National Institute for Health and Care Excellence

Final

Perioperative care in adults

[C] Evidence review for preoperative risk stratification tools

NICE guideline NG180

Evidence reviews underpinning recommendations 1.3.1 and 1.3.2 in the NICE guideline

August 2020

Final

This evidence review was developed by the National Guideline Centre

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1 Preoperative risk stratification tools

1.1 Review question: Which validated preoperative risk stratification tools best identify increased risk of mortality and morbidity in adults who will be undergoing surgery?

1.2 Introduction

The conundrum facing all perioperative clinicians when evaluating patients for surgery remains how best to evaluate and quantify the risk of undergoing the anticipated procedure. There are a number of reasons why this is a key element of evaluation during the preoperative clinical encounter. Firstly, establishing objective understanding of the anticipated mortality and morbidity risk allows and directs discussions with other involved clinicians about the appropriateness of the planned surgery and whether it should proceed as planned, should be abbreviated, or whether alternative non-surgical options should be considered. Secondly, being able to quantify morbidity risk allows planning for post-operative destination, discussions about quality of life and recovery or convalescence and to give insight to the patient about the anticipated clinical course. Understanding these elements allows frank discussions about what the patients actually wish to achieve from the surgical encounter. Furthermore this opens the discussions amongst all parties for shared decision making about the best outcome decision that will meet the goals of the involved parties.

Thus it becomes incumbent on perioperative clinicians to find robust, reliable and accurate tools that will allows us to determine bespoke perioperative risk for each individual patient allowing these discussions and decisions to proceed smoothly. Current practice appears to be that many perioperative clinicians use risk stratification tools but not in a uniform or unified fashion. Different tools are used with different sensitivities and specificities and are not uniformly applied to all surgical populations. There does not exist a national recommendation or standard on which tools to use, how they should be applied, nor even that a risk stratification tool should be consistently used in the perioperative setting at all.

The committee agreed this was a fundamental aspect that required investigation of existing evidence around such tools with the intention to set a recommendation standard in this area of perioperative care.

1.3 PICO table

For full details see the review protocol in Appendix A:.

Table 1: PICO characteristics of review question

Population	Adults 18 years and over undergoing surgery.
Risk tool	Validated risk stratification tools: • P-POSSUM score (Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity) • SORT (Surgical Outcome Risk Tool) • NSQIP (National Surgical Quality Improvement Program) universal surgical risk calculator
Target condition	• Mortality • Morbidity
Outcome measures	• Sensitivity, specificity, predictive values • Area under the ROC curve (c-statistic)

	• Predicted risk versus observed risk (calibration)
Study design	• Prospective and retrospective cohort studies

1.4 Clinical evidence

1.4.1 Included studies

Sixty studies were included in the review;[11, 14, 17, 18, 20, 22, 24, 25, 27, 32, 33, 37, 39, 43, 45, 47, 48, 51, 54, 56, 57, 59, 61-63, 65, 69, 70, 74, 78, 84, 88, 93, 94, 101, 105, 110, 116, 118, 120, 136, 138, 142, 149, 151, 155, 157, 161, 162, 165, 166, 170, 171, 177, 179, 182, 183, 186, 187, 189] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

See also the study selection flow chart in Appendix C: and study evidence tables in Appendix D:.

1.4.2 Excluded studies

See the excluded studies list in appendix J.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Population	Risk tool	Outcomes
Baker 2018[11]	Patients scheduled for surgery under general anaesthetic (GA) with entry into the Peritoneum. N=298	ACS NSQIP risk calculator	Morbidity • c-statistic
Bennett-Guerrero 2003[14]	Two cohorts of patients undergoing major, non-cardiac surgery over the same time interval. N=1056 (USA) N=1539(UK)	P-POSSUM	Mortality • calibration
Blair 2018[17]	Retrospective review of a single institution, multi-surgeon, database of all patients undergoing partial nephrectomy (PN) for renal cell carcinoma. N=470	ACS NSQIP risk calculator	Mortality • calibration Complications • calibration
Bodea 2018[18]	Elective surgery patients undergoing elective Pancreaticoduodenectomy for periampullary malignant tumours. N=113	P-POSSUM	Mortality • c-statistic • calibration Morbidity • c-statistic • calibration
Bonaventura 2019[20]	Patients undergoing cholecystectomy for acute cholecystitis N=271	Charlson Comorbidity index	Morbidity • c-statistic
Boyd 2019[22]	Women patients 18 years or older undergoing surgery for pelvic organ prolapse or incontinence by all routes.	ACS NSQIP risk calculator	Morbidity • c-statistic

Study	Population	Risk tool	Outcomes
	N=731		
Bronheim 2018[24]	Adult patients undergoing posterior lumbar decompression surgery N=52,066	ASA	Mortality • c-statistic Morbidity • c-statistic
Brooks 2005[25]	A cohort of higher-risk patients scheduled to undergo surgical procedures. N=949	POSSUM P-POSSUM Surgical risk score	Mortality • c-statistic • calibration
Bulow 2019[27]	Patients treated with hip arthroplasty for a femoral neck fracture. N=43,224	Charlson Comorbidity index	Mortality • c-statistic
Cengiz 2014[32]	Consecutive patients undergoing colorectal cancer surgery between 2002 and 2012 in third-level healthcare centres. N=335	POSSUM P- POSSUM	Mortality • c-statistic
Chun 2018[33]	Patients who had undergone spinal surgery for various spine diseases at a single tertiary care centre. N=217	POSSUM E-PASS	Complications • c-statistic
Cologne 2015[37]	Consecutive laparoscopic colon resections performed on an elective basis from by two colorectal surgeons at a tertiary referral centre. N=116	ACS NSQIP risk calculator	Mortality • calibration Any complication • calibration
Dahlke 2014[39]	Data obtained from the ACS NSQIP participant file 2011 release for patients undergoing a broad range of surgeries across all surgical	ACS NSQIP risk calculator	Morbidity • c-statistic

Study	Population	Risk tool	Outcomes
	specialities. N=238649		
Donati 2004[43]	Data were collected from all patients, with no age limits imposed, who underwent any type of elective or emergency surgical procedure in two different hospitals. N=1936	POSSUM P-POSSUM ASA classification	Mortality • c-statistic
Dutta 2011[45]	Patients undergoing oesophago-gastric cancer resections. N=121	POSSUM P- POSSUM	Mortality • c-statistic • calibration Any complication • c-statistic • calibration
Egberts 2011[47]	The medical records of 143 patients with cutaneous melanoma who underwent a radical lymph node dissection (RLND). N=143	POSSUM	Mortality • calibration Any complication • calibration
Egberts 2011[48]	The medical records of patients undergoing surgery for inflammatory bowel disease (IBD). N=191	POSSUM	Mortality • calibration Any complication • calibration
Filip 2014[51]	Patients diagnosed with oesophageal cancer in whom surgery was performed. N=137	POSSUM P-POSSUM ASA classification Charlson Comorbidity index	Mortality • calibration Morbidity • c-statistic • calibration
Fu 2019[54]	Patients who underwent total shoulder arthroplasty were identified in the NSQIP.	ASA classification Charlson Comorbidity index	Morbidity • c-statistic

Study	Population	Risk tool	Outcomes
	N=10,527		
Goffi 1999[56]	Patients admitted during one year period for major elective or emergency operations, benign or malignant. N=187	ASA classification	Morbidity & morbidity combined • c-statistic
Golan 2018[57]	Patients in prospectively maintained database who underwent open RC with either ileal conduit or orthotopic neobladder urinary diversion for bladder cancer. N=954	ACS NSQIP risk calculator	Mortality • c-statistic • calibration Morbidity • c-statistic • calibration
Haga 2011[59]	Patients who received any elective procedure. N=5272	POSSUM P-POSSUM E-PASS	Morbidity • c-statistic
Hightower 2010[61]	Patients undergoing major abdominal cancer surgery. N=32	ASA classification	Morbidity • c-statistic
Hirose 2014[62]	Consecutive patients who underwent spinal surgery. N=601	POSSUM E-PASS	Mortality • c-statistic Morbidity • c-statistic
Hirose 2015[63]	Retrospective review of consecutive patients who underwent spinal surgery. N=275	E-PASS	Mortality • c-statistic
Hobson 2007[65]	All patients undergoing surgery in the emergency theatre of the Leicester general hospital over a 4-month period. N=163	POSSUM P-POSSUM	Mortality • c-statistic Morbidity • c-statistic

Study	Population	Risk tool	Outcomes
Huisman 2014[69]	Recruitment took place in 6 different countries at 11 medical centers between September 2008 and January 2012 and included cancer patients scheduled for elective surgery. N=263	ASA classification	Morbidity • c-statistic
Igari 2013[70]	Patients undergoing general surgical procedures at Ohta Nishinouchi General Hospital. N=593	POSSUM P-POSSUM	Mortality • calibration Morbidity • calibration
Jones 1992[74]	Patients admitted to the high-dependency unit immediately after surgery. N=117	POSSUM	Mortality • c-statistic • calibration Morbidity • c-statistic • calibration
Katlic 2019[78]	Geriatric surgical patients undergoing major elective surgery including cardiac, thoracic, vascular, orthopaedic, surgical oncology, general surgery, urologic and neurologic. N=1025	ASA Score Charleston Comorbidity index	Complication • c-statistic
Kim 2018[84]	Patients undergoing total shoulder arthroplasty or reverse total shoulder arthroplasty. N=90,491	Charleston Comorbidity index	Mortality • c-statistic Morbidity • c-statistic
Kong 2013[88]	Major colorectal operations performed at Geelong hospital and Western Hospital from 2008-2010 N=863	POSSUM P-POSSUM	Mortality • calibration

Study	Population	Risk tool	Outcomes
Kwok 2011[93]	Data from ACS NSQIP including very elderly patients aged 80+ undergoing emergency colon surgery. N=1730	ASA classification Surgical risk scale	Mortality • c-statistic • calibration
Lakomkin 2018[94]	Patients undergoing spinal tumour resection. N=2,170	ASA score Charlston Comorbidity Index	Mortality • c-statistic
Lima 2019[101]	Patients over 60 years old scheduled to undergo elective procedures under general, regional or combined anaesthesia for general, gynaecological, plastic, vascular, or orthopaedic surgeries. N=235	P-POSSUM	Mortality • c-statistic
Moonesinghe 2013[110]	Study of surgical patients age 65 years or older who presented to the participating hospital. N=594	ASA classification	Morbidity • c-statistic
Markovic 2018[105]	Pilot study included patients who were being prepared for one of the major non-cardiac surgeries under general anaesthesia. N=78	ASA classification ACS NSQIP risk calculator SORT	Mortality • c-statistic
Neary 2007[116]	A consecutive cohort of patients who needed non-elective, non-cardiac surgery. N=2349	P-POSSUM Surgical Risk Score	Mortality • c-statistic • calibration
Ngulube 2019[118]	Patients aged 18 years and above undergoing a major general surgical procedure as defined by the British United Provident Association, with timing ranging from elective to emergency. N=181	POSSUM P-POSSUM	Mortality • c-statistic • calibration Morbidity • c-statistic • calibration

Study	Population	Risk tool	Outcomes
Organ 2002[120]	All surgical patients undergoing a surgical procedure. N=229	P-POSSUM	Mortality • c-statistic • calibration
Reis 2019[137]	Patients admitted to surgical ICU after open vascular surgery. N=833	POSSUM	Mortality • c-statistic • calibration
Rivard 2016[138]	Patients who underwent laparotomy on the gynecologic oncology service at a single academic hospital. N=1094	ACS NSQIP risk calculator	Mortality • c-statistic • calibration Complications • c-statistic • calibration
Saafan 2019[142]	Patients presenting to ER and diagnosed and operated for perforated duodenal ulcers. N=152	ASA classification	Morbidity • c-statistic
Shaker 2019[149]	Gynaecologic oncology patients aged >70 years undergoing laparotomy. N=200	ACS NSQIP risk calculator	Mortality • c-statistic Morbidity • c-statistic
Sharrock 2017[151]	Consecutive hospital admissions of patients aged 70 or over admitted as an emergency for abdominal surgery. N=193	P-POSSUM ASA classification	Mortality • c-statistic • calibration Morbidity • c-statistic
Simpson 2018[155]	Patients over 80 years old undergoing emergency laparotomy N=103	P-POSSUM	Mortality • c-statistic
Slim 2006[157]	Patients undergoing open or	POSSUM	Mortality

Study	Population	Risk tool	Outcomes
	laparoscopic surgery (electively or on emergent basis) for colorectal cancers or diverticular disease. N=1421	P-POSSUM	• c-statistic • calibration
Suresh 2019[161]	Patients who underwent panniculectomy. N=264	ACS NSQIP risk calculator	Morbidity • c-statistic
Sutton 2002[162]	All patients admitted under the care of three surgeons. N=1946	ASA classification Surgical Risk Scale	Mortality • c-statistic
Teeuwen 2011[165]	Patients older than 15 years undergoing colorectal resection between January 2003 and January 2008 in the Radboud University Nijmegen Medical Centre. N=734	POSSUM P-POSSUM	Mortality • Calibration Morbidity • Calibration
Teoh 2017[166]	All patients undergoing minimally invasive surgery on the gynecologic oncology service. N=876	ACS NSQIP risk calculator	Mortality • c-statistic • calibration Complications • c-statistic • calibration
Tominaga 2016[170]	Patients over 70 years of age diagnosed with colorectal cancer and underwent curative colorectal resection from a single hospital. N=239	E-PASS	Mortality • calibration
Tran Ba Loc 2010[171]	Patients, at least 65 years old, undergoing major colorectal surgery. N=1186	POSSUM P-POSSUM Surgical risk score	Mortality • c-statistic • calibration Complications • c-statistic

Study	Population	Risk tool	Outcomes
			• calibration SRS • c-statistic • calibration
Vather 2006[177]	Consecutive patients undergoing a major colorectal operation between January 2002 and October 2005 at the participating hospital. N=308	POSSUM P-POSSUM	Mortality • c-statistic
Wang 2014[179]	Consecutive patients treated surgically in the study centre following a diagnosis of hilar cholangiocarcinoma. N=100	POSSUM P-POSSUM E-PASS	Mortality • c-statistic • calibration Complications • c-statistic • calibration E-PASS • c-statistic • calibration
Wang 2017[182]	Geriatric patients (age>60 years) with isolated spinal stenosis who underwent lumbar surgery. N=242	ACS-NSQIP risk calculator	Mortality • c-statistic
Wani 2005[183]	Patients of diagnosed calcular disease of biliary tract over an 18 month period. N=500	POSSUM	Mortality • prognostic accuracy • correlation Morbidity • prognostic accuracy • correlation
Wolters 2006[186]	Patients received an aorto-bi-iliac or an aroto-bifemoral graft due to arterial occlusive disease.	POSSUM ASA classification	Mortality • c-statistic Morbidity

Study	Population	Risk tool	Outcomes
	N=107		• c-statistic
Yap 2018[187]	Patients aged 19 years and older admitted for preoperative evaluation and cardiopulmonary risk stratification before non-cardiac surgery. N=424	ACS NSQIP risk calculator	Mortality • c-statistic
Zattoni 2019[189]	Patients over 70 years old undergoing emergency abdominal surgery under general anaesthesia. N=110	ASA classification Charleston Comorbidity index	Mortality • c-statistic

See Appendix D:for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

1.1 Discrimination

Table 3: Clinical evidence profile

Risk tool	No of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Concordance statistic (c-stat: median, range)	Quality
Mortality								
POSSUM	13	10811	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	82% (47-95)	Very low
P-POSSUM	18	15579	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	81% (56-94)	Very low
NSQIP	8	241905	No serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	83%	Low

Risk tool	No of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Concordance statistic (c-stat: median, range)	Quality
							(62-97)	
E-PASS	2	5372	Serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision	83% (82-84)	Low
ASA	7	58056	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	77% (59-93)	Very low
Charlson	4	136995	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	77% (58-86)	Very low
SORT	1	78	Serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision	80%	Low
SRS	5	8160	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	85% (66-95)	Very low
Morbidity (composite outcome)								
POSSUM	9	2673	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	75% (56-84)	Very low
P-POSSUM	1	113	Serious risk of bias	No serious inconsistency	No serious indirectness	Cannot be assessed	61%	Low
NSQIP	8	4819	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	62.5% (55-88)	Very low
E-PASS	3	1093	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	67% (59-68)	Very low
ASA	9	64846	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	69% (52-78)	Very low
Charlson	4	103357	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	64% (56-69)	Very low

GRADE was conducted with emphasis on c-statistic as this was the primary measures agreed for decision making
a) Risk of bias was assessed using the PROBAST checklist. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b) Inconsistency was assessed by visual inspection of a plotted summary of c-statistics and for overlap of confidence intervals where reported.
c) The judgement of precision was based on visual inspection of the confidence region of the c-statistic, where variation in confidence intervals was reported.

