetron versus placebo, Outcome 8: Postoperative wound infection

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.8.1 NA dose						
Eberhart 2006	0	80	1	76	100.0%	0.32 [0.01 , 7.66]
Subtotal (95% CI)		**80**		**76**	**100.0%**	**0.32 [0.01 , 7.66]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.71 (P = 0.48)						
Total (95% CI)		**80**		**76**	**100.0%**	**0.32 [0.01 , 7.66]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.71 (P = 0.48)						
Test for subgroup differences: Not applicable						



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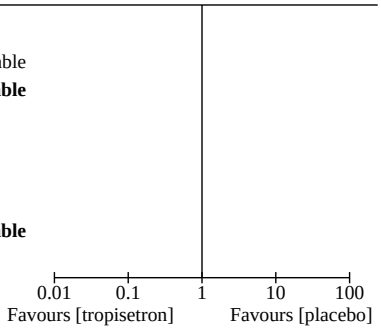
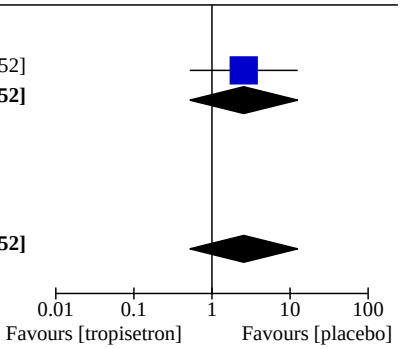
Analysis 18.9. Comparison 18: Tropisetron versus placebo, Outcome 9: Arrhythmia

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.9.1 High dose						
Contreras Dominguez 2008	0	25	0	25		Not estimable
Subtotal (95% CI)		**25**		**25**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**25**		**25**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 18.10. Comparison 18: Tropisetron versus placebo, Outcome 10: Visual disturbances

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.10.1 High dose						
Purhonen 1997	5	48	2	49	100.0%	2.55 [0.52 , 12.52]
Subtotal (95% CI)		**48**		**49**	**100.0%**	**2.55 [0.52 , 12.52]**
Total events:	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.15 (P = 0.25)						
Total (95% CI)		**48**		**49**	**100.0%**	**2.55 [0.52 , 12.52]**
Total events:	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.15 (P = 0.25)						
Test for subgroup differences: Not applicable						



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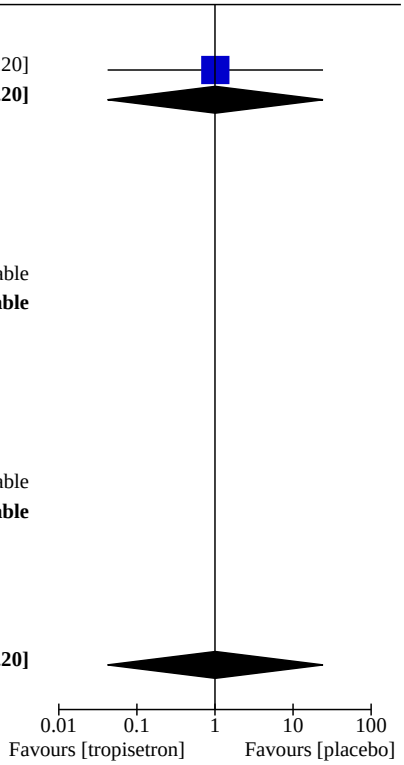
Analysis 18.11. Comparison 18: Tropisetron versus placebo, Outcome 11: QT prolongation

Study or Subgroup	Tropisetron Events	Tropisetron Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.11.1 Low dose						
Capouet 1996	1	97	0	32	100.0%	1.01 [0.04 , 24.20]
Subtotal (95% CI)		**97**		**32**	**100.0%**	**1.01 [0.04 , 24.20]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 1.00)						
18.11.2 Recommended dose						
Capouet 1996	0	95	0	32		Not estimable
Subtotal (95% CI)		**95**		**32**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
18.11.3 High dose						
Capouet 1996	0	96	0	33		Not estimable
Subtotal (95% CI)		**96**		**33**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**288**		**97**	**100.0%**	**1.01 [0.04 , 24.20]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 1.00)						
Test for subgroup differences: Not applicable						



ADDITIONAL TABLES

Table 1. Recommended, low, and high doses of antiemetic drugs

Drug	Dose*	Cut-off (lower, upper limit)**	Low dose	Recommended dose	High dose
Amisulpride	5 mg to 10 mg IV	NR	< 5 mg	5 mg to 10 mg	> 10 mg
Aprepitant	40 mg per os	NR	< 40 mg	40 mg	> 40 mg
Casopitant	150 mg per os	NR	< 150 mg	150 mg	> 150 mg
Dexamethasone	4 mg to 5 mg IV	NR	< 4 mg	4 mg to 5 mg	> 5 mg
Dimenhydrinate	1 mg/kg IV	NR	< 1 mg/kg	1 mg/kg	> 1 mg/kg
Dolasetron	12.5 mg IV	NR	< 12.5 mg	12.5 mg	> 12.5 mg
Droperidol	0.625 mg to 1.25 mg IV	See FDA[1] 2.5 mg IV	< 0.625 mg	0.625 mg to 1.25 mg	> 1.25 mg
Fosaprepitant	NR	NR	NR	NR	NR

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Table 1. Recommended, low, and high doses of antiemetic drugs *(Continued)*

Granisetron	0.35 mg to 3 mg IV	NR	< 0.35 mg	0.35 mg to 3 mg	> 3 mg
Haloperidol	0.5 mg to < 2 mg IM/IV	See FDA < 2 mg	< 0.5 mg	0.5 mg to < 2 mg	2 mg (cut-off)
Meclizine	50 mg per os	NR	< 50 mg	50 mg	> 50 mg
Methylprednisolone	40 mg IV	NR	< 40 mg	40 mg	> 40 mg
Metoclopramide	25 mg to 50 mg IV	10 mg[(2)]	< 25 mg (10 mg cut-off)	25 mg to 50 mg	> 50 mg
Ondansetron	4 mg IV, 8 mg ODT	NR for PONV (32 mg for other[(3)])	< 4 mg IV, < 8 mg ODT	4 mg IV, 8 mg ODT	> 4 mg IV, > 8 mg ODT, (32 mg cut-off)
Palonosetron	0.075 mg IV	NR	< 0.075 mg	0.075 mg	> 0.075 mg
Perphenazine	5 mg IV	NR	< 5 mg	5 mg	> 5 mg
Promethazine	6.25 mg to 12.5 mg IV	NR	< 6.25 mg	6.25 mg to 12.5 mg	> 12.5 mg
Ramosetron	0.3 mg IV	NR	< 0.3 mg	0.3 mg	> 0.3 mg
Rolapitant	70 mg to 200 mg per os	NR	< 70 mg	70 mg to 200 mg	> 200 mg
Scopolamine	Transdermal patch	NR	NA	NA	NA
Tropisetron	2 mg IV	NR	< 2 mg	2 mg	> 2 mg

* Recommended doses are based on Gan 2014; for amisulpride, we used data from a dose-finding study (Kranke 2013).
** Cut-off limits are based on those reported in Gan 2014.
(1) FDA black box warning.
(2) Metoclopramide at a dose of 10 mg is not effective in reducing the incidence of PONV.
(3) 32 mg single IV dose for chemotherapy-induced nausea (FDA warning).
Abbreviations: IM = intramuscular; IV = intravenous; NA = not applicable; NR = not reported; ODT = orally disintegration tablets; per os = per oral.

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Table 2. Monitoring and reporting of any (severe) adverse events

Study ID	Any AE				SAE		Ris of bias	
	1. Did the study report "any AE"?	1.1 Did the authors proactively monitor for any AE?	1.2 Did the authors simply provide spontaneous reporting (passively) of AEs by participants?	1.3 Did the authors report all relevant (class-specific) AEs?	2. Did the study report "SAEs"?	2.1 Did the authors define SAEs according to an accepted international classification?	RoB (any AE)	RoB (SAE)
	Y/N (if Y, 1.1 -> 1.3; if N, go to 2)	Y/N	Y/N	Y/N	Y/N (if Y, 2.1; if N, go to 3)	Y/N		
Ahn 2002	Y	Y	N	Y	N		low	NA
Altorjay 2011	Y	unclear	unclear	Y	N		unclear	NA
Ansari 2010	Y	unclear	unclear	N	N		high	NA
Bailey 1990	Y	Y	N	Y	Y	N	low	high
Bang 2016	N				Y	N	NA	high
Bhatnagar 2007	Y	unclear	unclear	Y	N		unclear	NA
Bianchin 2007	Y	unclear	unclear	Y	Y	N	unclear	high
Biedler 1998	Y	unclear	unclear	Y	N		unclear	NA
Biswas 2003	Y	unclear	unclear	N	N		high	NA
Candiotti 2008	Y	unclear	unclear	Y	Y	N	unclear	high
Capouet 1996	Y	Y	N	N	N		unclear	NA
Chen 2006	Y	unclear	unclear	Y	N		unclear	NA
DAngelo 2005	Y	unclear	unclear	N	N		high	NA
Diemunsch 1997	N				Y	N	NA	high

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Table 2. Monitoring and reporting of any (severe) adverse events *(Continued)*

Diemunsch 1998	N				Y	N	NA	high
Diemunsch 2007	Y	Y	N	Y	Y	N	low	high
Dua 2004	Y	unclear	unclear	N	N		high	NA
Dua 2014	Y	unclear	unclear	N	N		high	NA
Eberhart 2006	N				Y	N	NA	high
Fortney 1998	Y	N	Y	N	N		high	NA
Gan 2005	Y	unclear	unclear	N	Y	N	high	high
Gan 2007	Y	Y	N	Y	Y	N	low	high
Gan 2009	Y	unclear	unclear	N	N		high	NA
Gan 2017	Y	Y	N	N	Y	N	unclear	high
Green 2012	Y	Y	N	N	N		low	NA
Gugale 2016	Y	unclear	unclear	N	N		high	NA
Hanaoka 2004	Y	Y	N	N	Y	Y	unclear	low
Helmers 1993	Y	Y	N	Y	N		low	NA
Hessami 2012	Y	unclear	unclear	N	N		high	NA
Ibrahim 2013	N				Y	N	NA	high
Joe 2009	Y	unclear	unclear	N	N		high	NA
Jones 2006	Y	unclear	unclear	N	N		high	NA
Kaja 2014	N				Y	N	NA	high
Kim 1992	Y	unclear	unclear	N	N		high	NA
Kocamanoglu 2005	N				Y	N	NA	high

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Table 2. Monitoring and reporting of any (severe) adverse events *(Continued)*

Koivuranta 1997	N				Y	N	NA	high
Koivuranta 1999	N				Y	N	NA	high
Kothari 2000	Y	unclear	unclear	N	N		high	NA
Kovac 1992	Y	unclear	unclear	N	N		high	NA
Koyuncu 2017	Y	Y	N	N	N		unclear	NA
Kranke 2013	Y	unclear	unclear	unclear	Y	N	unclear	high
Krobbuaban 2008	Y	unclear	unclear	N	N		high	NA
Kyokong 1999	Y	unclear	unclear	N	N		high	NA
Laha 2013	Y	Y	N	N	N		unclear	NA
Lee 2008a	N				Y	N	NA	high
Lee 2008b	Y	unclear	unclear	N	N		high	NA
Lee SY 2001	Y	unclear	unclear	N	N		high	NA
Lee SY 2002	Y	Y	N	Y	N		low	NA
Morris 1998	Y	unclear	unclear	N	N		high	NA
Moussa 2007	Y	Y	N	N	N		unclear	NA
Murphy 2011a	Y	Y	N	Y	N		low	NA
NKO101287	Y	unclear	unclear	Y	Y	N	unclear	high
NKT102245	Y	Y	N	Y	Y	Y	low	low
NKT102260	Y	Y	N	Y	Y	Y	low	low
NKT102552	Y	Y	N	Y	Y	Y	low	low
Ozmen 2002	Y	unclear	unclear	N	N		high	NA

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Table 2. Monitoring and reporting of any (severe) adverse events *(Continued)*

PALO-04-07	Y	Y	N	N	Y	N	unclear	high
Papadima 2013	N				Y	N	NA	high
Papadimitriou 2001	Y	Y	N	N	Y	N	unclear	high
Park 2006	Y	Y	N	N	N		unclear	NA
Scholz 1998	Y	unclear	unclear	N	Y	N	high	high
Segelman 2016	Y	N	Y	N	N		high	NA
Shah 1972	Y	Y	N	N	N		unclear	NA
Singla 2010	Y	unclear	unclear	Y	N		unclear	NA
Sung 1993	Y	N	Y	N	N		high	NA
Tarantino 2015	Y	unclear	unclear	Y	Y	Y	unclear	low
Tzeng 2000	Y	Y	N	N	N		unclear	NA
Wadood 2014	Y	unclear	unclear	N	N		high	NA
Wagner 1996	Y	Y	N	N	N		unclear	NA
Warriner 1997	N				Y	N	NA	high
Wattwil 2003	Y	Y	N	N	N		unclear	NA
Yuksek 2003	Y	unclear	unclear	N	N		high	NA
Zhou 2012	Y	unclear	unclear	N	N		high	NA

Abbreviations: N = no; NA = not applicable; Y = yes.

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Table 3. Most common dosages, routes, and time points of administration of single drugs of direct interest (primary outcome: vomiting)

Drug	Dose	Dose category	Route	Timing
Amisulpride	5 to 10 mg	rec	IV	at induction of AN
Aprepitant	40 mg	rec	PO	before surgery
Casopitant	150 mg	rec	PO	before surgery
Dexamethasone*	4 to 5 mg	rec	IV	at induction of AN
Dimenhydrinate	< 1 mg/kg	low	IV/IM	at induction of AN/before surgery
Dolasetron	12.5 mg	rec	IV	end of surgery
Droperidol	0.625 to 1.25 mg	rec	IV	at induction of AN
Fosaprepitant	150 mg	NA	IV	at induction of AN
Granisetron	0.35 to 3 mg	rec	IV	all time points
Haloperidol	0.5 to < 2 mg	rec	IV	at induction of AN
Metoclopramide	25 to 50 mg	low	IV	at induction of AN
Ondansetron (IV)	4 mg	rec	IV	at induction of AN
Ondansetron (PO)	8 mg	rec	PO	before surgery
Palonosetron	0.075 mg	rec	IV	at induction of AN
Promethazine**	< 6.25 mg	low	IV	at induction of AN
Ramosetron (IV)	0.3 mg	rec	IV	end of surgery
Rolapitant	70 to 200 mg	rec	PO	before surgery
Scopolamine	1.5 mg	NA	TD	before surgery
Tropisetron (IV)*	2 mg	rec	IV	at induction of AN

The table reported the most commonly used doses, routes, and time points of administration of drugs of direct interest for vomiting.
*Most of the studies investigated high doses, but recommended were also effective.
**Not used in any of the included studies with recommended dose.
Abbreviations: AN = anaesthesia; IM = intramuscular; IV = intravenous; NA = not applicable; PO = per oral; rec = recommended; TD = transdermal.