1.2 Calibration

Risk tool	No of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Observed/Expected ratio (median, range)	Quality
Mortality								
POSSUM	10	5252	Serious risk of bias	Serious inconsistency	No serious indirectness	not estimable	0.86 (0-1.73)	Very low
P-POSSUM	10	8029	Serious risk of bias	Serious inconsistency	No serious indirectness	not estimable	1.03 (0.56-15.87)	Very low
NSQIP	4	2634	Serious risk of bias	Serious inconsistency	No serious indirectness	not estimable	1.23 (0.64-1.28)	Very low
E-PASS	1	100	Serious risk of bias	No serious inconsistency	No serious indirectness	not estimable	1	Low
ASA	1	1186	Serious risk of bias	No serious inconsistency	No serious indirectness	not estimable	1.08	Low
SRS	1	949	Serious risk of bias	No serious inconsistency	No serious indirectness	not estimable	0.81	Low
Morbidity (composite outcome)								
POSSUM	9	3356	Serious risk of bias	Serious inconsistency	No serious indirectness	not estimable	1 (0.8-1.44)	Very low
NSQIP	5	3510	Serious risk of bias	Serious inconsistency	No serious indirectness	not estimable	1.06 (0.76-1.84)	Very low

a) Risk of bias was assessed using the PROBAST checklist. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b) Inconsistency was assessed by visual inspection of a plotted summary where reported.
c) The judgement of precision was not possible in the absence of the confidence region of the O/E ratio, summary ratios were downgraded due to this limitation.
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1.3 Economic evidence

1.3.1 Included studies

No health economic studies were included.

1.3.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix H:.

1.4 Evidence statements

1.4.1 Clinical evidence statements

Risk tools mortality concordance

Thirteen studies reported an accuracy of 47-95% with POSSUM predicting mortality, with a median c-statistic of 82% (n=10811, Very low quality evidence)

Eighteen studies reported an accuracy of 56-94% with P-POSSUM predicting mortality, with a median c-statistic of 81% (n=15579, Very low quality evidence)

Eight studies reported an accuracy of 62-97% with NSQIP predicting mortality, with a median c-statistic of 83% (n=241905, Low quality evidence)

Two studies reported an accuracy of 82-84% with E-PASS for predicting mortality, with a median c-statistic of 83% (n=5372, Low quality evidence)

Seven studies reported an accuracy of 59-93% with ASA for predicting mortality, with a median c-statistic of 77% (n=58056, Very low quality evidence)

Four studies reported an accuracy of 58-86% with Charlson Comorbidity Index for predicting mortality, with a median c-statistic of 77% (n=136995, Very low quality evidence)

One study reported an accuracy of 80% with SORT for predicting mortality (n=78, Very low quality evidence)

Five studies reported an accuracy of 66-93% with SRS for predicting mortality of, with a median c-statistic of 85% (n=8160, Very low quality evidence)

Risk tools morbidity concordance

Nine studies reported an accuracy of 56-84% with POSSUM for predicting morbidity, with a median c-statistic of 75% (n=2673, Very low quality evidence)

One study reported an accuracy of 61% with P-POSSUM for predicting morbidity (n=113, Low quality evidence)

Eight studies reported an accuracy of 55-88% with NSQIP for predicting morbidity, with a median c-statistic of 62.5% (n=4819, Very low quality evidence)

Three studies reported an accuracy of 59-68% with E-PASS for predicting morbidity, with a median c-statistic of 67% (n=1093, Very low quality evidence)

Ten studies reported an accuracy of 52-93% with ASA for predicting morbidity, with a median c-statistic of 69% (n=66792, Very low quality evidence)

Four studies reported an accuracy of 56-69% with Charlson Comorbidity Index for predicting morbidity, with a median c-statistic of 64% (n=103357, Very low quality evidence)

Risk tools mortality calibration

Ten studies reported a predictive accuracy of POSSUM for mortality with median O/E ratio of 0.86 (n=5252, Very low quality evidence)

Ten studies reported a predictive accuracy of P-POSSUM for mortality with median O/E ratio of 1.03 (n=8029, Very low quality evidence)

Four studies reported a predictive accuracy of NSQIP for mortality with median O/E ratio of 1.23 (n=2634, Very low quality evidence)

One study reported a predictive accuracy of E-PASS for mortality with median O/E ratio of 1 (n=100, Low quality evidence)

One study reported a predictive accuracy of ASA for mortality with median O/E ratio of 1.08 (n=1186, Low quality evidence)

One study reported a predictive accuracy of SRS for mortality with median O/E ratio of 0.81 (n=949, Low quality evidence)

Risk tools morbidity calibration

Nine studies reported a predictive accuracy of POSSUM for morbidity with median O/E ratio of 1 (n=3356, Very low quality evidence)

Five studies reported a predictive accuracy of NSQIP for morbidity with median O/E ratio of 1.06 (n=3510, Very low quality evidence)

1.4.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.5 The committee's discussion of the evidence

Please see recommendations 1.3.1 – 1.3.2 in the guideline.

1.5.1 Interpreting the evidence

1.5.1.1 The outcomes that matter most

The committee highlighted that a key goal of preoperative risk assessment is to identify and stratify those at increased risk of mortality and morbidity. As such, the main outcomes included in this evidence review was the predictive accuracy of risk tools, as measured by

sensitivity, specificity, predictive values, c-statistic data, and predicted risk versus observed risk (calibration data). The risk prediction tools do not predict or report specific morbidities, rather morbidity rate as a composite outcome.

1.5.1.2 The quality of the evidence

The quality of evidence varied from low to very low. Studies were downgraded for risk of bias inconsistency and imprecision. Risk of bias was generally serious or very serious due to unclear methodology in terms of blinding of risk tool and outcome data. A large proportion of the available concordance data had no reported variance data (such as 95% CI). As such, many of the outcomes were downgraded for a subsequent risk of inconsistency and possible imprecision. Due to the method of reporting and analysis of the calibration data with observed/expected ratios, it was also not possible to ascertain variance data. These outcomes were subsequently downgraded due to the uncertainty around outcome precision.

1.5.1.3 Benefits and harms

The committee agreed that an accurate risk prediction tool can have benefits in directing discussions between clinicians about the appropriateness of the planned surgery and whether it should proceed as planned, should be abbreviated, or whether alternative non-surgical options should be considered. Additionally, the committee suggested that being able to quantify morbidity risk allows planning for post-operative destination, discussions about recovery or convalescence and the anticipated clinical course. Effective risk tools can subsequently have a benefit on patient experience and postoperative quality of life. One possible disadvantage (harm) of using risk tools is underestimating mortality or morbidity risk, which may lead to insufficient attention to preventable risks, insufficient monitoring or surgery being performed when alternative options may be more appropriate. Another potential harm is over-estimating operative risk, which can lead to unnecessary over-vigilance and possibly reluctance on the part of the patient (and maybe clinician) to commence surgery. Thus using accurate risk prediction was seen by the GC as vital to maximise benefits and minimise harms.

The committee discussed the results and utility of the risk tools reviewed and agreed that a concordance (c-statistic) of >80% represents a good level of predictive accuracy, with results of >90% demonstrating an excellent test. The committee added that a test yielding <70% accuracy would be considered poor. The committee also noted that calibration data showing a test observed/expected ratio of 0.9-1.1 would be considered a fair level of accuracy, adding that it would be better to overestimate the event rate than to underestimate morbidity or mortality.

The committee agreed that tools such as POSSUM, P-POSSUM, NSQIP, E-PASS and SRS showed a fair level of accuracy for mortality with median c-statistic of ~85%. The committee highlighted that there was notable inconsistency in the accuracy of tools in the prediction of mortality and morbidity, with most tools ranging from ~60% to ~90% accuracy for predicting mortality.

The committee noted that all tools were less accurate in predicting morbidity showing a predictive accuracy of ~60-70%, but agreed that this was expectedly lower than the accuracy in predicting mortality and could still be informative for a healthcare professional and patient scheduled to undergo surgery.

The committee agreed that the evidence on risk tool calibration showed significant inconsistency between studies, limiting the utility of these results. As such, the committee weighted the majority of their discussions on the benefits and harms of risk tools on risk tool concordance evidence.

The committee considered that the noted variation in results could be due to the heterogeneity in study populations, with included studies providing risk prediction for a range

of varied types of surgery. This was a notable concern to the committee, and while they felt confident that risk tools can have a benefit in the preoperative setting in predicting morbidity and mortality, they were not able to determine which risk tool should be used.

1.5.2 Cost effectiveness and resource use

No economic evaluations were identified for this question.

All of the different risk tools are freely available, and therefore do not have a cost associated with using them. Although they require some time to complete, the committee stated it would usually take less than 5 minutes during a preoperative assessment. The different types of risk tools do require different information, for example, some require information on the adult's haemoglobin levels, however, all of these tests are already carried out as part of preoperative assessment.

The committee highlighted that if a risk tool is not accurate at estimating mortality and morbidity, then the wrong people may be given targeted interventions before surgery (incorrectly identified as high risk), or the wrong people may not be receiving interventions they should have (incorrectly identified as low risk). These targeted interventions vary, but could require being referred to a Consultant Anaesthetist, Cardiologist or Care of the Elderly specialist, or being admitted to a specialist area after surgery. Therefore, the committee highlighted the importance of accurately identifying who is at risk, as these downstream interventions can have a high cost associated with them, or quality of life could be lost from people not receiving interventions they require.

A recommendation was made to use a validated risk tool as part of a preoperative assessment. The committee agreed that the most commonly used tools such as P-POSSUM, NSQIP, E-PASS and SORT showed similar level of accuracy in predicting mortality and therefore will not lead to differences in the downstream interventions that are implemented in relation to patient risk. As current practice already involves using a validated risk tool as part of a preoperative assessment, the recommendation will not have a substantial resource impact.

1.5.3 Other factors the committee took into account

The committee recognised that it may be more appropriate to use a surgery specific risk tool rather than a generic tool. In addition, the committee agreed that the tool could simply be recording the American Society of Anaesthesiologists status of the patient for lower risk, less complex surgery.

The committee noted that a validated risk stratification tool can also help to frame discussions about risk with the person having surgery. Planned surgery is recognised as a 'teachable moment' when patients are more receptive and motivated to undertake healthy lifestyle changes such as smoking cessation or increasing the exercise they undertake. Healthcare professionals involved in the perioperative pathway can be trained to use motivational behavioural change techniques to help support these interactions with patients.

The committee noted that a validated risk stratification tool can also help to frame discussions about risk with the person having surgery as well as the wider perioperative team on the impact of surgical management on overall outcome. They agreed that the risk of postoperative morbidity is an important concern for people when they are making decisions about surgery. The committee noted that the recommendation was applicable to people undergoing dental surgery.

The committee considered that the findings of risk tools could have an influence over allocation of resources, although this would not be solely based on the risk tool findings, but alongside clinical assessment and judgement.

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Appendices

Appendix A: Review protocols

Table 4: Review protocol: Preoperative risk stratification tools

ID	Field	Content
0.	PROSPERO registration number	Not registered
1.	Review title	Which validated preoperative risk stratification tools best identify increased risk of mortality and morbidity in adults who will be undergoing surgery?
2.	Review question	Which validated preoperative risk stratification tools best identify increased risk of mortality and morbidity in adults who will be undergoing surgery?
3.	Objective	To determine which validated preoperative risk stratification tools best identify increased risk of mortality and morbidity in adults who will be undergoing surgery.
4.	Searches	Medline, Embase, The Cochrane Library
5.	Condition or domain being studied	Perioperative care
6.	Population	Inclusion: Adults 18 years and over undergoing surgery. Exclusion: • children and young people aged 17 years and younger • surgery for burns, traumatic brain injury or neurosurgery
7.	Test	Validated risk stratification tools: • P-POSSUM score (Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity) • SORT (Surgical Outcome Risk Tool) • NSQIP (National Surgical Quality Improvement Program) universal surgical risk calculator
8.	Comparator/Reference standard/Confounding factors	n/a
9.	Types of study to be included	Prospective and retrospective cohort studies
10.	Other exclusion criteria	• derivation studies • internal validation studies • non-English language studies • studies published before 2000
11.	Context	n/a

12.	Primary outcomes (critical outcomes)	Mortality Morbidity	
13.	Secondary outcomes (important outcomes)	n/a	
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5).	
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.	
16.	Strategy for data synthesis	GRADEpro used to assess the quality of evidence for each outcome.	
17.	Analysis of sub-groups	Subgroups: • older adults (over 60)	
18.	Type and method of review	☐	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☒	Risk prediction

19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	[x]		
22.	Anticipated completion date	[x]		
23.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☐	☑
		Piloting of the study selection process	☐	☑
		Formal screening of search results against eligibility criteria	☐	☑
		Data extraction	☐	☑
		Risk of bias (quality) assessment	☐	☑
		Data analysis	☐	☑
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail POC@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
25.	Review team members	From the National Guideline Centre: Ms Kate Ashmore Ms Kate Kelley Ms Sharon Swaine Mr Ben Mayer Ms Maria Smyth Mr Vimal Bedia Mr Audrius Stonkus Ms Madelaine Zucker Ms Margaret Constanti Ms Annabelle Davis Ms Lina Gulhane		

26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.	
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.	
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage].	
29.	Other registration details	[n/a]	
30.	Reference/URL for published protocol	[Give the citation and link for the published protocol, if there is one.]	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Perioperative care, surgery, risk prediction	
33.	Details of existing review of same topic by same authors	[n/a]	
34.	Current review status	☐	Ongoing
		☒	Completed but not published
		☐	Completed and published
		☐	Completed, published and being

			updated
		☐	Discontinued
35.	Additional information	[n/a]	
36.	Details of final publication	www.nice.org.uk	

Table 5: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[115] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland).

	• Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'. • Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. For example, economic evaluations based on observational studies will be excluded, when the clinical review is only looking for RCTs,

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2018.[115]

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 30 May 2019	Exclusions
Embase (OVID)	1974 – 30 May 2019	Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 5 of 12 CENTRAL to 2019 Issue 5 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 4 of 4	None

Medline (Ovid) search terms

1.	exp Preoperative Care/ or Preoperative Period/
2.	(pre-operat* or preoperat* or pre-surg* or presurg*).ti,ab.
3.	((before or prior or advance or pre or prepar*) adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
4.	or/1-3
5.	limit 4 to English language
6.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
7.	5 not 6
8.	letter/
9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/8-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animals/ not humans/

20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/18-24
26.	7 not 25
27.	Decision Support Techniques/
28.	Health Status Indicators/
29.	(POSSUM or "Physiological and Operative Severity Score").ti,ab.
30.	SORT.ti,ab.
31.	"Surgical Outcome Risk Tool".ti,ab.
32.	((risk* or predict* or prognos*) adj2 (tool* or rule* or index* or indices or score* or scoring or scale* or model* or system* or algorithm* or stratif* or criteria or calculat*)).ti,ab.
33.	or/27-32
34.	26 and 33

Embase (Ovid) search terms

1.	*preoperative care/ or *preoperative period/
2.	(pre-operat* or preoperat* or pre-surg* or presurg*).ti,ab.
3.	((before or prior or advance or pre or prepar*) adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
4.	or/1-3
5.	limit 4 to English language
6.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
7.	5 not 6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	case report/ or case study/
12.	(letter or comment*).ti.
13.	or/8-12
14.	randomized controlled trial/ or random*.ti,ab.
15.	13 not 14
16.	animal/ not human/
17.	nonhuman/
18.	exp Animal Experiment/
19.	exp Experimental Animal/
20.	animal model/
21.	exp Rodent/
22.	(rat or rats or mouse or mice).ti.
23.	or/15-22
24.	7 not 23
25.	Health Status Indicator/
26.	(POSSUM or "Physiological and Operative Severity Score").ti,ab.

27.	SORT.ti,ab.
28.	"Surgical Outcome Risk Tool".ti,ab.
29.	((risk* or predict* or prognos*) adj2 (tool* or rule* or index* or indices or score* or scoring or scale* or model* or system* or algorithm* or stratif* or criteria or calculat*)).ti,ab.
30.	or/25-29
31.	24 and 30

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Preoperative Care] this term only
#2.	MeSH descriptor: [Preoperative Period] this term only
#3.	MeSH descriptor: [Perioperative Nursing] this term only
#4.	(pre-operative* or preoperative* or preop* or pre-op* or pre-surg* or presurg*):ti,ab
#5.	(before or prior or advance) near/3 (surg* or operat* or anaesthes* or anesthes*):ti,ab
#6.	(or #1-#5)
#7.	MeSH descriptor: [Decision Support Techniques] this term only
#8.	MeSH descriptor: [Health Status Indicators] this term only
#9.	(POSSUM or "Physiological and Operative Severity Score"):ti,ab
#10.	SORT:ti,ab
#11.	"Surgical Outcome Risk Tool":ti,ab
#12.	((risk* or predict* or prognos*) near/2 (tool* or rule* or index* or indices or score* or scoring or scale* or model* or system* or algorithm* or stratif* or criteria or calculat*)):ti,ab
#13.	(or #7-#12)
#14.	#6 and #13

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to the perioperative care population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional health economics searches were run on Medline and Embase.

Table 7: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 30 May 2019	Exclusions Health economics studies
Embase	2014 – 30 May 2019	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 02 May 2019 NHSEED - Inception to 02 May 2019	None

Medline (Ovid) search terms

1.	exp Preoperative Care/ or exp Perioperative Care/ or exp Perioperative Period/ or exp Perioperative Nursing/

2.	((pre-operative* or preoperative* or preop* or pre-op* or pre-surg* or presurg*) adj3 (care* or caring or treat* or nurs* or monitor* or recover* or medicine)).ti,ab.
3.	((perioperative* or peri-operative* or intraoperative* or intra-operative* or intrasurg* or intra-surg* or peroperat* or per-operat*) adj3 (care* or caring or treat* or nurs* or monitor* or recover* or medicine)).ti,ab.
4.	((postoperative* or postop* or post-op* or post-surg* or postsurg*) adj3 (care* or caring or treat* or nurs* or monitor* or recover* or medicine)).ti,ab.
5.	((care* or caring or treat* or nurs* or recover* or monitor*) adj3 (before or prior or advance or during or after) adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
6.	1 or 2 or 3 or 4 or 5
7.	(intraoperative* or intra-operative* or intrasurg* or intra-surg* or peroperat* or per-operat* or perioperat* or peri-operat*).ti,ab.
8.	((during or duration) adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
9.	7 or 8
10.	postoperative care/ or exp Postoperative Period/ or exp Perioperative nursing/
11.	(postop* or post-op* or post-surg* or postsurg* or perioperat* or peri-operat*).ti,ab.
12.	(after adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
13.	(post adj3 (operat* or anaesthes* or anesthes*)).ti,ab.
14.	10 or 11 or 12 or 13
15.	exp Preoperative Care/ or Preoperative Period/
16.	(pre-operat* or preoperat* or pre-surg* or presurg*).ti,ab.
17.	((before or prior or advance or pre or prepar*) adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
18.	15 or 16 or 17
19.	6 or 9 or 14 or 18
20.	letter/
21.	editorial/
22.	news/
23.	exp historical article/
24.	Anecdotes as Topic/
25.	comment/
26.	case report/
27.	(letter or comment*).ti.
28.	or/20-27
29.	randomized controlled trial/ or random*.ti,ab.
30.	28 not 29
31.	animals/ not humans/
32.	exp Animals, Laboratory/
33.	exp Animal Experimentation/
34.	exp Models, Animal/
35.	exp Rodentia/
36.	(rat or rats or mouse or mice).ti.
37.	or/30-36
38.	19 not 37
39.	limit 38 to English language
40.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)

41.	39 not 40
42.	economics/
43.	value of life/
44.	exp "costs and cost analysis"/
45.	exp Economics, Hospital/
46.	exp Economics, medical/
47.	Economics, nursing/
48.	economics, pharmaceutical/
49.	exp "Fees and Charges"/
50.	exp budgets/
51.	budget*.ti,ab.
52.	cost*.ti.
53.	(economic* or pharmaco?economic*).ti.
54.	(price* or pricing*).ti,ab.
55.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
56.	(financ* or fee or fees).ti,ab.
57.	(value adj2 (money or monetary)).ti,ab.
58.	or/42-57
59.	41 and 58

Embase (Ovid) search terms

1.	*preoperative period/ or *intraoperative period/ or *postoperative period/ or *perioperative nursing/ or *surgical patient/
2.	((pre-operative* or preoperative* or preop* or pre-op* or pre-surg* or presurg*) adj3 (care* or caring or treat* or nurs* or monitor* or recover* or medicine)).ti,ab.
3.	((perioperative* or peri-operative* or intraoperative* or intra-operative* or intrasurg* or intra-surg* or peroperat* or per-operat*) adj3 (care* or caring or treat* or nurs* or monitor* or recover* or medicine)).ti,ab.
4.	((care* or caring or treat* or nurs* or recover* or monitor*) adj3 (before or prior or advance or during or after) adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
5.	1 or 2 or 3 or 4
6.	peroperative care/ or exp peroperative care/ or exp perioperative nursing/
7.	(intraoperative* or intra-operative* or intrasurg* or intra-surg* or peroperat* or per-operat* or perioperat* or peri-operat*).ti,ab.
8.	((during or duration) adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
9.	6 or 7 or 8
10.	postoperative care/ or exp postoperative period/ or perioperative nursing/
11.	(postop* or post-op* or post-surg* or postsurg* or perioperat* or peri-operat*).ti,ab.
12.	(after adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
13.	(post adj3 (operat* or anaesthes* or anesthes*)).ti,ab.
14.	10 or 11 or 12 or 13
15.	exp preoperative care/ or preoperative period/
16.	(pre-operat* or preoperat* or pre-surg* or presurg*).ti,ab.
17.	((before or prior or advance or pre or prepar*) adj3 (surg* or operat* or anaesthes* or anesthes*)).ti,ab.
18.	15 or 16 or 17

19.	5 or 9 or 14 or 18
20.	letter.pt. or letter/
21.	note.pt.
22.	editorial.pt.
23.	case report/ or case study/
24.	(letter or comment*).ti.
25.	or/20-24
26.	randomized controlled trial/ or random*.ti,ab.
27.	25 not 26
28.	animal/ not human/
29.	nonhuman/
30.	exp Animal Experiment/
31.	exp Experimental Animal/
32.	animal model/
33.	exp Rodent/
34.	(rat or rats or mouse or mice).ti.
35.	or/27-34
36.	19 not 35
37.	limit 36 to English language
38.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
39.	37 not 38
40.	health economics/
41.	exp economic evaluation/
42.	exp health care cost/
43.	exp fee/
44.	budget/
45.	funding/
46.	budget*.ti,ab.
47.	cost*.ti.
48.	(economic* or pharmaco?economic*).ti.
49.	(price* or pricing*).ti,ab.
50.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
51.	(financ* or fee or fees).ti,ab.
52.	(value adj2 (money or monetary)).ti,ab.
53.	or/40-52
54.	39 and 53

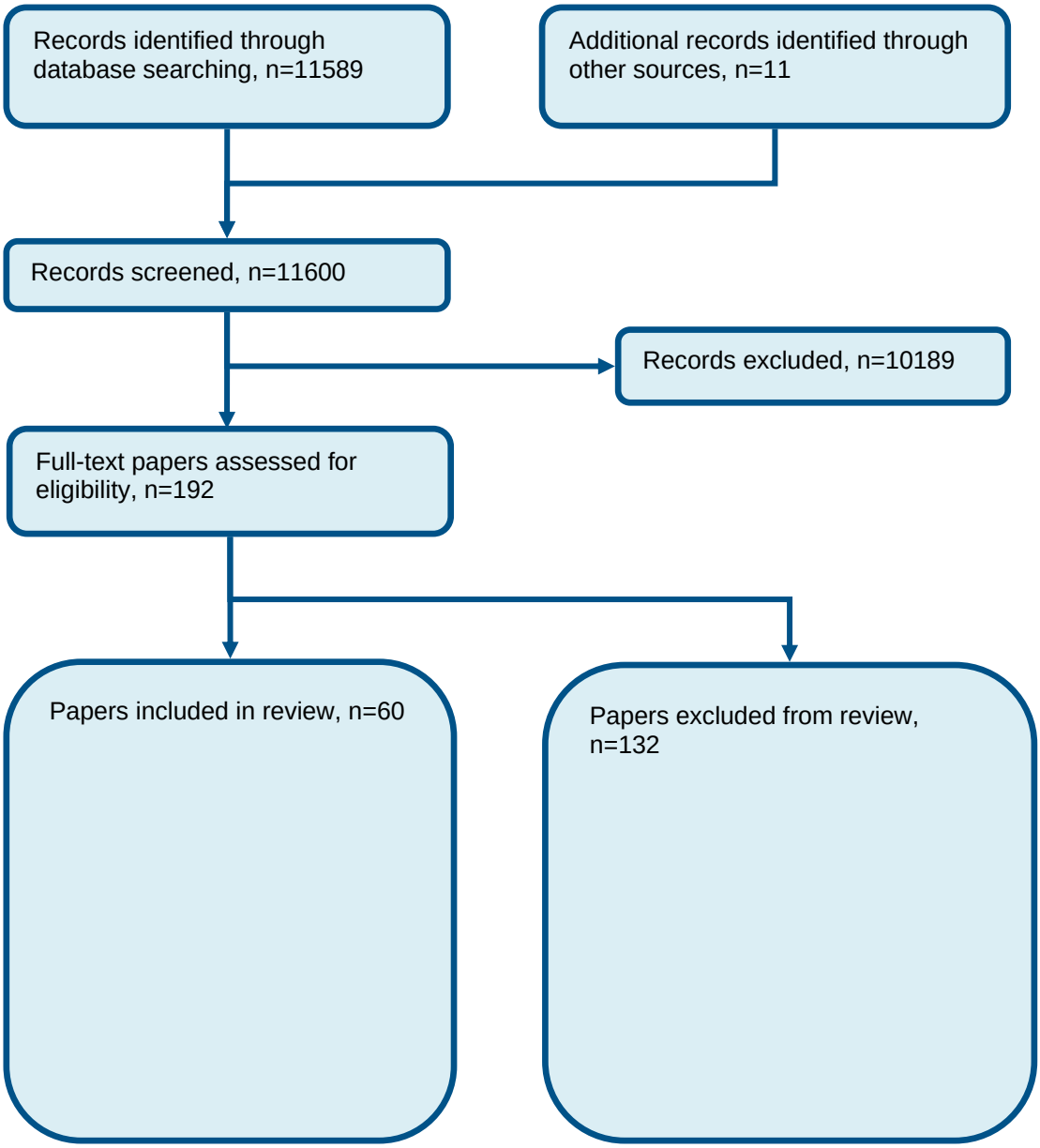
NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Preoperative Care EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Perioperative Care EXPLODE ALL TREES
#3.	MeSH DESCRIPTOR Perioperative Period EXPLODE ALL TREES

#4.	MeSH DESCRIPTOR Perioperative Nursing EXPLODE ALL TREES
#5.	(((perioperative* or peri-operative* or intraoperative* or intra-operative* or intrasurg* or intra-surg* or peroperat* or per-operat*) adj3 (care* or caring or treat* or nurs* or monitor* or recover* or medicine)))
#6.	(((care* or caring or treat* or nurs* or recover* or monitor*) adj3 (before or prior or advance or during or after) adj3 (surg* or operat* or anaesthes* or anesthes*)))
#7.	(((pre-operative* or preoperative* or preop* or pre-op* or pre-surg* or presurg*) adj3 (care* or caring or treat* or nurs* or monitor* or recover* or medicine)))
#8.	(((postoperative* or postop* or post-op* or post-surg* or postsurg*) adj3 (care* or caring or treat* or nurs* or monitor* or recover* or medicine)))
#9.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10.	(* IN HTA)
#11.	(* IN NHSEED)
#12.	#9 AND #10
#13.	#9 AND #11
#14.	MeSH DESCRIPTOR Intraoperative Care EXPLODE ALL TREES
#15.	#1 OR #2 OR #3 OR #4 OR #14
#16.	((intraoperative* or intra-operative* or intrasurg* or intra-surg* or peroperat* or per-operat* or perioperat* or peri-operat*))
#17.	(((during or duration) adj3 (surg* or operat* or anaesthes* or anesthes*)))
#18.	((postop* or post-op* or post-surg* or postsurg* or perioperat* or peri-operat*))
#19.	((after adj3 (surg* or operat* or anaesthes* or anesthes*)))
#20.	((post adj3 (operat* or anaesthes* or anesthes*)))
#21.	((pre-operat* or preoperat* or pre-surg* or presurg*))
#22.	(((before or prior or advance or pre or prepar*) adj3 (surg* or operat* or anaesthes* or anesthes*)))
#23.	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24.	#10 AND #23
#25.	#11 AND #23
#26.	#12 OR #13 OR #24 OR #25