APPENDICES

Appendix 1. Search strategies

Ovid MEDLINE(R) ALL <1946 to 23 April 2020>

1 nausea/

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2 vomiting/

3 "postoperative nausea and vomiting"/

4 (nausea* or nauseous* or inappeten* or PONV or emet* or vomit* or emesis or retch*).ti,ab,kf,hw.

5 1 or 2 or 3 or 4

6 Postoperative Care/

7 exp Postoperative Period/

8 exp Anesthesia/

9 "postoperative nausea and vomiting"/

10 exp Postoperative Complications/

11 Anesthesia Recovery Period/

12 (an?esth* or postoperat* or post operat* or postsurg* or post surg* or PONV or ((after or following) adj2 (surg* or operat*))).ti,ab,kf,hw.

13 6 or 7 or 8 or 9 or 10 or 11 or 12

14 exp Antiemetics/

15 exp Serotonin 5-HT3 Receptor Antagonists/

16 exp Dopamine D2 Receptor Antagonists/

17 exp Adrenal Cortex Hormones/

18 exp Histamine H1 Antagonists/

19 exp Cholinergic Antagonists/

20 Amisulpride/

21 Aprepitant/

22 exp Dexamethasone/

23 Dimenhydrinate/

24 Droperidol/

25 Granisetron/

26 Haloperidol/

27 Meclizine/

28 exp Methylprednisolone/

29 Metoclopramide/

30 Ondansetron/

31 Palonosetron/

32 Perphenazine/

33 Promethazine/

34 Scopolamine/

35 Tropisetron/

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36 (antiemesis or anti emesis or antiemetic* or anti emetic* or antiemetogenic or anti emetogenic or (ALIZAPRIDE or AMISULPRIDE or APREPITANT or BETAMETHASONE or BROMOPRIDE or CASOPITANT or CHLORPROMAZINE or CP-122,721 or CYCLIZINE or DEHYDROBENZPERIDOL or DEXAMETHASONE or DIMENHYDRINATE or DOLASETRON or DOMPERIDONE or DROPERIDOL or FOSAPREPITANT or GRANISETRON or HALOPERIDOL or MECLIZINE or MECLOZINE or METHYLPREDNISOLONE or METOCLOPRAMIDE or NETUPITANT or ONDANSETRON or PALONOSETRON or PERPHENAZINE or PREDNISOLONE or PROCHLORPERAZINE or PROMETHAZINE or RAMOSETRON or ROLAPITANT or SULPIRIDE or TANDOSPIRONE or TIAPRIDE or TRANSDERMAL SCOPOLAMINE or TRIMEPRAZINE or TRIMETHOBENZAMIDE or TROPISETRON or VESTIPITANT)).ti,ab,kf,hw.

37 (serotonin 5 HT3 receptor antagonist* or 5 HT3 antagonist* or corticosteroid* or antihistamine* or antihistaminic* or H1 receptor blockader* or anticholinergic* or anti-cholinergic* or cholinergic antagonist* or cholinergic blocking agent* or Barhemsys or APD421 or Emend or MK-0517 or MK-0869 or L-754030 or GSK-525060 or methylfluorprednisolone or hexadecadrol or Decaject or Decameth or Dexasone or Dexpak or Millicorten or Oradexon or Hexadrol or DMH or Dramanate or Dramamine or Gravol or Anzemet or Anemet or MDL-73147EF or dehidrobenzperidol or dehydrobenzperidol or DHB or Inapsine or Droleptan or emend for injection or MK-0517 or L-785,298 or Kytril or BRL-43694 or Haldol or Antivert or Metipred or Urbason or Maxolon or Reglan or Zofran or ODT or Zuplenz or GR-38032F or RS-25259 or RS-25233 or Aloxi or Decentan or Trilafon or promethazin* or proazamine or Phenergan or Diprazin or Nasea or YM-060 or Varubi or scopolamine or hyoscine or Transderm Scop or Scopoderm TTS or Navoban or ICS-205-930 or azasetron or benzquinamide or buspirone or cetirizine or diclectin or diphenol or dixyrazine or doxylamine or levomepromazine or olanzapine or oxybutynin or penehyclidine or thiethylperazine).ti,ab,kf,hw.

38 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37

39 ((randomized controlled trial or controlled clinical trial).pt. or randomi?ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.)

40 5 and 13 and 38 and 39

Ovid Embase <1974 to 23 April 2020>

1 nausea/

2 vomiting/

3 "nausea and vomiting"/

4 exp "postoperative nausea and vomiting"/

5 (nausea* or nauseous* or inappeten* or PONV or emet* or vomit* or emesis or retch*).ti,ab,kw.

6 1 or 2 or 3 or 4 or 5

7 postoperative care/

8 postanesthesia care/

9 postoperative analgesia/

10 postoperative period/

11 exp anesthesia/

12 exp "postoperative nausea and vomiting"/

13 exp postoperative complication/

14 anesthetic recovery/

15 (an?esth* or postoperat* or post operat* or postsurg* or post surg* or PONV or ((after or following) adj2 (surg* or operat*))).ti,ab,kw.

16 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15

17 exp antiemetic agent/

18 serotonin 3 antagonist/

19 dopamine 2 receptor blocking agent/

20 exp corticosteroid/

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21 exp histamine H1 receptor antagonist/

22 exp cholinergic receptor blocking agent/

23 amisulpride/

24 aprepitant/

25 exp dexamethasone/

26 dimenhydrinate/

27 droperidol/

28 granisetron/

29 haloperidol/

30 meclozine/

31 methylprednisolone/

32 metoclopramide/

33 ondansetron/

34 palonosetron/

35 perphenazine/

36 promethazine/

37 scopolamine/

38 tropisetron/

39 (antiemesis or anti emesis or antiemetic* or anti emetic* or antiemetogenic or anti emetogenic or (ALIZAPRIDE or AMISULPRIDE or APREPITANT or BETAMETHASONE or BROMOPRIDE or CASOPITANT or CHLORPROMAZINE or CP-122,721 or CYCLIZINE or DEHYDROBENZPERIDOL or DEXAMETHASONE or DIMENHYDRINATE or DOLASETRON or DOMPERIDONE or DROPERIDOL or FOSAPREPITANT or GRANISETRON or HALOPERIDOL or MECLIZINE or MECLOZINE or METHYLPREDNISOLONE or METOCLOPRAMIDE or NETUPITANT or ONDANSETRON or PALONOSETRON or PERPHENAZINE or PREDNISOLONE or PROCHLORPERAZINE or PROMETHAZINE or RAMOSETRON or ROLAPITANT or SULPIRIDE or TANDOSPIRONE or TIAPRIDE or TRANSDERMAL SCOPOLAMINE or TRIMEPRAZINE or TRIMETHOBENZAMIDE or TROPISETRON or VESTIPITANT)).ti,ab,kw.

40 (serotonin 5 HT3 receptor antagonist* or 5 HT3 antagonist* or corticosteroid* or antihistamine* or antihistaminic* or H1 receptor blockader* or anticholinergic* or anti-cholinergic* or cholinergic antagonist* or cholinergic blocking agent* or Barhemsys or APD421 or Emend or MK-0517 or MK-0869 or L-754030 or GSK-525060 or methylfluorprednisolone or hexadecadrol or Decaject or Decameth or Dexasone or Dexpak or Millicorten or Oradexon or Hexadrol or DMH or Dramanate or Dramamine or Gravol or Anzemet or Anemet or MDL-73147EF or dehidrobenzperidol or dehydrobenzperidol or DHB or Inapsine or Droleptan or emend for injection or MK-0517 or L-785,298 or Kytril or BRL-43694 or Haldol or Antivert or Metipred or Urbason or Maxolon or Reglan or Zofran or ODT or Zuplenz or GR-38032F or RS-25259 or RS-25233 or Aloxi or Decentan or Trilafon or promethazin* or proazamine or Phenergan or Diprazin or Nasea or YM-060 or Varubi or scopolamine or hyoscine or Transderm Scop or Scopoderm TTS or Navoban or ICS-205-930 or azasetron or benzquinamide or buspirone or cetirizine or diclectin or diphenol or dixyrazine or doxylamine or levomepromazine or olanzapine or oxybutynin or penehyclidine or thiethylperazine).ti,ab,kw.

41 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40

42 ((crossover procedure or double blind procedure or single blind procedure).sh. or (crossover* or cross over*).ti,ab. or placebo*.ti,ab,sh. or (doubl* adj blind*).ti,ab. or (controlled adj3 (study or design or trial)).ti,ab. or allocat*.ti,ab. or trial*.ti,ab. or randomized controlled trial.sh. or random*.ti,ab.) not ((exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.))

43 6 and 16 and 41 and 42

Cochrane Central Register of Controlled Trials: Issue 4 of 12, April 2020
#1 MeSH descriptor: [Nausea] explode all trees
#2 MeSH descriptor: [Vomiting] explode all trees

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#3 MeSH descriptor: [Postoperative Nausea and Vomiting] explode all trees
#4 (nausea* or nauseous* or inappeten or PONV or emet* or vomit* or emesis):ti,ab,kw
#5 #1 or #2 or #3 or #4
#6 MeSH descriptor: [Postoperative Care] explode all trees
#7 MeSH descriptor: [Postoperative Period] explode all trees
#8 MeSH descriptor: [Anesthesia] explode all trees
#9 MeSH descriptor: [Postoperative Nausea and Vomiting] explode all trees
#10 MeSH descriptor: [Postoperative Complications] explode all trees
#11 MeSH descriptor: [Anesthesia Recovery Period] explode all trees
#12 ((anesth* or anaesth* or postoperat* or post next operat* or postsurg* or post next surg* or PONV) or ((after or following) NEAR/2 (surg* or operat*))):ti,ab,kw
#13 #6 or #7 or #8 or #9 or #10 or #11 or #12
#14 MeSH descriptor: [Antiemetics] explode all trees
#15 MeSH descriptor: [Serotonin 5-HT3 Receptor Antagonists] explode all trees
#16 MeSH descriptor: [Dopamine D2 Receptor Antagonists] explode all trees
#17 MeSH descriptor: [Adrenal Cortex Hormones] explode all trees
#18 MeSH descriptor: [Histamine H1 Antagonists] explode all trees
#19 MeSH descriptor: [Cholinergic Antagonists] explode all trees
#20 MeSH descriptor: [Amisulpride] explode all trees
#21 MeSH descriptor: [Aprepitant] explode all trees
#22 MeSH descriptor: [Dexamethasone] explode all trees
#23 MeSH descriptor: [Dimenhydrinate] explode all trees
#24 MeSH descriptor: [Droperidol] explode all trees
#25 MeSH descriptor: [Granisetron] explode all trees
#26 MeSH descriptor: [Haloperidol] explode all trees
#27 MeSH descriptor: [Meclizine] explode all trees
#28 MeSH descriptor: [Methylprednisolone] explode all trees
#29 MeSH descriptor: [Metoclopramide] explode all trees
#30 MeSH descriptor: [Ondansetron] explode all trees
#31 MeSH descriptor: [Palonosetron] explode all trees
#32 MeSH descriptor: [Perphenazine] explode all trees
#33 MeSH descriptor: [Promethazine] explode all trees
#34 MeSH descriptor: [Scopolamine] explode all trees
#35 MeSH descriptor: [Tropisetron] explode all trees
#36 (antiemesis or anti next emesis or antiemetic* or antiemetogenic or anti next emetic* or ALIZAPRIDE or AMISULPRIDE or APREPITANT or BETAMETHASONE or BROMOPRIDE or CASOPITANT or CHLORPROMAZINE or CP-122,721 or CYCLIZINE or DEHYDROBENZPERIDOL or DEXAMETHASONE or DIMENHYDRINATE or DOLASETRON or DOMPERIDONE or DROPERIDOL or FOSAPREPITANT or GRANISETRON or HALOPERIDOL or MECLIZINE or MECLOZINE or METHYLPREDNISOLONE or METOCLOPRAMIDE or NETUPITANT or ONDANSETRON or PALONOSETRON or PERPHENAZINE or PREDNISOLONE or PROCHLORPERAZINE or PROMETHAZINE or RAMOSETRON or ROLAPITANT or SULPIRIDE or TANDOSPIRONE or TIAPRIDE or TRANSDERMAL next SCOPOLAMINE or TRIMEPRAZINE or TRIMETHOBENZAMIDE or TROPISETRON or VESTIPITANT):ti,ab,kw
#37 (serotonin next 5 next HT3 next receptor next antagonist* or 5 next HT3 next antagonist* or corticosteroid* or antihistamine* or antihistaminic* or H1 next receptor next blockader* or anticholinergic* or anti next cholinergic* or cholinergic next antagonist* or cholinergic next blocking next agent* or Barhemsys or APD421 or Emend or MK 0517 or MK 0869 or L 754030 or GSK 525060 or methylfluorprednisolone or hexadecadrol or Decaject or Decameth or Dexasone or Dexpak or Millicorten or Oradexon or Hexadrol or DMH or Dramanate or Dramamine or Gravol or Anzemet or Anemet or MDL 73147EF or dehidrobenzperidol or dehydrobenzperidol or DHB or Inapsine or Droleptan or emend for injection or MK 0517 or L 785,298 or Kytril or BRL 43694 or Haldol or Antivert or Metipred or Urbason or Maxolon or Reglan or Zofran or ODT or Zuplenz or GR 38032F or RS 25259 or RS 25233 or Aloxi or Decentan or Trilafon or promethazin* or proazamine or Phenergan or Diprazin or Nasea or YM 060 or Varubi or scopolamine or hyoscine or Transderm next Scop or Scopoderm next TTS or Navoban or ICS 205 930 or azasetron or benzquinamide or buspirone or cetirizine or diclectin or diphenol or dixyrazine or doxylamine or levomepromazine or olanzapine or oxybutynin or penehyclidine or thiethylperazine):ti,ab,kw
#38 #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37
#39 #5 and #13 and #38 in Trials

CINAHL Ebsco <1981 to 23 April 2020>
S1 (MH "Nausea and Vomiting+")
S2 TX (nausea* or nauseous* or inappeten* or PONV or emet* or vomit* or emesis or retch*)
S3 S1 OR S2
S4 (MH "Postoperative Care+")
S5 (MH "Postoperative Period")
S6 (MH "Anesthesia+")