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of risk tools



Appendix D: Clinical evidence tables

Reference	Baker 2018[11]
Study type	Prospective Cohort study
Study sample	Patients were prospectively enrolled from March 2014-2015 and eligible if they were undergoing an abdominal operation
Inclusion criteria	298 patients deemed eligible by their surgical oncologist as an appropriate surgical candidate, and the operation was planned under GA with entry into the Peritoneum.
Exclusion criteria	Patients excluded if they underwent an emergent operation
Risk tools	ACS NSQIP
Outcome	90 day morbidity
Results	ACS NSQIP any complication – OR = 1.042 (CI 1.030-1.116), P value = <0.0001, c-statistic = 0.6061

Reference	Bennett-Guerrero 2003[14]
Study type	Prospective Cohort study of risk prediction tool
Study sample	2 cohorts of patients undergoing major, non-cardiac surgery over the same time interval (August 1996 to June 1998). One cohort included patients undergoing surgery at the Mount Sinai Hospital, New York and the second cohort included patients undergoing surgery at the Queen Alexandra hospital and St Mary's hospital in Portsmouth.
Inclusion criteria	Patients undergoing major, non-cardiac surgery. USA (n=1056). UK (n=1539).
Exclusion criteria	None provided
Risk tools	P-POSSUM
Outcome	Mortality – in hospital mortality
Results	UK cohort - predicted mortality rate = 10.2%, observed mortality rate = 9.9 US cohort - predicted mortality rate = 7.8%, observed mortality rate = 2.1% UK cohort - predicted no. of deaths = 156, Observed number of deaths = 152 US cohort – predicted no. of deaths = 82, observed no. of deaths = 22

Reference	Blair 2018[17]
Study type	Retrospective review of cohort
Study sample	Retrospective review of a single institution, multi-surgeon, database of all patients undergoing PN for renal cell carcinoma from February 1998 to June 2015.
Inclusion criteria	470 Patients undergoing PN for renal cell carcinoma. 272 males and 198 women with a median age of 57 years
Exclusion criteria	Patients were excluded if complete records were not available and if the pathology of the tumor was determined to be anything other than RCC.
Risk tools	ACS NSQIP surgical risk calculator
Outcome	30 days overall complications and mortality
Results	Comparing predicted vs observed outcomes for all patients, the risk of overall complications were significantly under estimated (9.16% vs 16.81%, p<0.001) by the NSQIP. 95% CI = -7.65 (-7.07, -7.33). Mortality = (0.33 vs 0.21%, p<0.001) 95% CI = 0.12 (0.09-0.16).

Reference	Bodea 2018[18]
Study type	Retrospective cohort study
Study sample	Elective surgery patients at the Surgical Clinic no. 3 Cluj Romania between July 2013- December 2015.
Inclusion criteria	113 Participants undergoing elective Pancreaticoduodenectomy for periampullary malignant tumors. 64 males and 49 females, aged between 22-81 (median of 64).
Exclusion criteria	No exclusion criteria provided
Risk tools	P-POSSUM
Outcome	Mortality Morbidity
Results	The c-statistic was 0.61 for morbidity and 0.61 for mortality. Comparing the observed and estimated morbidity and mortality, statistical significant results (p=0.05 and p=0.03, respectively) Morbidity =ROC sensibility 0.65 [CI95% (0.562, 0.735)] and specificity 0.5 [CI95% (0.388, 0.606)]

Reference	Bonaventura 2019[20]
Study type	Retrospective cohort study

Reference	Bonaventura 2019[20]
Study sample	Patients undergoing cholecystectomy for acute cholecystitis at the surgery unit of Ospedale Policlinico San Martino hospital between 2005 and 2013.
Inclusion criteria	271 patients undergoing cholecystectomy for acute chloecystitis
Exclusion criteria	Patients who were younger than 18 were excluded
Risk tools	CCI ASA
Outcome	In hospital complications
Results	CCI in hospital complications – c-statistic = 0.662 (p= 0.0086) ASA in hospital complications – OR = 1.92 (CI 1.04-3.54) p=<0.001

Reference	Boyd 2019[22]
Study type	Retrospective cohort study
Study sample	Records of patients who underwent pelvic reconstructive and incontinence surgery in a single tertiary centre from July 2014 to July 2017 were reviewed
Inclusion criteria	731 women patients 18 years or older undergoing surgery for pelvic organ prolapse or incontinence by all routes were included
Exclusion criteria	Non pelvic reconstructive procedures or procedures with same day hospital discharge were excluded.
Risk tools	ACS NSQIP risk calculator
Outcome	30 day Mortality
Results	NSQIP mortality – 0 event rate NSQIP any complication - C statistic = 0.547 (p 0.039), BS = 35.037
Comments	Women only and excluded all same day DC patients

Reference	Bronheim 2018[24]
Study type	Retrospective review of cohort
Study sample	Retrospective review of ACS-NSQIP database from 2006 to 2014
Inclusion criteria	52,066 adult patients undergoing posterior lumbar decompression surgery
Exclusion criteria	None provided
Risk tools	ASA score

Reference	Bronheim 2018[24]
Outcome	30 days mortality and morbidity
Results	c-statistic results as a predictor for any complication = 0.770 SE 0.023 (P= <0.001 CI= 0.726 - 0.815) c-statistic results as a predictor for mortality = 0.800 SE 0.002 (P= <0.001 CI= 0.796 - 0.804)

Reference	Brooks 2005[25]
Study type	Retrospective review of cohort
Study sample	All 3048 consecutive patients undergoing surgical procedures under the care of a single consultant surgeon working at a district general hospital between February 1999 and September 2002 were considered for analysis.
Inclusion criteria	A cohort of 949 higher-risk patients remained and was used in this analysis.
Exclusion criteria	Patients at low risk of death were excluded from analysis, including 1185 patients undergoing day-case procedures, 149 children and 765 young patients undergoing minor or intermediate inpatient procedures.
Risk tools	POSSUM P-POSSUM Surgical risk score
Outcome	Mortality
Results	ROC AUC (95% CI) POSSUM: 0·92 (0·90 to 0·95) P-POSSUM: 0·92 (0·90 to 0·95) SRS: 0·89 (95 per cent c.i. 0·86 to 0·93) Actual mortality rate: 8.4% Expected mortality rate: POSSUM: 12.6% P-POSSUM: 7.3% SRS: 5.9%

Reference	Bulow 2019[27]
Study type	Retrospective review of cohort

Reference	Bulow 2019[27]
Study sample	Retrospective review of patients from the Swedish Hip Arthroplasty register between 2005 and 2012
Inclusion criteria	43,224 patients treated with hip arthroplasty for a femoral neck fracture
Exclusion criteria	None provided
Risk tools	CCI
Outcome	30 and 90 days mortality and long term mortality – 1 year post op
Results	c-statistic 30 day mortality = 0.59 c-statistic 90 day mortality = 0.59 c-statistic 1 year mortality = 0.58

Reference	Cengiz 2014[32]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	335 consecutive patients undergoing colorectal cancer surgery between 2002 and 2012 in third-level healthcare centres. Male patients (n = 196) consisted 58.5% of all patients and 38.2% (n = 128) of all patients were over 70 years of age. Number of elective surgeries or curative resection was 279 (83.3%) or 265 (79.1%), respectively.
Inclusion criteria	Consecutive patients undergoing colorectal cancer surgery
Exclusion criteria	None provided
Risk tools	Possum P-possum ACPGBI scores
Outcome	Mortality within postoperative 30-days that extend the duration of hospital stay.
Results	Mortality and morbidity were observed in 17 and 109 patients, respectively. Mortality predictive scores: POSSUM: c-statistic = 89.7, 95% CI = 86.0-92.8, sensitivity = 88.2, specificity = 78.6. P-POSSUM: c-statistic = 90.4, 95% CI = 86.7-93.3, sensitivity = 94.1, specificity = 73.0 ACPGBI score: c-statistic = 78.1, 95% CI = 73.3-82.4, sensitivity = 76.5, specificity = 70.8

Reference	Chun 2018[33]
Study type	Retrospective case control study

Reference	Chun 2018[33]
Study sample	Patients who had undergone surgery at a single tertiary care centre.
Inclusion criteria	217 patients who had undergone spinal surgery for various spine diseases. 103 men and 114 women with a mean age of 57.0 years.
Exclusion criteria	None included
Risk tools	E-PASS POSSUM
Outcome	Postoperative complications within 1 month after surgery
Results	The c-statistic for predicted post-operative complications was 0.588 for the E-PASS and 0.721 for the POSSUM.

Reference	Cologne 2015[37]
Study type	Retrospective cohort study
Study sample	Consecutive laparoscopic colon resections performed on an elective basis from April 2011 through July 2014 by two colorectal surgeons at a tertiary referral centre
Inclusion criteria	116 patients were included if they were older than 18 years, if the procedure was performed by one of the 2 specified surgeons, if a preoperative ACS risk score was calculated and if completed postoperative medical records were available.
Exclusion criteria	None provided
Risk tools	ACS NSQIP risk calculator
Outcome	Mortality Any complication
Results	Observed vs predicted risk for any complication = (17.3% vs 19.4%, p=0.05), mortality = (1.07% vs 0.83%, p=0.86).

Reference	Dahlke 2014[39]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	Data obtained from the ACS NSQIP participant file 2011 release for patients undergoing a broad range of surgeries across all surgical specialities.
Inclusion criteria	238,649 patients were included for analysis if they underwent a general surgery. 58.8% female with a median age of 54.1 years.
Exclusion criteria	None provided

Reference	Dahlke 2014[39]
Risk tools	ACS NSQIP – All information
Outcome	Overall Morbidity
Results	AUC/c-statistic for overall morbidity = 0.861

Reference	Donati 2004[43]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	Data were collected from all patients, with no age limits imposed, who underwent any type of elective or emergency surgical procedure in two different hospitals. N=1936
Inclusion criteria	Patients who underwent any type of elective or emergency surgical procedure/
Exclusion criteria	Patients having cardiac surgery or Caesarean delivery were excluded.
Risk tools	POSSUM P-POSSUM ASA
Outcome	Overall mortality
Results	AUC/c-statistic (SE, 95% CI) POSSUM: 0.915 (SE 0.016, CI 0.884–0.947) P-POSSUM: 0.912 (SE 0.033, CI 0.898–0.924) ASA: 0.810 (SE 0.044, CI 0.792–0.828)

Reference	Dutta 2011[45]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	121 Patients undergoing oesophago-gastric cancer resections in Glasgow Royal Infirmary from January 2005 to May 2009
Inclusion criteria	Patients undergoing oesophago-gastric curative cancer resections who had data to score the POSSUM, P-POSSUM, O-POSSUM, and mGPS models were included in the study
Exclusion criteria	None provided
Risk tools	Possum P-possum

Reference	Dutta 2011[45]
Outcome	Mortality and Morbidity Both short term and long term survival were recorded
Results	Observed morbidity was 49%, whereas POSSUM predicted post-operative morbidity in 60%, giving an overall standardised morbidity ratio of 0.25 and 0.71. ROC analysis for the POSSUM morbidity equation (c-statistic 0.639, 95% CI 0.541–0.737, P = 0.008) ROC analysis for the P-POSSUM mortality equation gave c-statistic 0.808 (95% CI 0.55–1.06, P = 0.020), POSSUM (c-statistic 0.759, 95% CI 0.48–1.04, P = 0.051)

Reference	Egberts 2011[48]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	The medical records of 191 patients undergoing surgery for IBD at the Department of General Surgery and Thoracic Surgery at the University Hospital of Kiel from 2004 to 2009 were analysed retrospectively. There were a total of 191 patients (81 male and 110 female) with a mean age of 38.1 years (range 5–75). There were 158 patients operated on for Crohn's disease and 33 patients for UC
Inclusion criteria	Patients with a histologically proven MC or CU and an abdominal surgery were included.
Exclusion criteria	Patients who presented with a perianal affection and were treated with proctological techniques (seton drainage, fistula repair, etc.) without abdominal surgery were excluded from this study.
Risk tools	Possum
Outcome	Mortality Morbidity
Results	The overall complication rate was 27.7%, and the mortality was 0.5%. The morbidity rate predicted by POSSUM was 28.4% and the mortality rate 7.2%.

Reference	Egberts 2011[47]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	The medical records of 143 patients with cutaneous melanoma who underwent a radical lymph node dissection (RLND) at the Department of General Surgery and Thoracic Surgery at the University Hospital of Kiel from 1985 to 2008 were analysed retrospectively. There were 143 patients (59 male, 84 female) with a mean age of 58.1 years (range: 20–89 years)

Reference	Egberts 2011[47]
Inclusion criteria	Patients with cutaneous melanoma who underwent a radical lymph node dissection (RLND)
Exclusion criteria	None provided
Risk tools	Possum
Outcome	Mortality Morbidity
Results	The actual mortality rate was 0% whereas the rate estimated by POSSUM was 8.3%. The POSSUM (ie predicted) morbidity rate for all patients together was 32.9% and the observed morbidity for all patients was similar at 28.0%.

Reference	Filip 2014[51]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	Patients diagnosed with oesophageal cancer in whom surgery was performed between January 2004 and March 2013
Inclusion criteria	Patients diagnosed with oesophageal cancer in whom surgery was performed. Out of 137 patients diagnosed with oesophageal cancer, esophagectomy was performed in 43 cases.
Exclusion criteria	Patients with unresectable tumours on laparotomy or thoracotomy or those with palliative surgery were excluded
Risk tools	POSSUM Charlson Age adjusted Charlson ASA score
Outcome	Mortality and Morbidity within 30 days after surgery
Results	Postoperative mortality (11.62%) was best predicted by POSSUM score (10.48; 95% CI 9.37 -11.66). The observed morbidity was 58.13%, higher than that expected by POSSUM (48.24%; 95%CI, 44.82-51.66) with a morbidity ratio O/E of 1.2. Expected mortality for P-POSSUM was 2.71 (95%CI, 2.31 - 3.12), O-POSSUM was 6.83 (95%CI, 6.21-7.25), whereas the observed mortality in our series was 11.62%, thus giving a mortality ratio observed/expected of 1.1 for POSSUM, 4.28 for P-POSSUM and 1.7 for O-POSSUM. The observed morbidity given was 58.13%, higher than that expected by the POSSUM (48.24%; 95%CI, 44.82 - 51.66) with a morbidity ratio O/E of 1.2. c-statistic for morbidity p-value POSSUM score 0.826 (0.67-0.92) 0.0001 Physiological score 0.74 (0.58-0.86) 0.0014

Reference	Filip 2014[51]
	Operative score 0.607 (0.44-0.75) 0.21 Charlson comorbidity index 0.608 (0.44-0.75) 0.21 Age adjusted Charlson index 0.736 (0.58-0.85) 0.0018
Comments	Unclear what outcome is being predicted for c-statistic, presumed morbidity.