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S7 (MH "Postoperative Complications+")
S8 (MH "Anesthesia Recovery")
S9 TX (anesth* or anaesth* or postoperat* or post operat* or postsurg* or post surg* or PONV or ((after or following) N2 (surg* or operat*)))
S10 S4 OR S5 OR S6 OR S7 OR S8 OR S9
S11 (MH "Antiemetics+")
S12 (MH "Serotonin Antagonists+")
S13 (MH "Dopamine Antagonists+")
S14 (MH "Adrenal Cortex Hormones+")
S15 (MH "Histamine H1 Antagonists+")
S16 (MH "Cholinergic Antagonists+")
S17 (MH "Dexamethasone")
S18 (MH "Dimenhydrinate")
S19 (MH "Droperidol")
S20 (MH "Granisetron")
S21 (MH "Haloperidol")
S22 (MH "Meclizine")
S23 (MH "Methylprednisolone")
S24 (MH "Metoclopramide")
S25 (MH "Ondansetron")
S26 (MH "Perphenazine Hydrochloride")
S27 (MH "Promethazine")
S28 (MH "Scopolamine")
S29 TX (antiemesis or anti emesis or antiemetic* or anti emetic* or antiemetogenic or anti emetogenic or (ALIZAPRIDE or AMISULPRIDE or APREPITANT or BETAMETHASONE or BROMOPRIDE or CASOPITANT or CHLORPROMAZINE or CP-122,721 or CYCLIZINE or DEHYDROBENZPERIDOL or DEXAMETHASONE or DIMENHYDRINATE or DOLASETRON or DOMPERIDONE or DROPERIDOL or FOSAPREPITANT or GRANISETRON or HALOPERIDOL or MECLIZINE or MECLOZINE or METHYLPREDNISOLONE or METOCLOPRAMIDE or NETUPITANT or ONDANSETRON or PALONOSETRON or PERPHENAZINE or PREDNISOLONE or PROCHLORPERAZINE or PROMETHAZINE or RAMOSETRON or ROLAPITANT or SULPIRIDE or TANDOSPIRONE or TIAPRIDE or TRANSDERMAL SCOPOLAMINE or TRIMEPRAZINE or TRIMETHOBENZAMIDE or TROPISETRON or VESTIPITANT))
S30 TX (serotonin 5 HT3 receptor antagonist* or 5 HT3 antagonist* or corticosteroid* or antihistamine* or antihistaminic* or H1 receptor blockader* or anticholinergic* or anti-cholinergic* or cholinergic antagonist* or cholinergic blocking agent* or Barhemsys or APD421 or Emend or MK-0517 or MK-0869 or L-754030 or GSK-525060 or methylfluorprednisolone or hexadecadrol or Decaject or Decameth or Dexasone or Dexpak or Millicorten or Oradexon or Hexadrol or DMH or Dramanate or Dramamine or Gravol or Anzemet or Anemet or MDL-73147EF or dehidrobenzperidol or dehydrobenzperidol or DHB or Inapsine or Droleptan or emend for injection or MK-0517 or L-785,298 or Kytril or BRL-43694 or Haldol or Antivert or Metipred or Urbason or Maxolon or Reglan or Zofran or ODT or Zuplenz or GR-38032F or RS-25259 or RS-25233 or Aloxi or Decentan or Trilafon or promethazin* or proazamine or Phenergan or Diprazin or Nasea or YM-060 or Varubi or scopolamine or hyoscine or Transderm Scop or Scopoderm TTS or Navoban or ICS-205-930 or azasetron or benzquinamide or buspirone or cetirizine or diclectin or diphenol or dixyrazine or doxylamine or levomepromazine or olanzapine or oxybutynin or penehyclidine or thiethylperazine)
S31 S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30
S32 S3 AND S10 AND S31
S33 ((MM "Randomized Controlled Trials") OR (MM "Random Assignment") OR (MM "Prospective Studies+") OR (MM "Clinical Trial Registry") OR (MM "Double-Blind Studies") OR (MM "Single-Blind Studies") OR (MM "Triple-Blind Studies") OR (MM "Multicenter Studies") OR (MM "Placebos")) OR (random* or placebo* or trial*)
S34 S32 AND S33

Appendix 2. Eligibility checklist

Author (Year)				
Journal				
Title				
Is the study eligible?	***Yes***	***No***	***Maybe***	**Note**
Type of study				

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(Continued)

RCT?	
Not quasi-RCT?	
Not cross-over study?	
Not retracted study (see clinicaltrials.gov) or authored by Fujii and colleagues?	
Not abstract only?	
Types of participants	
Adults (≥ 18 years)?	
General anaesthesia?	
Types of intervention	
Monotherapy, or	
augmentation study (different class), or	
combination study (same class)?	
Substance class(es):	*Name of drug(s):*_____
- 5-HT_3 receptor antagonists	
- D_2 receptor antagonists	
- NK_1 receptor antagonists	
- Corticosteroids	
- Antihistamines	
- Anticholinergics	
Drug allocated before onset of PONV?	
Similar baseline anaesthesia regimen in study's arms?	
Outcomes of interest	
Outcomes of interest reported?	

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Appendix 3. Data extraction form

RCT data extraction	Notes
Identification	
Study details:	
First author	
Year of publication	
Journal	
Country (location of study conduct)	
Number of centres	
Duration of study (date)	
Trial registry number	
Author's contact details (corresponding author):	
Author's name	
e-mail address	
Methods	
Study design	
Groups	
Population	
Inclusion criteria	
Exclusion criteria	
Significant group differences (baseline imbalance)? (Y/N)	

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(Continued)

Participant flow:
assessed for eligibility (n)
enrolled (n)
randomized (n/n)
received treatment (n/n)
analysed (n/n)
Prognostic variables and potential effect modifiers
Population and baseline characteristics:
Gender
Non-smoker
History of PONV/motion sickness
Type of general anaesthesia
Duration of anaesthesia
Use of perioperative opioids (if yes, which?)
Type of surgery
Significant imbalance between groups? (Y/N) *If yes, please define.*
Intervention
Dose
Time point of administration
Route of administration
Risk of bias (see Appendix 4: critical appraisal form)

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(Continued)

Allocation concealment						
Blinding of participants and personnel						
Blinding of outcome assessors						
Incomplete outcome data						
Funding source						
Sponsorship source						
Sponsorship involvement						
Outcome data						
Type of outcome	Definition of outcome	Observation time period	Intervention (events)	Intervention (n)	Control (events)	Control (n)
Vomiting (0 to 24 hours)						
Vomiting (0 to 6 hours)						
Vomiting (2 to 24 hours)						
Nausea						
Complete response						
Subjects with SAE						
Subjects with any AE						
Mortality						
Arrhythmia						
QT prolongation						
Extrapyramidal symptoms						

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(Continued)

Postoperative wound infection					
Headache					
Constipation					
Sedation/drowsiness					
Visual disturbances (e.g. blurred vision)					
Monitoring and reporting of (severe) adverse events:					
	Yes	No	Unclear	Risk of bias	Note
Did the authors actively monitor for AEs (any AE)?					
Did the authors simply provide spontaneous reporting of AEs that arose?					
Did the authors actively monitor only for defined AEs and other relevant AEs were not monitored?					
Did the authors define SAEs according to an accepted international classification and report the number of SAEs?					

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Appendix 4. Critical appraisal form

Author (year)			
Journal			
Title			
Risk of bias assessment (with quotes and/or statement)	***High risk of bias***	***Low risk of bias***	***Unclear risk of bias***
Random sequence generation (selection bias)			
State here the method used to generate the sequence			
Allocation concealment (selection bias)			
State here the method used to conceal allocation			
Blinding of participants and personnel (performance bias)			
Persons responsible for participants' care			
Participants			
Blinding of outcome assessment (detection bias)			
Outcome assessor			
Incomplete outcome data (attrition bias)			
Adequate, if dropout rate ≤ 15% and balanced between arms and reasons for missing values reported, and unrelated to the analysed outcome (data analysis described and imputation methods correct)			
Selective reporting (reporting bias)			
Adequate, if a prospectively registered study protocol is available and all pre-defined primary and secondary outcomes are also reported in the published study			
Other bias			
Other sources of bias (e.g. imbalance in baseline characteristics between study's arms)			

Appendix 5. Criteria for GRADEing the quality of evidence

The certainty of the evidence was assessed by two independent reviewers for the following domains and according to the following criteria:

Within-study risk of bias (study limitations): the contribution matrix was used to approximate the contribution of each piece of study to the NMA of relative treatment effects (Papakonstantinou 2018; Salanti 2014). A combination of study contributions with study risk of bias assessments (high, unclear, and low risk of bias) was used to evaluate study limitations for each NMA of relative treatment effect. We have assessed the quality level that contributed most to the NMA of treatment effect (majority RoB). In addition, we have compared the results of the NMA including all studies (primary analysis) with those obtained when only low risk of bias studies were included (sensitivity

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analysis). If the clinical impact between the primary and the sensitivity NMA of treatment effect with respect to the range of equivalence does not differ (location of point estimate and 95% CI), no concern due to study limitations has been assumed.

Across-studies bias (publication bias): the risk of across-studies bias was investigated on the comparison level and only when a sufficient number of studies per direct comparison was available. For pair-wise comparisons with 10 or more relevant studies, we investigated risk of bias across studies using funnel plots and contour-enhanced funnel plots. In addition, we performed exploratory analyses (e.g. Rücker's arcsine test for dichotomous data, trim and fill sensitivity meta-analysis) to further investigate funnel plot asymmetry. Based on these empirical examinations, we assumed two possible descriptions for across-studies bias: undetected or suspected.

Indirectness: the domain indirectness refers to the relevance of the included studies to the research question. Among all reported studies, study populations, interventions, outcomes, and study settings matched the inclusion criteria of the current systematic review. Thus, we concluded that there is no indirectness in any of the studies included in the current review.

Imprecision: the 95% confidence interval expressed the uncertainty of the relative NMA treatment effects. Imprecise treatment effects with a wide confidence interval may be associated with high uncertainty regarding the clinical decision. We considered the range of treatment effects included in the confidence interval and compared it with the respective range of equivalence. The inclusion of different clinical implications in the confidence interval indicates an imprecise NMA treatment effect, and down-rating for imprecision was required (Nikolakopoulou 2019).

Heterogeneity: we measured heterogeneity using the 95% prediction interval, which indicates where the true effect of a future study is expected to lie (Riley 2011). Similarly to imprecision, of highest importance for assessing NMA treatment effects with respect to heterogeneity is whether a clinical decision is substantially influenced (Nikolakopoulou 2019). We evaluated compatibility between confidence and prediction intervals in terms of the range of equivalence for the assessment of heterogeneity.

If heterogeneity was present, we investigated "dose of the intervention" as a potential effect modifier in a subgroup network meta-analysis. Different clinical decisions between NMA treatment effects of low, recommended, and high doses with respect to the range of equivalence were included in the final judgement on heterogeneity.

Incoherence: disagreement between direct and indirect evidence is termed incoherence. It cannot be tested in cases where only direct or indirect evidence exists. However, if only indirect evidence is present, there is always some concern, and we downgraded the comparison for incoherence (Nikolakopoulou 2019). In cases where more than 90% of the information comes from direct evidence, we assumed that incoherence was not a concern (Salanti 2017).

In other cases, we used two ways of judging incoherence. First, we used a local test (ratio of risk ratios (direct versus indirect), test for disagreement) to measure inconsistency. Because we recognized the low power of this test for inconsistency, as already described by others, we considered the implication of incoherence for clinical decisions as an alternative (Nikolakopoulou 2019). Thus, we compared the clinical interpretation of confidence intervals of direct and indirect effect estimates with respect to the range of equivalence (Nikolakopoulou 2019). If direct and indirect estimates (95% CIs) were incoherent, we assessed whether both estimates contribute importantly to the NMA treatment effect (Brignardello-Petersen 2019). The proportions of direct and indirect contributions to the NMA treatment effect were calculated using König's method provided by the R command netsplit in the R package netmeta. If direct and indirect estimates contributed in a way comparable to 30% to 70% contribution to the NMA treatment effect, and if 95% CIs of both estimates were different (incoherent) with respect to the range of equivalence, down-rating for incoherence was required. If there was a dominant estimate (> 70% contribution) and the 95% CI was similar to the 95% CI of the NMA estimate, no down-rating for incoherence was performed.

Summarizing judgements across the six domains: we considered our judgements on separate domains in conjunction rather than in isolation. We paid particular attention not to downgrade twice for the same aspect (Nikolakopoulou 2019). Salanti et al described the following overlapping domains: indirectness – incoherence, heterogeneity – incoherence, heterogeneity – imprecision, and heterogeneity – publication bias (Nikolakopoulou 2019). For overlapping domains, we downgraded only once.

Appendix 6. Code (abbreviations) of interventions

Code (abbreviations) of interventions

5-HT3 receptor antagonists:

azas = azasetron

dola = dolasetron

gran = granisetron

onda = ondansetron

palo = palonosetron (rs-25259)

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ramo = ramosetron

trop = tropisetron

D2 receptor antagonists:

aliz = alizapride

amis = amisulpride (APD421)

busp = buspirone

chlo = chlorpromazine

domp = domperidone

drop = droperidol

halo = haloperidol

levo = levomepromazine

meto = metoclopramide

olan = olanzapine

perp = perphenazine

proc = prochlorperazine

sulp = l-sulpiride

thie = thiethylperazine

trbe = trimethobenzamide

NK1 receptor antagonists:

apre = aprepitant

caso = casopitant

cp12 = cp-122,721

fosa = fosaprepitant

rola = rolapitant

vest = vestipitant

Corticosteroids:

dexa = dexamethasone

beta = betamethasone

meth = methylprednisolone

pred = prednisolone

Antihistamines (H1 receptor antagonists):

benz = benzquinamide

ceti = cetirizine

cycl = cylizine

dime = dimenhydrinate/ diphenhydramine

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dixy = dixyrazine

doxy = doxylamin/ diclectin

mecl = meclizine

prom = promethazine

Anticholinergics:

diph = diphenidol

oxyb = oxybutynin

pene = penehyclidine

scop = scopalamine (transdermal scopolamine, hyoscine)

WHAT'S NEW

Date	Event	Description
17 November 2020	Amended	Sources of support updated.

HISTORY

Protocol first published: Issue 11, 2017
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CONTRIBUTIONS OF AUTHORS

Stephanie Weibel (SW), Gerta Rücker (GR), Leopold HJ Eberhart (LE), Nathan L Pace (NP), Hannah M Hartl (HH), Olivia L Jordan (OJ) Debora Mayer (DM), Manuel Riemer (MR), Maximilian S Schaefer (MS), Diana Raj (DR), Insa L Backhaus (IB), Antonia Helf (AH), Tobias Schlesinger (TS), Peter Kienbaum (PKi), Peter Kranke (PKr).

Conceiving the review: SW, NP, GR, DR, IB, MS, PKi, LE, PKr (authors of the protocol).

Co-ordinating the review: SW.

Undertaking manual searches: SW, DM, MR, HH, AH, DR.

Screening search results: SW, DM, MR, HH, AH, DR, IB, MS, TS,

Organizing retrieval of papers: SW, DM, MR, HH, AH, DR, IB, MS, NP, LE, PKr.

Screening retrieved papers against inclusion criteria: SW, DM, MR, HH, AH, DR, IB, MS, LE.

Appraising quality of papers: SW, DM, MR, HH, AH, DR, IB, MS, LE.

Abstracting data from papers: SW, DM, MR, HH, AH, DR, IB, MS, LE.

Writing to authors of papers for additional information: SW.