Reference	Fu 2019[54]
Study type	Retrospective chart review of ACS NSQIP
Study sample	Data from the ACS NSQIP from 2005 to 2015 was extracted
Inclusion criteria	10,527 patients who underwent total shoulder arthroplasty were identified in the NSQIP
Exclusion criteria	Cases missing age, sex, height, weight and thise younger than 18 years old.
Risk tools	ASA score Modified Charlston Comorbidity Index
Outcome	30 day postoperative adverse event
Results	ASA any adverse event – c-statistic = 0.607 (0.587 – 0.627) mCCI any adverse event - c-statistic = 0.555 (0.536 – 0.575)

Reference	Goffi 1999[56]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	Patients admitted during one year period for major elective or emergency operations, benign or malignant. N=187
Inclusion criteria	Patients admitted during one year period for major elective or emergency operations, benign or malignant.
Exclusion criteria	Not reported
Risk tools	ASA
Outcome	Mortality and 30 days post-operative any complication combined
Results	AUC: 0.777

Reference	Golan 2018[57]

Reference	Golan 2018[57]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	Patients in prospectively maintained database who underwent open RC with either ileal conduit or orthotopic neobladder urinary diversion for bladder cancer between Jan 2007 and Dec 2016.
Inclusion criteria	954 patients undergoing radical cystectomy with uniary diversion Males = 752 and median age =70 (62-76)
Exclusion criteria	Patients who underwent a continent catherisable unirary diversion were not included.
Risk tools	ACS NSQIP risk calculator
Outcome	Mortality and 30 days post-operative any complication
Results	Predicted vs observed any complication= 30.7% vs 40.3% and mortality = 1.3% vs 2.2%. Any complication c-statistic = 0.58 (p<0.001), mortality c-statistic = 0.62 (p=0.02).

Reference	Haga 2011[59]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	Patients who received any of the 41 elective procedures were eligible for enrolment. These procedures comprised more than 90% of all scheduled operations in general surgery. Elective surgery was defined as surgery that did not require emergency surgery within 48 hours from admission. N=5272
Inclusion criteria	Patients who received any of the 41 elective procedures were eligible for enrolment
Exclusion criteria	Exclusion criteria were as follows: (1) patients who did not sign the consent forms to participate in this study; (2) those who had concomitant cancer of different organs; (3) those who had a history of cancer in the previous 5 years; and (4) those who received concomitant surgery in different surgical fields such as enucleation of an esophageal submucosal tumor via right thoracotomy and distal pancreatectomy for pancreatic cancer.
Risk tools	POSSUM P-POSSUM E-PASS
Outcome	Mortality
Results	AUC (95% CI) POSSUM: 0.74 (0.63-0.86) P-POSSUM: 0.81 (0.75-0.88) E-PASS: 0.82 (0.69-0.95)

Reference	Hightower 2010[61]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	Patients undergoing major abdominal cancer surgery. N=32
Inclusion criteria	Patients .18 yr of age screened in the Pre-anaesthesia Assessment Center scheduled for one of the following (frequency of surgery): Gastrectomy (3), Pancreatectomy (2), Radical cystectomy (14), Radical nephrectomy (1), Radical transabdominal tumour debulking (2), Pelvic exenteration (5), Low anterior resection (1), Retroperitoneal lymph node dissection (4)
Exclusion criteria	Any patient who is unable to exercise, deemed unacceptable for surgery after evaluation in the Pre-anaesthesia Assessment Center, surgery is cancelled for any reason, suffering any of the following within 3 months before visiting the Pre-anaesthesia Assessment Center: Myocardial infarction, Cerebrovascular event, Transient ischaemic attack, Pulmonary embolic event, Existing acute or chronic deep vein thrombosis, Pregnancy.
Risk tools	ASA
Outcome	Morbidity during 7-day post-op period
Results	Morbidity c-statistic = 0.688 ($p<0.038$), 95% CI= 0.52315 - 0.85185)

Reference	Hirose 2014[62]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	601 consecutive patients who underwent spinal surgery between January 2005 and December 2009 at Kumamoto University Hospital.
Inclusion criteria	Patients who underwent spinal surgery. The surgical procedures included laminoplasty and anterior fusion to treat cervical disorders (169 patients); posterior fusion for thoracic disorders (16 patients); laminectomy, posterior fusion, and discectomy for lumbar disorders (259 patients); resection of spinal tumors (117 patients); spinal fusion for scoliosis (27 patients); and curettage or spinal fusion for pyogenic spondylitis (13 patients). 327 were male and 274 were female, and their mean age was 58.7 years (range 7–88 years).
Exclusion criteria	None provided
Risk tools	POSSUM E-PASS
Outcome	Mortality and Morbidity
Results	The ROC curves of each model for the detection of postoperative complications were evaluated - the c-statistic of predicted

Reference	Hirose 2014[62]
	morbidity rate (PMR) for E-PASS was 0.668 (95% CI 0.596–0.739) and higher than for POSSUM (0.588; 95% CI 0.513–0.663).

Reference	Hirose 2015[63]
Study type	A single centre retrospective cohort study
Study sample	Retrospective review of 275 consecutive patients who underwent spinal surgery between Jan 2008 and Dec 2009 at Kumamoto University Hospital.
Inclusion criteria	275 patients undergoing spinal surgery. The same 4 surgeons performed the procedures. 146 male and 129 females, mean age was 59.7 years.
Exclusion criteria	None provided
Risk tools	E-PASS
Outcome	Total postoperative morbidities
Results	Total postoperative morbidities, c-statistic = 0.681

Reference	Hobson 2007[65]
Study type	Prospective comparison study
Study sample	All patients undergoing surgery in the emergency theatre of the Leicester general hospital over a 4-month period from June to September 2003.
Inclusion criteria	163 patients undergoing surgery in the emergency theatre including general surgery, gynaecology, renal, urology and vascular.
Exclusion criteria	None provided
Risk tools	POSSUM P-POSSUM
Outcome	30 day mortality 60 day/in hospital mortality
Results	30 day mortality, c-statistic = POSSUM - 0.946, P-POSSUM - 0.940. In hospital Mortality, c-statistic = POSSUM – 0.932, P-POSSUM – 0.928.

Reference	Huisman 2014[69]
Study type	Prospective cohort study

Reference	Huisman 2014[69]
Study sample	Recruitment took place in 6 different countries at 11 medical centers between September 2008 and January 2012 and included 263 cancer patients scheduled for elective surgery
Inclusion criteria	A cohort of cancer patients aged 70 or over who were candidate for elective surgery under general anesthesia, were invited to take part by the local coordinator. The median age of this cohort was 76 years (Range: 70–96) and 66.5% of patients were female. The majority of surgical procedures were laparotomies (n = 156; 59.3%) and breast cancer surgeries (n = 76; 28.9%).
Exclusion criteria	Patients requiring emergency surgical management (within 24 hours) were excluded from this study. Medical centres that included less than 10 patients were excluded from analysis, which resulted in the analysis of 263 patients
Risk tools	Timed up and go ASA classification
Outcome	Mortality and 30 day morbidity
Results	In a univariable logistic regression analysis the TUG and ASA were not predictive of 30-day mortality. For morbidity - Sensitivity of a high TUG was 42.0% and specificity was 89.8%. The c-statistic was 0.66 (95%-CI = 0.57–0.75; p<0.001). Sensitivity of ASA ≥3 was 57.1% and specificity was 58.5%. The c-statistic was 0.58 (95%-CI = 0.49–0.67, p = 0.09).

Reference	Igari 2013[70]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	Patients undergoing general surgical procedures at Ohta Nishinouchi General Hospital between April 2003 and March 2009
Inclusion criteria	593 Patients aged ≥80 years who underwent surgery under general anaesthesia. 287 male and 387 females, mean age 83 years.
Exclusion criteria	None provided
Risk tools	POSSUM P-POSSUM
Outcome	Postoperative morbidity and mortality within 30 days post operatively
Results	POSSUM - Observed/expected morbidity ratio was 1.44 and mortality ratio was 0.98 P-POSSUM – the O/E ratio was 1.0.

Reference	Jones 1992[74]

Reference	Jones 1992[74]
Study type	Retrospective cohort analysis of risk prediction tools
Study sample	From January to June 1990, patient admissions were recorded to the high-dependency unit. N=117
Inclusion criteria	Patients admitted to the high-dependency unit immediately after surgery
Exclusion criteria	Analysis excluded 13 patients admitted with multiple injuries following trauma
Risk tools	POSSUM
Outcome	Postoperative morbidity and mortality (30 days)
Results	POSSUM Mortality AUC: 0.753 (+/−0.081) Morbidity AUC: 0.82 Observed: Mortality 13/117, morbidity 59/117 Expected: Mortality 20/117, morbidity 59/117

Reference	Katlic 2019[78]
Study type	Retrospective cohort study
Study sample	Patients aged ≥75 years who presented to Sinai Hospital of Baltimore for major elective surgery between September 2012 and July 2016
Inclusion criteria	1025 geriatric surgical patients undergoing major elective surgery including cardiac, thoracic, vascular, orthopaedic, surgical oncology, general surgery, urologic and neurologic.
Exclusion criteria	None provided
Risk tools	Charleston Comorbidity index ASA Score Fried's 5 point frailty score
Outcome	Any NSQIP complication
Results	Fried’s 5 point frailty – c-statistic = 0.70 (p=0.680) ASA score – c-statistic = 0.70 (p=0.755) CCI – c-statistic = 0.64 (p=0.008)

Reference	Kim 2018[84]
Study type	Retrospective cohort study
Study sample	The national inpatient sample from the USA was queried for patients who underwent a total shoulder arthroplasty or reverse total shoulder arthroplasty between 2002 and 2014
Inclusion criteria	90,491 patients undergoing total shoulder arthroplasty or reverse total shoulder arthroplasty
Exclusion criteria	None provided
Risk tools	Charlston comorbidity index
Outcome	Any inpatient complication and mortality
Results	CCI mortality – c-statistic = 0.827 (CI 0.774-0.88) CCI any complication – c-statistic = 0.691 (CI 0.680-0.703)

Reference	Kong 2013[88]
Study type	Temporal validation of a prospective observational study and the external validation was a retrospective observational study
Study sample	Major colorectal operations performed at Geelong hospital and Western Hospital from 2008-2010
Inclusion criteria	474 major colorectal operations performed at Geelong hospital (temporal validation) and 389 cases at Western Hospital (external validation)
Exclusion criteria	Patients undergoing surgery for reversal of colostomy or ileostomy, diverting stoma formation, transanal endoscopic microsurgery, and laparotomy or laparscopy with washout of peritoneal cavity.
Risk tools	POSSUM P-POSSUM ACPGBI
Outcome	Mortality
Results	Temporal validation (of BH tool) dataset POSSUM: mortality c-statistic = 0.790 p=<0.001 P-POSSUM: mortality c-statistic = 0.801 p=0.88 ACPGBI: mortality c-statistic = 0.721 p= 0.006 External validation (of BH tool) dataset POSSUM: mortality c-statistic = 0.696 p=<0.0001

Reference	Kong 2013[88]
	P-POSSUM: mortality c-statistic = 0.681 p=0.13 ACPGBI: mortality c-statistic = 0.658 p=<0.0001

Reference	Kwok 2011[93]
Study type	Retrospective cohort
Study sample	Data from ACS NSQIP N=1730
Inclusion criteria	Very elderly patients aged 80+ undergoing emergency colon surgery
Exclusion criteria	Not reported
Risk tools	ASA Surgical risk scale
Outcome	Mortality
Results	Overall mortality was 489 (28%)

Tool	C-statistic	Goodness of fit (p value)
ASA	0.66	0.14
Surgical risk scale	0.66	0.14

Reference	Lakomkin 2018[94]
Study type	Retrospective chart review of ACS NSQIP
Study sample	Data from ACA NSQIP from 2008 to 2014
Inclusion criteria	2,170 patients undergoing spinal tumor resection
Exclusion criteria	None provided
Risk tools	ASA score Modified Charlston Comorbidity Index
Outcome	30 day Mortality
Results	ASA – mortality – 'not predictive of any adverse event' CCI – mortality OR = 1.24 (CI= 1.12 – 1.36) P value= <0.001, c-statistic = 0.860

Reference	Lima 2019[101]
Study type	Prospective observational study
Study sample	Patients scheduled to undergo elective surgery during a 3 month period at a University hospital
Inclusion criteria	235 patients over 60 years old scheduled to undergo elective procedures under general, regional or combined anaesthesia for general, gynaecological, plastic, vascular, or orthopaedic surgeries at a university hospital were enrolled.
Exclusion criteria	Patients who were admitted to ICU immediately after surgery, submitted to emergency or urgent surgery procedures, unable to speak or understand the Portuguese language or incapable of signing the informed consent were excluded.
Risk tools	P-POSSUM
Outcome	30 day Mortality
Results	P-POSSUM 30 day mortality AUROC = 0.563

Reference	Moonesinghe 2013[110]
Study type	Prospective observational study
Study sample	Study of surgical patients age 65 years or older who presented to the Johns Hopkins Hospital anesthesia preoperative evaluation center for elective surgery during a 1-year period (June 22, 2005 to July 1, 2006). N=594
Inclusion criteria	Patients were recruited on selected days of the week with days of the week rotated on a regular basis. Using this sampling method, a total of 666 eligible patients were identified on the days sampled; 21 declined participation in the study and 2 participants requested removal from the study after enrolment.
Exclusion criteria	Patients with Parkinson disease (n = 2), previous stroke (n = 11), a Mini-Mental Status Examination score <18 (n = 2), and those taking carbidopa/levodopa, donepezil hydrochloride, or antidepressants (n = 34) because previous studies have found that these medications cause symptoms that are potentially collinear with domains of frailty.
Risk tools	ASA
Outcome	Surgical complications
Results	ASA AUROC = 0. 0.626

Reference	Markovic 2018[105]
Study type	Retrospective chart review
Study sample	Pilot study included patients who were being prepared for one of the major non-cardiac surgeries under general anaesthesia. N=78

Reference	**Markovic 2018[105]**
Inclusion criteria	Patients who were being prepared for extensive non-cardiac surgeries under general anaesthesia.
Exclusion criteria	Not reported
Risk tools	ASA NSQIP SORT
Outcome	Mortality
Results	Mortality

Test	Event rate (%)	C-statistic (95% CI)
ASA		0.669 (0.506-0.832)
NSQIP	14 (18%)	0.813 (0.702-0.924)
SORT		0.797 (0.671-0.924)

Comments	Population/surgery characteristics unclear

Reference	**Neary 2007[116]**
Study type	Prospective observational cohort study
Study sample	The study was performed at Gloucestershire Royal Hospital, a district hospital with 700 beds, and was approved by the Hospital Audit Committee. N=2349
Inclusion criteria	The study included a consecutive cohort of patients who needed non-elective, non-cardiac surgery in the 12 months from 1 July 2001.
Exclusion criteria	Not reported
Risk tools	P-POSSUM Surgical Risk Score
Outcome	Mortality (30d) Morbidity
Results	Expected/Observed mortality