Translating non-English papers: IB, SW, MS, LE, MR.

Obtaining and screening data on unpublished studies: SW, OJ.

Managing data for the review: SW, OJ.

Entering data into Review Manager 5 (RevMan 5): SW, OJ.

Analysing RevMan statistical data: SW, NP, OJ.

Performing other statistical analysis not using RevMan 5: SW, GR, NP, OJ.

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Interpreting data: SW, NP, GR, DR, IB, MS, PKi, LE, PKr, TS.

Making statistical inferences: SW, GR, NP.

Writing the review: SW, NP, GR, LE, MS, DR, PKr.

Securing funding for the review: SW, PKr.

Serving as guarantor for the review (one author): PKr.

Taking responsibility for reading and checking the review before submission: SW, GR, LE, NP, HH, OJ, DM, MR, MS, DR, IB, AH, TS, PKi, PKr.

DECLARATIONS OF INTEREST

General note: our review team included several experts in the field (NLP, DR, MSS, PKi, LHJE, AH, TS, PKr). Review authors (LHJE, PKr) who were involved in the conduct of studies related to the current review did not assess the relevant studies for inclusion or exclusion and were not allowed to extract data or critically appraise the quality of the relevant studies.

Stephanie Weibel has no conflict of interest regarding the topic of this review. Stephanie Weibel is an academic researcher. She has received personal payments for consultancies and lecture fees from Genelux Corporation, San Diego, California, USA (ended March 2014). Genelux Corporation does not produce any products for the intervention of interest in this review. She was involved in the conduct of phase 3 clinical trials related to the current review ("Amisulpride (APD421)" (NCT02646566 NCT02449291 Kranke 2018), and she was involved in a meta-analysis on the incidence of postoperative nausea and vomiting that was published recently (Schaefer 2016). She received funding through a one-time payment from B. Braun-Stiftung, Melsungen, Germany. The B. Braun-Stiftung is an independent and non-profit foundation. She has received lecture fees (topic: systematic reviews and meta-analyses) from the University of Marburg (2017, 2020).

Gerta Rücker is employed as a statistician at the Institute of Medical Biometry and Statistics of the Medical Center at the University of Freiburg. She received payment for a one-day course on statistical methods in meta-analysis from the Grünenthal Group, Aachen, Germany.

Nathan L Pace has no conflict of interest regarding the topic of this review. Nathan L Pace is a non-practising anaesthetist and statistician faculty member of the University of Utah, receives no private practice income, and has no commercial relationships. He has received payment for development of educational presentations (Barash, Cullen, Stoelting, CLINICAL ANESTHESIA, 8th edition) and has provided consultancy (St Marks Hospital, Salt Lake City, Utah, USA) on topics unrelated to the current review. He has received supplements to attend Cochrane meetings. He also has stocks and shares in companies that have no interest in the topic of this review (TIAA-CREF, Fidelity, Vanguard, USAA, MorganStanley).

Leopold Eberhart is employed as a clinical and academic anaesthetist with a clinical and research focus on postoperative pain management and postoperative nausea and vomiting. He has no conflict of interest regarding the topic of this review. Leopold Eberhart has received lecture fees (from Baxter GmbH and Fresenius GmbH) and payment for lectures (from Gruenenthal GmbH, Baxter GmbH and Fresenius, GmbH) and has provided consultancy (for Gruenenthal GmbH and ratiopharm GmbH) for topics not related to the current review. He holds a board membership with Gruenenthal GmbH Deutschland, which does not have an interest in the topic of this review. He has been involved in the conduct of phase 2 and phase 3 clinical trials related to the current review ("Amisulpride (APD421)" (NCT02646566 NCT02449291 Kranke 2018 Gan 2017 Kranke 2013; "Vestipitant (GW597599)" (NCT01507194); "Buspiron" (Kranke 2012); IMPACT study (Apfel 2004)). He was an author of several papers on postoperative nausea and vomiting.

Hannah Hartl has no conflict of interest regarding the topic of this review. Hannah Hartl is a medical student.

Olivia Jordan has no conflict of interest regarding the topic of this review. Olivia Jordan is a medical student.

Debora Mayer has no conflict of interest regarding the topic of this review. Debora Mayer is a medical student.

Manuel Riemer has no conflict of interest regarding the topic of this review. Manuel Riemer is a medical student.

Maximilian S Schaefer has no conflict of interest regarding the topic of this review. Maximilian S Schaefer is an attending anaesthesiologist. He was involved in a meta-analysis on the incidence of postoperative nausea and vomiting published recently (Schaefer 2016).

Diana Raj has no conflict of interest regarding the topic of this review. Diana Raj is a consultant in clinical anaesthesiology and a Trustee and Secretary of West of Scotland Anaesthetic Teaching (WOSAT), Scottish Charity SC04663.

Insa Linnea Backhaus has no conflict of interest regarding the topic of this review. Insa Linnea Backhaus earned her PhD in Public Health and is an academic researcher.

Antonia Helf has no conflict of interest regarding the topic of this review. Antonia Helf is a clinical investigator and academic researcher. She was involved in the conduct of phase 3 clinical trials related to the current review ("Amisulpride (APD421)" (NCT02646566 NCT02449291)).

Tobias Schlesinger has no conflict of interest. Tobias Schlesinger is a clinical investigator and academic researcher.

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Peter Kienbaum is employed as a clinical and academic anaesthetist and has been holding the position of vice chairman of the anaesthesia department for 10 years. His clinical and research work focuses on cardiovascular effects of anaesthetics and recovery after anaesthesia. Peter Kienbaum has been consulting for Baxter Germany, Air Liquide Germany, Orion Pharma Germany, and TEVA ratiopharm Germany, with respect to inhaled anaesthetics and other issues not related to this review. He authored several trial papers unrelated to the current review and was involved in a meta-analysis on the incidence of postoperative nausea and vomiting published recently (Schaefer 2016).

Peter Kranke is employed as a clinical and academic anaesthetist with a clinical and research focus on obstetric anaesthesia and postoperative nausea and vomiting. He has received lecture fees (from MSD, ratiopharm, Covidien) and has provided consultancy (to MSD, Ratiopharm, Covidien) on topics unrelated to the current review. He has received lecture fees and provided consultancy to Fresenius GmbH. This company manufactures propofol, which may be effective as an antiemetic in reducing PONV. He acted as a consultant for Acacia Ltd. He has been involved in the conduct of phase 2 and phase 3 clinical trials related to the current review ("Amisulpride (APD421)" (NCT02646566 NCT02449291 Kranke 2018 Gan 2017 Kranke 2013); "Vestipitant (GW597599)" (NCT01507194); "Buspiron" (Kranke 2012); IMPACT study (Apfel 2004)). He was author of several trial papers and of the consensus guidelines for management of postoperative nausea and vomiting. He has published research reports and editorial views on the topic under review and was involved in a meta-analysis on the incidence of postoperative nausea and vomiting published recently (Schaefer 2016).

SOURCES OF SUPPORT

Internal sources

- Stephanie Weibel, Germany

  Department of Anaesthesia and Critical Care, University of Würzburg, Würzburg, Germany
- Yvonne Jelting, Germany

  Department of Anaesthesia and Critical Care, University of Würzburg, Würzburg, Germany
- Nathan Leon Pace, USA

  Department of Anesthesiology, University of Utah, Salt Lake City, UT, USA
- Gerta Rücker, Germany

  Institute for Medical Biometry and Statistics, Faculty of Medicine and Medical Center – University of Freiburg, Freiburg, Germany
- Diana Raj, UK

  Department of Anaesthesia, Intensive Care Medicine and Pain Medicine, Queen Elizabeth University Hospital, Glasgow, UK
- Insa Linnea Backhaus, Italy

  Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
- Maximilian S Schaefer, Germany

  Department of Anaesthesiology, University Hospital Düsseldorf, Düsseldorf, Germany
- Peter Kienbaum, Germany

  Department of Anaesthesiology, University Hospital Düsseldorf, Düsseldorf, Germany
- Leopold HJ Eberhart, Germany

  Department of Anaesthesiology & Intensive Care Medicine, Philipps-University Marburg, Marburg, Germany
- Peter Kranke, Germany

  Department of Anaesthesia and Critical Care, University of Würzburg, Würzburg, Germany

External sources

- B. Braun-Stiftung, Germany

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The protocol to the review was prospectively published in 2017 (Weibel 2017). We deviated from the protocol in the following points.

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- Types of studies: we have planned in the protocol that eligible studies must be published in a peer-reviewed journal. We changed this restriction and decided to include all studies that were published as full-text articles independent of a peer-review process. Peer review may be one reason for publication bias (selective publication of positive and significant results).
- Types of participants: we have defined in the protocol that we include adult participants (≥ 18 years) undergoing any type of surgery under general anaesthesia. During full-text screening, we have recognized that many studies have not reported any eligibility criteria or lower bound of age for study participants, or have used other definitions of "adults" starting with 15, 16, or 17 years. Because we are interested in the adult population in the biological sense, we extended our inclusion criteria for age as follows: for each study enrolling participants younger than 18 and reporting the mean age with SD, we assumed that a majority of participants are 18 or older, and that the study is eligible for this review, when the lower bound of the confidence interval (mean age ± 1.5 SD) is 18 or greater (Chebyshev's inequality). Similarly, if the study reports the median and the IQR of age with the lower bound of the IQR 18 or greater, then we can state that a majority of participants are 18 or older.
- New secondary outcome: complete response (number of participants without vomiting, nausea, or need for rescue treatment within 24 hours postoperatively). Complete response is an important outcome for participants in the postoperative period.
- Searching other resources: we have scanned the reference lists of included studies only of the following relevant systematic reviews Carlisle 2006a; De Oliveira 2013; Liu 2015; Tricco 2015a; Tricco 2015b. We have not scanned the reference lists of all included studies in the current review, and we have not contacted trial authors for further relevant studies in the field.
- Overall risk of bias summary: we have summarized the risk of bias for each study depending on judgements for the items 'sequence generation', 'blinding of participant, personnel, and outcome assessors', and 'incomplete outcome data'. At the protocol stage, we had planned to use the item 'allocation concealment' instead of 'sequence generation'. However, we judged only 69 studies (12%) that used either central allocation or sequentially numbered opaque sealed envelopes (SNOSE) as having low risk of bias for allocation concealment. In contrast, a total of 282 studies (48%) have reported adequate methods for sequence generation such as random numbers tables or computer-generated random numbers. We believe that most authors of previous studies were unaware of the definition and reporting standards of methods for allocation concealment. Most study authors have reported on sequence generation and blinding but not on allocation concealment. The term 'SNOSE' was used only in more recent studies. Therefore, we decided to use 'sequence generation' instead of 'allocation concealment', because we assume that allocation concealment may have worked in many more studies included in this systematic review. Reporting of methods used for allocation concealment is the real problem.
- Assessment of clinical and methodological heterogeneity within treatment comparisons: we had planned to use descriptive statistics as reported in the Characteristics of included studies table to assess whether studies within each pair-wise comparison are homogenous enough with respect to potential effect modifiers (risk of bias, intervention details, funding source), so that the assumption of homogeneity might be plausible. Finally, for the effect modifiers 'risk of bias' and 'dose of intervention', we accepted heterogeneity (see inclusion criteria of this review) and assessed the impact of these effect modifiers in either sensitivity analysis (risk of bias) or subgroup analysis (dose). Due to the quantity of data and lack of information for the effect modifier 'funding source' in many studies, an objective and reliable assessment of the distribution of this effect modifier within all comparisons was not possible. In general, we assumed that for all included studies, the study populations, interventions, outcomes, and study settings matched the inclusion criteria of the current systematic review. Thus, we concluded that there is no relevant clinical and methodological heterogeneity within treatment comparisons in the current review.
- Assessment of transitivity across treatment comparisons: we had planned to assess the assumption of transitivity by comparing the distribution of potential effect modifiers (see data extraction form 'Potential effect modifiers') across the different pair-wise comparisons. In case of intransitivity (e.g. substantially imbalanced distribution of effect modifiers among comparisons), we did not want to perform NMA. Finally, for the effect modifiers 'risk of bias' and 'dose of intervention', we accepted differences in the distribution of these effect modifiers across treatment comparisons (see inclusion criteria of this review) and assessed the impact of these effect modifiers in either sensitivity analysis (risk of bias) or subgroup analysis (dose). Due to the quantity of data and lack of information for the effect modifier 'funding source' in many studies, an objective and reliable assessment of the distribution of this effect modifier within all comparisons was not possible. In general, we assumed that for all included studies, the study populations, interventions, outcomes, and study settings matched the inclusion criteria of the current systematic review. Thus, we concluded that there is no relevant clinical and methodological heterogeneity across treatment comparisons (intransitivity) in the current review.
- Net heat plot: to locate sources of inconsistency, we had planned to use net heat plots. However, data were too complex to visualize net heat plots in a meaningful manner.
- Subgroup analyses: in case of heterogeneity or inconsistency, we had planned to explore potential effect modifiers as possible sources. Due to the complex nature of the review, we decided to perform only the subgroup analysis 'dose of the interventions'. In addition, we have added a table summarizing the most commonly used dosages, routes, and time points of administration of single drugs of direct interest for the primary outcome vomiting and have reported this information in the Effects of interventions section.
- Methods for analysing additive dose effects: we have added the analysis to test the assumption whether the effects of combined dose categories (e.g. low + recommended, low + recommended + high, recommended + high) are additive sums of their individual categories.
- Reporting of effect estimates: we decided the process/method of selection of effect estimates for reporting in the Effects of interventions section at the review stage after performing the analyses. Selection was not driven by specific results.
- Sensitivity analyses: we included two new sensitivity analyses on funding (funding source 'industry', funding source 'non-industry'). We added one new sensitivity analysis on 'single drugs only' including only study arms investigating single drugs and excluding study arms investigating combinations of drugs. This analysis compared the robustness of network effect estimates of the primary network meta-analysis and the sensitivity analysis including single drugs only (which is the basic analysis for the subgroup analysis of dose).

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- 'Summary of findings' table and GRADE: at the protocol stage, we had planned to use the four-step approach by Puhan and colleagues (Puhan 2014). However, new and more efficient methods suitable for large NMAs have appeared during preparation of this paper (CINeMA: Nikolakopoulou 2019; Papakonstantinou 2018; Salanti 2014; Salanti 2017). We have used CINeMA, which enhances feasibility of performance of this review.
- Yvonne Jelting was involved in the protocol but was no longer an author of the review. Hannah Hartl, Antonia Helf, Olivia, Jordan, Debora Mayer, Manuel Riemer, and Tobias Schlesinger were not authors of the protocol.

INDEX TERMS

Medical Subject Headings (MeSH)

Anesthesia, General [*adverse effects]; Antiemetics [*therapeutic use]; Drug Therapy, Combination; *Network Meta-Analysis; Placebos [therapeutic use]; Postoperative Nausea and Vomiting [*prevention & control]; Randomized Controlled Trials as Topic

MeSH check words

Adult; Female; Humans; Male

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