Expected mortality risk	Observed mortality	
	P-POSSUM	SRS

Reference	Neary 2007[116]		
	<10	42 of 2075 (2·0)	83 of 2217 (3·7)
	10-20	22 of 96 (23)	34 of 92 (37)
	20-30	13 of 46 (28)	
	30-40	18 of 34 (52)	17 of 30 (57)
	40-50	7 of 28 (25)	
	50-60	8 of 22 (36)	3 of 5 (60)
	60-70	9 of 13 (69)	
	70-80	7 of 11 (64)	4 of 5 (80)
	80-90	5 of 11 (45)	
	90-10	10 of 13 (77)	
	c-statistic for P-POSSUM mortality = 0.90 (0.87–0.93) c-statistic for SRS mortality = 0.85 (0.82–0.89)		

Reference	Ngulube 2019[118]
Study type	Prospective observational cohort study
Study sample	The study included all consecutively admitted patients undergoing a variety of major general surgical operations at Parirenyatwa Group of Hospitals (PGH) and Harare Central Hospital (HCH) over a 9 month period from January to September of 2015.
Inclusion criteria	181 patients (123 males, 58 females) aged 18 years and above undergoing a major general surgical procedure as defined by the British United Provident Association, with timing ranging from elective to emergency were included. Mean age 47 (SD 18.7)
Exclusion criteria	Below the age of 18 years, if managed conservatively, if it was a day case or any procedure categorised as minor and any case falling outside the scope of general surgery. Those also excluded were patients with more than 1 missing result or those requiring admission into a critical care unit post operatively but failed because of shortage of beds and those operated on by surgical trainees with less than 2 years experience.
Risk tools	POSSUM P-POSSUM
Outcome	Mortality

Reference	Ngulube 2019[118]
	Morbidity
Results	c-statistic for POSSUM morbidity = 0.775 (p<0.0001). O:E ratio = 0.88 c-statistic for POSSUM mortality = 0.818 (p=0.818). O:E ratio = 0.74 c-statistic for P-POSSUM mortality = 0.814 (p<0.000) O:E ratio = 1.06

Reference	Organ 2002[120]
Study type	Prospective observational cohort study
Study sample	All surgical patients undergoing a surgical procedure admitted to the Royal Brisbane Hospital intensive care facility in 1999 were reviewed retrospectively.
Inclusion criteria	All surgical patients undergoing a surgical procedure.
Exclusion criteria	Patients on whom no operation had been performed were excluded. Those in the category of trauma were also excluded because trauma patients were excluded from Copeland's original data-set and subsequent studies. Neurosurgical patients were not evaluated in our study as most were treated in a separate unit not contributing to the ICF database.
Risk tools	P-POSSUM
Outcome	Mortality
Results	c-statistic for P-POSSUM mortality = 0.68 (0.57–0.78) O:E ratio = 0.68 Observed deaths: 28/229, Expected deaths: 49.9/225

Reference	Reis 2019[137]
Study type	Retrospective cohort study
Study sample	All patients admitted to surgical ICU after open vascular surgery from January 2006 to July 2013 in a large academic hospital.
Inclusion criteria	833 patients admitted to surgical ICU after open vascular surgery from January 2006 to July 2013
Exclusion criteria	None provided
Risk tools	POSSUM
Outcome	Hospital mortality

Reference	**Reis 2019[137]**
Results	POSSUM hospital mortality – observed/expected ration of 0.98 (43/44) and AUROC = (0.829)

Reference	**Rivard 2016[138]**
Study type	Retrospective chart review
Study sample	Patients who underwent laparotomy on the gynecologic oncology service at a single academic hospital from January 2009 to December 2013. N=1094
Inclusion criteria	Patients undergoing laparotomy
Exclusion criteria	Not reported
Risk tools	NSQIP
Outcome	Mortality Complications
Results	
Comments	Low overall mortality event rate.

Outcome	Event rate (%)	Odds ratio (95%CI)	C-statistic	Bier score
Mortality	9 (0.8)	1.18 (1.08-1.29)	0.851	0.007
Any complication	368 (33.6)	1.06 (1.04-1.08)	0.635	0.323

Reference	**Saafan 2019[142]**
Study type	Retrospective chart review
Study sample	Retrospective chart review of all perforated duodenal ulcer patients at Hamad general hospital (Doha) and Alwakra hospital in Qatar using the hospitals administrative electronic database between January 2014 and December 2017.
Inclusion criteria	152 patients presenting to ER and diagnosed and operated for perforated duodenal ulcers
Exclusion criteria	Patients < 14 years old or with perforated other organs were excluded
Risk tools	ASA score (≥ 3)
Outcome	30 day post op morbidity
Results	ASA 30 day morbidity – c-statistic =0.69 (0.55–0.83), p=0.009, sensitivity = 58.82% (36.01–78.39) and Specificity = 75.56 (67.66–82.03)

Reference	Saafan 2019[142]
Comments	Male patients only and includes patients over 14 years old. Low risk of bias

Reference	Shaker 2019[149]
Study type	Retrospective review of cohort
Study sample	Retrospective review ACS NSQIP database from 2009 to 2013
Inclusion criteria	200 gynaecologic oncology patients 70+ years older undergoing laparotomy.
Exclusion criteria	None provided
Risk tools	ACS NSQIP surgical risk calculator
Outcome	30 days any complications and mortality
Results	Mortality = OR 1.12 (1.01-1.25), P value= 0.03, C statistic = 0.811, Brier score = 0.015 Any complication = OR 1.06(1.02 – 1.09), P value = 0.003, C statistic = 0.652, Brier score = 0.237
Comments	Female patients only of 70+ years old

Reference	Sharrock 2017[151]			
Study type	Retrospective cohort study			
Study sample	Consecutive hospital admissions were recorded between 02 January 2014 and 25 August 2015. N=193			
Inclusion criteria	Patients were eligible if they were aged 70 or over when admitted as an emergency for abdominal surgery.			
Exclusion criteria	Not reported			
Risk tools	P-POSSUM ASA			
Outcome	Mortality			
Results	Mortality			
	Outcome	Correlation	c-statistic	P value
	P-POSSUM			
	Correlation with days to death	-0.28		0.21
	Mortality		0.784	<0.001

Reference	Sharrock 2017[151]		
	ASA		
	Mortality	0.771	<0.001

Reference	Simpson 2018[155]
Study type	Retrospective review of cohort
Study sample	Retrospective review of the National Emergency Laparotomy Database between January 2014 to September 2016
Inclusion criteria	103 patients over 80 years old undergoing emergency laparotomy
Exclusion criteria	None provided
Risk tools	P-POSSUM
Outcome	Inpatient, 30 day and 90 day mortality
Results	Inpatient mortality = c-statistic 0.51, 30 day mortality = c-statistic 0.75, 90 day mortality c-statistic = 0.75
Comments	Patients over 80 years old.

Reference	Slim 2006[157]			
Study type	Prospective cohort study			
Study sample	Patients operated on for colorectal malignant or diverticular diseases, whether electively or on emergency basis, within a 4-month period. N=1421			
Inclusion criteria	Patients undergoing open or laparoscopic surgery (electively or on emergent basis) for colorectal cancers or diverticular disease.			
Exclusion criteria	Inflammatory bowel diseases or benign polyps, because both of those conditions require specific management, and other rare colorectal diseases (volvulus, chronic constipation, etc) because they involve specific therapeutic aspects.			
Risk tools	POSSUM P-POSSUM			
Outcome	Mortality			
Results	Mortality			
	Outcome	Predicted %	Observed % (95% CI)	c-statistic
	POSSUM	11.3	3.4 (2.5-4.44)	n/a
	P-POSSUM	4.7		0.82

Reference	Suresh 2019[161]
Study type	Retrospective chart review study
Study sample	All patients undergoing panniculectomy procedure at Duke University Hospital from 2005 to 2016
Inclusion criteria	264 patients who underwent panniculectomy from 2005 – 2016 were included
Exclusion criteria	None provided
Risk tools	NSQIP risk calculator
Outcome	30 day post-operative any complications
Results	NSQIP risk calculator any complication – c-statistic =0.6193

Reference	Sutton 2002[162]
Study type	Retrospective chart review study
Study sample	All patients admitted under the care of three surgeons between May 1997 and October 1999 were assessed. N=1946
Inclusion criteria	Patients transferred to the care of the firm while an inpatient and those whose care was on a shared basis with another firm were included.
Exclusion criteria	1351(31%) did not have an operation and were therefore excluded from further analysis
Risk tools	ASA Surgical Risk Scale
Outcome	Mortality
Results	AUC: ASA 0.93 (0.90–0.97) SRS 0.95 (0.93–0.97)

Reference	Teeuwen 2011[165]
Study type	Retrospective case-control study
Study sample	Patients older than 15 years undergoing colorectal resection between January 2003 and January 2008 in the Radboud University Nijmegen Medical Centre. N=734

Reference	Teeuwen 2011[165]
Inclusion criteria	Not reported
Exclusion criteria	Not reported
Risk tools	POSSUM P-POSSUM
Outcome	Mortality Morbidity
Results	

Outcome	Predicted %	Observed %
Mortality		
POSSUM	17	8.9
P-POSSUM	5.9	
Morbidity		
POSSUM	46	39.4

Reference	Teoh 2017[166]
Study type	A retrospective chart review
Study sample	All patients undergoing minimally invasive surgery on the gynecologic oncology service from January 1, 2009, to December 30, 2013. N=876
Inclusion criteria	Gynaecology oncology patients undergoing minimally invasive surgery
Exclusion criteria	Not reported
Risk tools	ACS NSQIP
Outcome	Mortality Any complication
Results	

Outcome	Event rate (%)	Odds ratio (95%CI)	C-statistic
Mortality	0	n/a	n/a
Any complication	100 (11.4)	1.08 (0.99-1.18)	0.57

Reference	Tominaga 2016[170]
Study type	Retrospective cohort
Study sample	Between January 2009 and August 2013, patients diagnosed with colorectal cancer and underwent curative colorectal resection at the Department of Surgical Oncology of Nagasaki University Graduate School of Biological Sciences. N=239
Inclusion criteria	Patients over 70 years of age diagnosed with colorectal cancer and underwent curative colorectal resection
Exclusion criteria	Not reported
Risk tools	E-PASS
Outcome	Mortality (Survival)
Results	

E-PASS score	Survival (%)	P value
<0.2	82.9	<0.001
≥0.2	54.9	

Reference	Tran Ba Loc 2010[171]
Study type	Retrospective cohort study
Study sample	From 2002 to 2004, elderly patients undergoing major colorectal surgery in France were enrolled. N=1186
Inclusion criteria	Patients, at least 65 years old, undergoing major colorectal surgery.
Exclusion criteria	Patients without POSSUM or follow-up data
Risk tools	POSSUM P-POSSUM Surgical risk score
Outcome	Mortality Morbidity
Results	

Outcome	O/E ratio	P value*	c-statistic (95% CI)
Morbidity			

Reference	Tran Ba Loc 2010[171]			
	POSSUM Morality	1.22	0.001	0.75 (0.70, 0.80)
	P-POSSUM	1.23	0.584	0.86 (0.81, 0.92)
	SRS	1.08	0.3	0.78 (0.70, 0.86)

Reference	Vather 2006[177]
Study type	Retrospective cohort study
Study sample	Consecutive patients undergoing a major colorectal operation between January 2002 and October 2005 at the participating hospital. N=308
Inclusion criteria	Patients undergoing a major colorectal operation
Exclusion criteria	Patients with incomplete data
Risk tools	POSSUM P-POSSUM
Outcome	Mortality
Results	Outcome: POSSUM — c-statistic: 0.789 — SE: 0.068 Outcome: P-POSSUM — c-statistic: 0.786 — SE: 0.068

Reference	Wang 2014[179]
Study type	Retrospective cohort
Study sample	Consecutive patients treated surgically in the study centre following a diagnosis of hilar cholangiocarcinoma. N=100
Inclusion criteria	Only patients with histologically confirmed cholangiocarcinoma were included.
Exclusion criteria	Patients who underwent liver transplantation were not included in this study
Risk tools	POSSUM P-POSSUM E-PASS

Reference	Wang 2014[179]
Outcome	Mortality Morbidity
Results	

Outcome	O/E ratio	P value*	c-statistic
Morbidity			
POSSUM	1.00 (52/52)	0.488	0.843 (0.768-0.919)
Morality			
POSSUM	1.11 (10/9)	0.520	0.863 (0.766-0.961)
P-POSSUM	1.00 (10/10)	0.721	0.848 (0.740-0.956)
E-PASS	1.00 (10/10)	0.671	0.842 (0.735-0.949)

* Goodness of fit

Reference	Wang 2017[182]
Study type	Retrospective cohort
Study sample	Geriatric patients who underwent lumbar surgery between January 2014 and December 2016 N=242
Inclusion criteria	Elderly patients (age>60 years) with isolated spinal stenosis who underwent conventional laminectomy without fusion.
Exclusion criteria	Age <60 y Lumbar spondylolisthesis Not treated with conservative therapy for 3 mo Glasgow Coma scale score <3. Conventional decompressive laminecomy with fusion.
Risk tools	ACS-NSQIP
Outcome	Mortality Any complication
Results	c-statistic:

Outcome	Event rate (%)	C-statistic (95% CI)
Mortality	2 (0.8)	0.972 (0.929, 1.000)
Any complication	106 (43.8)	0.683 (0.615,0.751)

<table>
<tr><td>Reference</td><td>Wani 2005[183]</td></tr>
<tr><td>Study type</td><td>Retrospective cohort study</td></tr>
<tr><td>Study sample</td><td>Patients of diagnosed calcular disease of biliary tract over an 18 month period.
N=500</td></tr>
<tr><td>Inclusion criteria</td><td>The types of surgeries performed were categorized into three groups :
TYPE-I: Cholecystectomy/ Cholecystostomy only.
TYPE.II: Cholecystectomy with CBD exploration with T tube drainage,
TYPE-III: Cholecystectomy with papillotomy/sphincteropeasty/choledochoduodenostomy or choledocho jujenostomy.</td></tr>
<tr><td>Exclusion criteria</td><td>All the operations performed were open procedures and no laparoscopic operation is included.</td></tr>
<tr><td>Risk tools</td><td>POSSUM scoring system</td></tr>
<tr><td>Outcome</td><td>Morbidity
Mortality</td></tr>
<tr><td>Results</td><td>Predictive accuracy
<table>
<tr><td>Outcome</td><td>Sensitivity</td><td>Specificity</td></tr>
<tr><td>Mortality</td><td>62%</td><td>94%</td></tr>
<tr><td>Morbidity</td><td>60%</td><td>99%</td></tr>
</table>
Correlation
<table>
<tr><td>Predicted rate (%)</td><td>Observed rate
Mortality (%)</td><td>
Morbidity (%)</td></tr>
<tr><td>80</td><td>96</td><td>99</td></tr>
<tr><td>70</td><td>84</td><td>87</td></tr>
<tr><td>60</td><td>72</td><td>74</td></tr>
<tr><td>50</td><td>60</td><td>62</td></tr>
<tr><td>40</td><td>48</td><td>50</td></tr>
<tr><td>30</td><td>36</td><td>37</td></tr>
<tr><td>20</td><td>24</td><td>25</td></tr>
<tr><td>10</td><td>12</td><td>12</td></tr>
</table>
Correlation between predicted and observed rates is significant, p<0.05</td></tr>
</table>

Reference	**Wolters 2006[186]**
Study type	Prospective cohort study
Study sample	From May 1996 to June 2000, patients meeting the inclusion criteria were included for analysis. N=107
Inclusion criteria	patients received an aorto-bi-iliac or an aroto-bifemoral graft due to arterial occlusive disease
Exclusion criteria	Not reported.
Risk tools	POSSUM ASA
Outcome	Mortality Morbidity
Results	Outcome: c-statistic Morbidity POSSUM: 0.561 ASA: 0.518 Morality POSSUM: 0.471 ASA: 0.590

Reference	**Yap 2018[187]**
Study type	Single-centre prospective validation cohort study.
Study sample	Patients admitted to St Luke's Medical Center-Quezon City from January 2016 to March 2017. N=424
Inclusion criteria	Patients aged 19 years and older admitted for preoperative evaluation and cardiopulmonary risk stratification before non-cardiac surgery. Surgeries eligible for inclusion included open, laparoscopic and percutaneous abdominal surgeries, anorectal surgeries, breast surgeries, thyroid surgeries, head and neck surgeries, orthopaedic surgeries, urologic surgeries, excision and incision biopsies of superficial masses, wound debridement, vascular surgeries, and neurosurgical procedures.

Reference	Yap 2018[187]
Exclusion criteria	Ophthalmologic and endoscopic procedures were excluded.
Risk tools	ACS NSQIP risk calculator
Outcome	Mortality Morbidity
Results	

Outcome	Total events	c-statistic
Mortality	12 (3%)	0.89
Morbidity	60 (14%)	0.88

Reference	Zattoni 2019[189]
Study type	Prospective observational study
Study sample	All patients 70 years or older consecutively admitted to the emergency unit with an urgent need for abdominal surgery between December 2-15 and May 2016
Inclusion criteria	110 patients over 70 years old undergoing emergency abdominal surgery under general anaesthesia were enrolled
Exclusion criteria	Patients who underwent only medical management or who were operated on for vascular, thoracic, gynaecological or urological conditions were excluded
Risk tools	Age adjusted CCI ASA score
Outcome	30 day mortality
Results	Age adjusted CCI ≥6 30 day mortality– sensitivity = 95.2% (76.2-99.9), specificity = 48.3% (37.6-59.2) c-statistic = 71.8 ASA ≥ 4 30 day mortality - sensitivity = 57.1% (34-78.2), specificity = 82% (72.5-89.4) c-statistic = 69.6 Age adjusted CCI ≥6 90 day mortality – sensitivity = 96% (79.6-99.9), specificity = 50.6% (39.5-61.6) c-statistic = 73.3 ASA ≥ 4 90 day mortality - sensitivity = 52% (31.3-72.2), specificity = 82.4% (72.6-89.8) c-statistic = 67.2

Appendix E: PROBAST checklist

Study	Overall rating	Model recalibrated or likely that calibration not needed?	Relevant performance measures?	Complexities in data accounted for?	Non-binary predictors handled appropriately?	Missing data handled appropriately?	All enrolled included in analysis?	Time interval between baseline and outcome appropriate?	Reasonable number of outcome events?	Outcome determined without knowledge of predictor information?	Outcome defined in same way for all?	Predictors excluded from outcome definition?	Pre-specified outcome used?	All relevant predictors analysed?	Predictors all available at time model meant to be used?	Predictor assessments made without knowledge of outcome data?	Predictors defined/ass' d same for all?	Similar health across participants?	Appropriate inc and exc?	Appropriate data sources?
Baker 2018[11]	Serious	Y	Y	Y	n/a	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Bennett-Guerrero 2003[14]	Low	Y	Y	Y	n/a	n/a	Y	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Blair 2018[17]	Serious	Y	Y	Y	n/a	n/a	Y	Y	Y	U	Y	Y	Y	Y	Y	U	Y	Y	Y	Y
Bodea 2018[18]	Serious	Y	Y	Y	n/a	n/a	Y	U	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y
Bonventura 2019[20]	Serious	Y	Y	Y	n/a	n/a	Y	U	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y
Boyd 2019[22]	Serious	Y	Y	n/a	n/a	U	U	U	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y

Overall rating	Serious	Serious	Serious	Serious	Very serious	Serious	Low	Low
Model recalibrated or likely that calibration not needed?	Y	Y	Y	Y	N	Y	Y	Y
Relevant performance measures?	Y	Y	Y	Y	Y	Y	Y	Y
Complexities in data accounted for?	Y	Y	n/a	n/a	Y	n/a	n/a	n/a
Non-binary predictors handled appropriately?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Missing data handled appropriately?	Y	n/a	Y	n/a	N	Y	Y	Y
All enrolled included in analysis?	Y	Y	Y	Y	N	Y	Y	Y
Time interval between baseline and outcome appropriate?	Y	U	Y	Y	Y	Y	Y	Y
Reasonable number of outcome events?	Y	Y	Y	Y	Y	N	Y	Y
Outcome determined without knowledge of predictor information?	Y	Y	Y	Y	Y	Y	Y	Y
Outcome defined in same way for all?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors excluded from outcome definition?	Y	Y	Y	Y	Y	Y	Y	Y
Pre-specified outcome used?	Y	Y	Y	Y	Y	Y	Y	Y
All relevant predictors analysed?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors all available at time model meant to be used?	U	Y	U	Y	Y	Y	Y	Y
Predictor assessments made without knowledge of outcome data?	U	Y	U	U	U	Y	U	U
Predictors defined/ass' d same for all?	Y	Y	Y	Y	Y	Y	Y	Y
Similar health across participants?	Y	Y	Y	Y	Y	Y	Y	Y
Appropriate inc and exc?	Y	Y	Y	Y	Y	Y	Y	Y
Appropriate data sources?	Y	Y	Y	Y	Y	Y	Y	Y
Study	Bronheim 2018[24]	Brooks 2005[25]	Bulow 2019[27]	Cengiz 2014[32]	Chun 2018[33]	Cologne 2015[37]	Dahlke 2014[39]	Donati 2004[43]

Overall rating	Low	Serious	Low	Low	Serious	Very serious	Low	Serious
Model recalibrated or likely that calibration not needed?	Y	Y	Y	Y	Y		Y	Y
Relevant performance measures?	Y	Y	Y	Y	Y	N	Y	Y
Complexities in data accounted for?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Non-binary predictors handled appropriately?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Missing data handled appropriately?	Y	Y	Y	Y	Y	Y	Y	Y
All enrolled included in analysis?	Y	Y	Y	Y	Y	Y	Y	Y
Time interval between baseline and outcome appropriate?	Y	U	Y	Y	Y	Y	Y	Y
Reasonable number of outcome events?	Y	Y	Y	Y	N	U	Y	Y
Outcome determined without knowledge of predictor information?	Y	Y	Y	Y	Y	Y	Y	Y
Outcome defined in same way for all?	Y	Y	Y	Y	Y	Y	Y	N
Predictors excluded from outcome definition?	Y	Y	Y	Y	Y	Y	Y	Y
Pre-specified outcome used?	Y	Y	Y	Y	Y	Y	Y	Y
All relevant predictors analysed?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors all available at time model meant to be used?	Y	Y	Y	Y	Y	Y	Y	Y
Predictor assessments made without knowledge of outcome data?	U	U	U	U	U	U	U	U
Predictors defined/ass' d same for all?	Y	Y	Y	Y	Y	Y	Y	Y
Similar health across participants?	Y	Y	Y	Y	Y	Y	Y	Y
Appropriate inc and exc?	Y	Y	Y	Y	Y	Y	Y	Y
Appropriate data sources?	Y	Y	Y	Y	Y	Y	Y	Y
Study	Dutta 2011[45]	Egberts 2011[47]	Egberts 2011[48]	Filip 2014[51]	Fu 2019[54]	Goffi 1999[56]	Golan 2018[57]	Haga 2011[59]

Overall rating	Serious	Serious	Very serious	Serious	Serious	Very serious	Low	Very serious
Model recalibrated or likely that calibration not needed?	Y	Y	Y	Y	Y	Y	Y	Y
Relevant performance measures?	Y	Y	Y	Y	Y	Y	Y	Y
Complexities in data accounted for?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Non-binary predictors handled appropriately?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Missing data handled appropriately?	Y	Y	Y	Y	Y	Y	Y	Y
All enrolled included in analysis?	Y	Y	Y	Y	Y	Y	Y	Y
Time interval between baseline and outcome appropriate?	Y	U	U	Y	Y	Y	Y	Y
Reasonable number of outcome events?	N	Y	N	N	N	N	Y	N
Outcome determined without knowledge of predictor information?	Y	Y	Y	Y	Y	Y	Y	Y
Outcome defined in same way for all?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors excluded from outcome definition?	Y	Y	Y	Y	Y	Y	Y	Y
Pre-specified outcome used?	Y	Y	Y	Y	Y	Y	Y	Y
All relevant predictors analysed?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors all available at time model meant to be used?	Y	Y	Y	Y	Y	Y	Y	Y
Predictor assessments made without knowledge of outcome data?	U	U	U	Y	Y	U	U	U
Predictors defined/ass' d same for all?	Y	Y	Y	Y	Y	Y	Y	Y
Similar health across participants?	Y	Y	Y	Y	Y	Y	Y	Y
Appropriate inc and exc?	Y	Y	Y	Y	U	U	Y	U
Appropriate data sources?	Y	Y	Y	Y	Y	Y	Y	Y
Study	Hightower 2010[61]	Hirose 2014[62]	Hirose 2015[63]	Hobson 2007[65]	Huisman 2014[69]	Igari 2013[70]	Jones 1992[74]	Katlic 2019[78]

Overall rating	Very serious	Very serious	Very serious	Serious	Serious	Serious	Serious	Serious
Model recalibrated or likely that calibration not needed?	Y	Y	Y	Y	Y	Y	Y	Y
Relevant performance measures?	Y	Y	Y	Y	Y	Y	Y	Y
Complexities in data accounted for?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Non-binary predictors handled appropriately?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Missing data handled appropriately?	U	Y	U	U	Y	Y	Y	Y
All enrolled included in analysis?	Y	Y	N	Y	Y	Y	Y	Y
Time interval between baseline and outcome appropriate?	U	U	U	Y	Y	Y	U	Y
Reasonable number of outcome events?	N	N	N	Y	N	N	Y	Y
Outcome determined without knowledge of predictor information?	Y	Y	Y	Y	Y	Y	Y	Y
Outcome defined in same way for all?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors excluded from outcome definition?	Y	Y	Y	Y	Y	Y	Y	Y
Pre-specified outcome used?	Y	Y	Y	Y	Y	Y	Y	Y
All relevant predictors analysed?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors all available at time model meant to be used?	Y	Y	Y	Y	Y	Y	Y	Y
Predictor assessments made without knowledge of outcome data?	U	U	U	U	U	Y	Y	Y
Predictors defined/ass' d same for all?	Y	Y	Y	Y	Y	Y	Y	Y
Similar health across participants?	Y	Y	Y	Y	Y	Y	N	Y
Appropriate inc and exc?	Y	Y	Y	U	Y	U	Y	U
Appropriate data sources?	Y	Y	Y	Y	Y	Y	Y	Y
Study	Kim 2018[84]	Kong 2013[88]	Kong 2015[89]	Kwok 2011[93]	Lakomkin 2018[94]	Lima 2019[101]	Markovic 2018[105]	Moonesinghe 2013[110]

Overall rating	Serious	Serious	Low	Very serious	Serious	Very serious	Very serious	Very serious
Model recalibrated or likely that calibration not needed?	Y	Y	Y	Y	Y	Y	Y	Y
Relevant performance measures?	Y	Y	Y	Y	Y	Y	Y	Y
Complexities in data accounted for?	n/a	n/a	n/a	n/s	n/a	n/a	U	n/a
Non-binary predictors handled appropriately?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Missing data handled appropriately?	Y	Y	Y	Y	Y	Y	Y	U
All enrolled included in analysis?	Y	Y	Y	Y	Y	Y	N	U
Time interval between baseline and outcome appropriate?	Y	Y	Y	U	Y	Y	Y	U
Reasonable number of outcome events?	Y	Y	Y	N	N	N	N	Y
Outcome determined without knowledge of predictor information?	Y	Y	Y	Y	Y	Y	Y	Y
Outcome defined in same way for all?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors excluded from outcome definition?	Y	Y	Y	Y	Y	Y	Y	Y
Pre-specified outcome used?	Y	Y	Y	Y	Y	Y	Y	Y
All relevant predictors analysed?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors all available at time model meant to be used?	Y	Y	Y	Y	Y	Y	Y	Y
Predictor assessments made without knowledge of outcome data?	U	Y	U	U	U	U	U	U
Predictors defined/ass' d same for all?	Y	Y	Y	Y	Y	Y	Y	Y
Similar health across participants?	Y	N	Y	Y	Y	Y	Y	Y
Appropriate inc and exc?	U	Y	Y	Y	Y	U	U	U
Appropriate data sources?	Y	Y	Y	Y	Y	Y	Y	Y
Study	Neary 2007[116]	Ngulube 2019[118]	Organ 2002[120]	Reis 2019[137]	Rivard 2016[138]	Saafan 2019[142]	Shaker 2019[149]	Sharrock 2017[151]

Overall rating	Serious	Very serious	Low	Serious	Serious	Serious	Very serious	Very serious
Model recalibrated or likely that calibration not needed?	Y	Y	Y	Y	Y	Y	Y	Y
Relevant performance measures?	Y	Y	Y	Y	Y	Y	Y	Y
Complexities in data accounted for?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Non-binary predictors handled appropriately?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Missing data handled appropriately?	Y	Y	Y	Y	Y	Y	Y	Y
All enrolled included in analysis?	Y	N	Y	Y	Y	Y	Y	N
Time interval between baseline and outcome appropriate?	Y	U	Y	Y	Y	Y	Y	Y
Reasonable number of outcome events?	Y	N	Y	Y	N	N	N	N
Outcome determined without knowledge of predictor information?	Y	Y	Y	Y	Y	Y	Y	Y
Outcome defined in same way for all?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors excluded from outcome definition?	Y	Y	Y	Y	Y	Y	Y	Y
Pre-specified outcome used?	Y	Y	Y	Y	Y	Y	Y	Y
All relevant predictors analysed?	Y	Y	Y	Y	Y	Y	Y	Y
Predictors all available at time model meant to be used?	Y	Y	Y	Y	Y	Y	Y	Y
Predictor assessments made without knowledge of outcome data?	U	Y	U	Y	U	U	U	Y
Predictors defined/ass' d same for all?	Y	Y	Y	Y	Y	Y	Y	Y
Similar health across participants?	Y	Y	Y	U	Y	Y	N	Y
Appropriate inc and exc?	U	Y	Y	Y	Y	Y	U	Y
Appropriate data sources?	Y	Y	Y	Y	Y	Y	Y	Y
Study	Simpson 2018[155]	Slim 2006[157]	Suresh 2019[161]	Sutton 2002[162]	Teeuwen 2011[165]	Teoh 2017[166]	Tominaga 2016[170]	Tran Ba Loc 2010[171]

Overall rating	Serious	Serious	Serious	Very serious	Serious	Serious	Low
Model recalibrated or likely that calibration not needed?	Y	Y	Y	Y	Y	Y	Y
Relevant performance measures?	Y	Y	Y	Y	Y	Y	Y
Complexities in data accounted for?	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Non-binary predictors handled appropriately?	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Missing data handled appropriately?	Y	Y	Y	U	Y	Y	Y
All enrolled included in analysis?	Y	Y	Y	U	Y	Y	Y
Time interval between baseline and outcome appropriate?	U	U	Y	Y	U	U	Y
Reasonable number of outcome events?	N	Y	N	N	N	N	Y
Outcome determined without knowledge of predictor information?	Y	Y	Y	Y	Y	Y	Y
Outcome defined in same way for all?	Y	Y	Y	Y	Y	Y	Y
Predictors excluded from outcome definition?	Y	Y	Y	Y	Y	Y	Y
Pre-specified outcome used?	Y	Y	Y	Y	Y	Y	Y
All relevant predictors analysed?	Y	Y	Y	Y	Y	Y	Y
Predictors all available at time model meant to be used?	Y	Y	Y	Y	Y	Y	Y
Predictor assessments made without knowledge of outcome data?	U	U	U	Y	Y	Y	Y
Predictors defined/ass' d same for all?	Y	Y	Y	Y	Y	Y	Y
Similar health across participants?	Y	Y	Y	Y	Y	Y	Y
Appropriate inc and exc?	Y	U	U	U	Y	Y	Y
Appropriate data sources?	Y	Y	Y	Y	Y	Y	Y
Study	Vather 2006[177]	Wang 2014[179]	Wang 2017[182]	Wani 2005[183]	Wolters 2006[186]	Yap 2018[187]	Zattoni 2019[189]

Appendix F: C-statistic plots

Figure 2: POSSUM

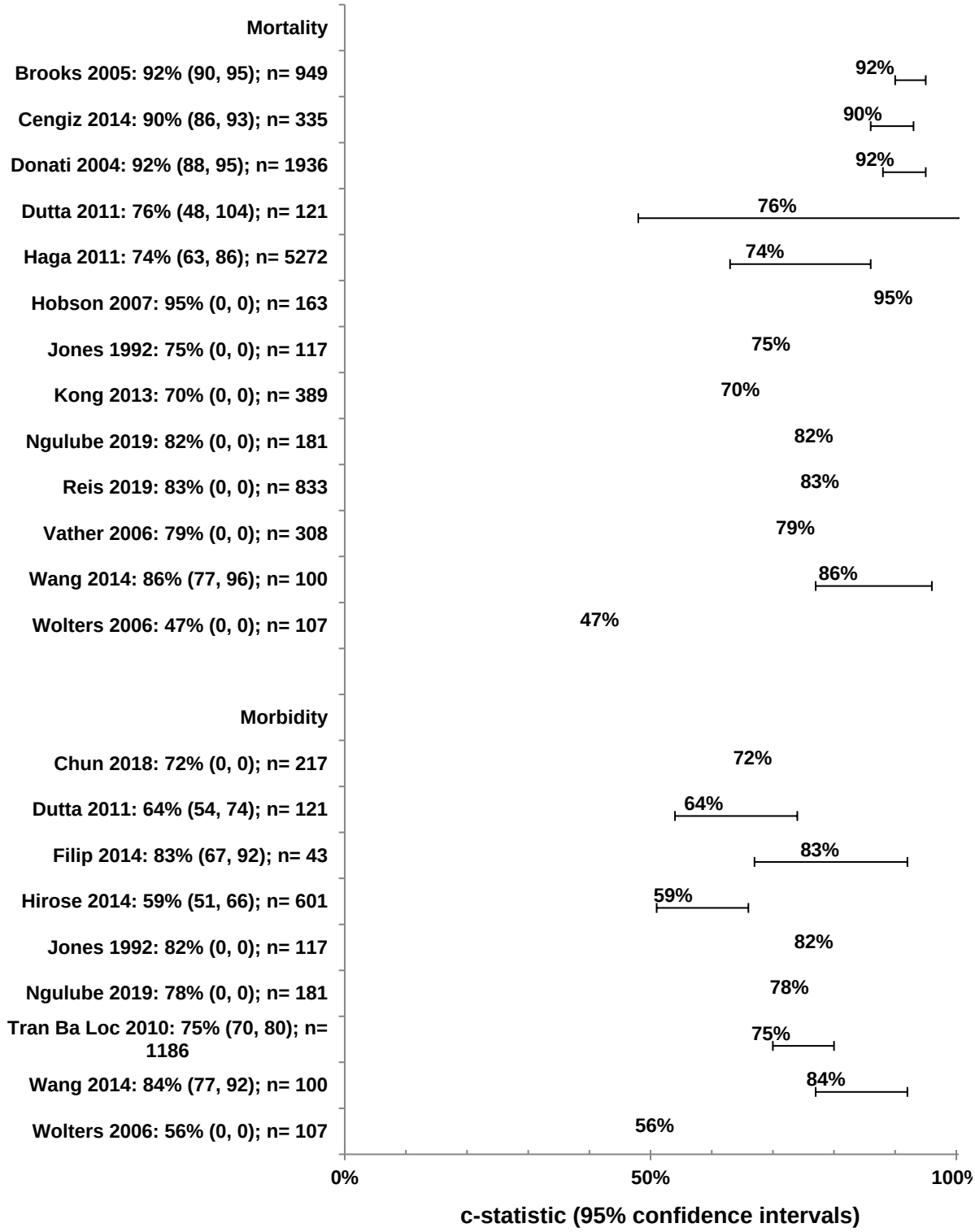


Figure 3: P-POSSUM

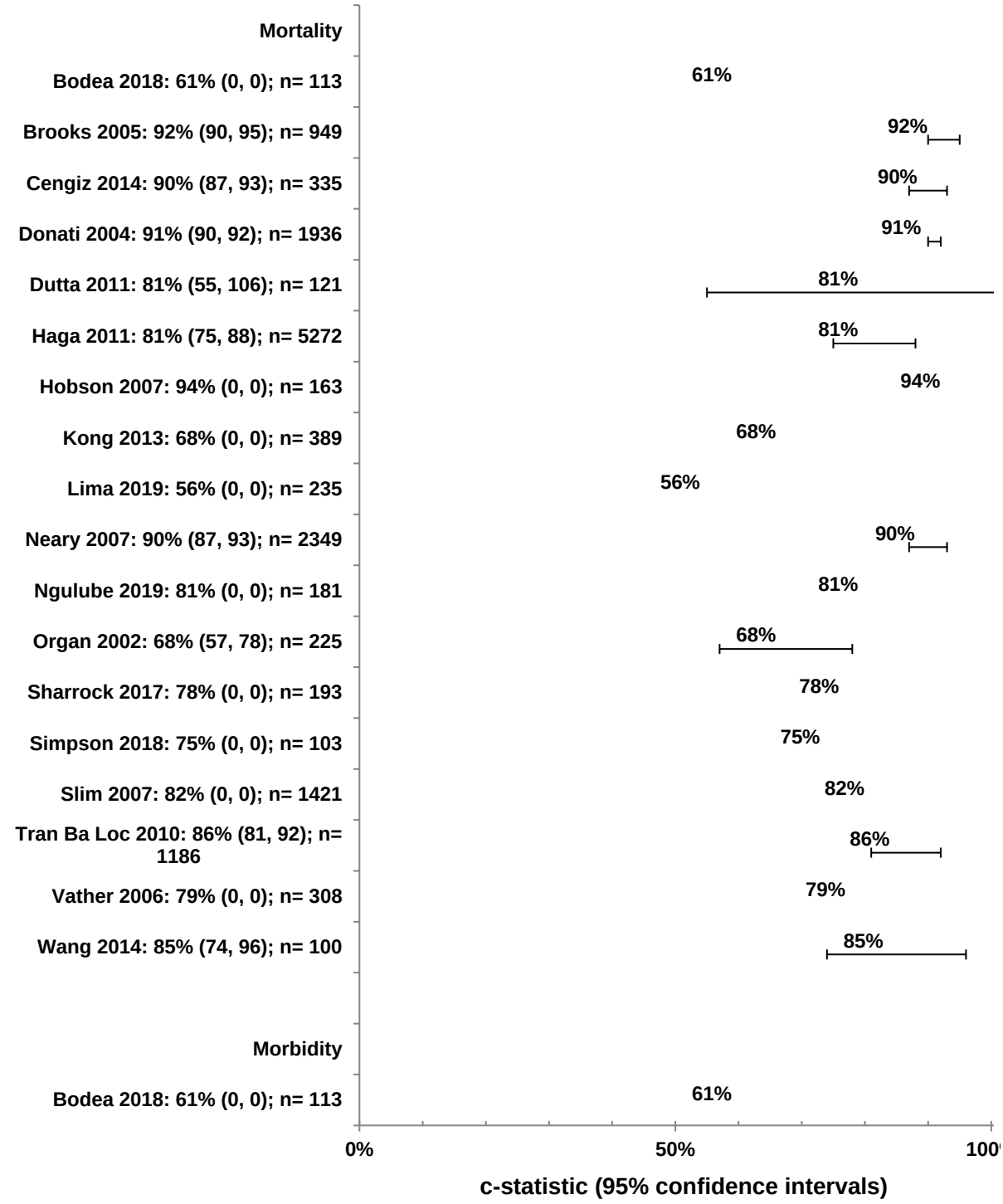


Figure 4: ACS NSQIP risk calculator

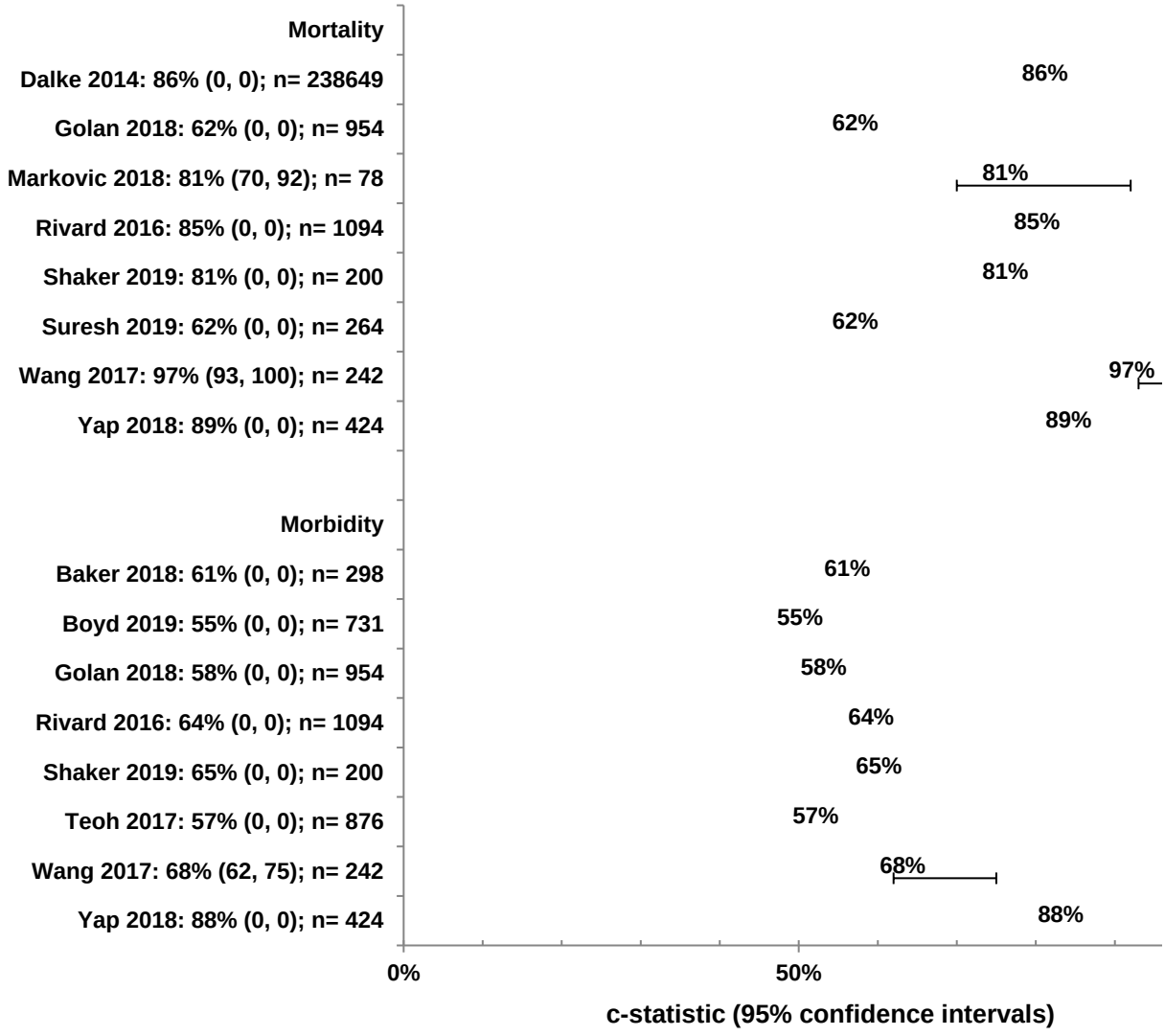


Figure 5: E-PASS

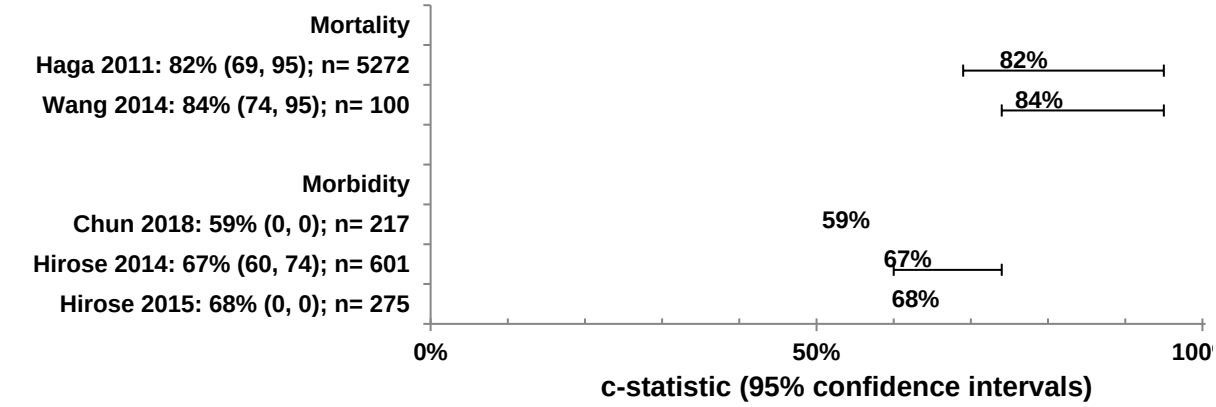


Figure 6: ASA

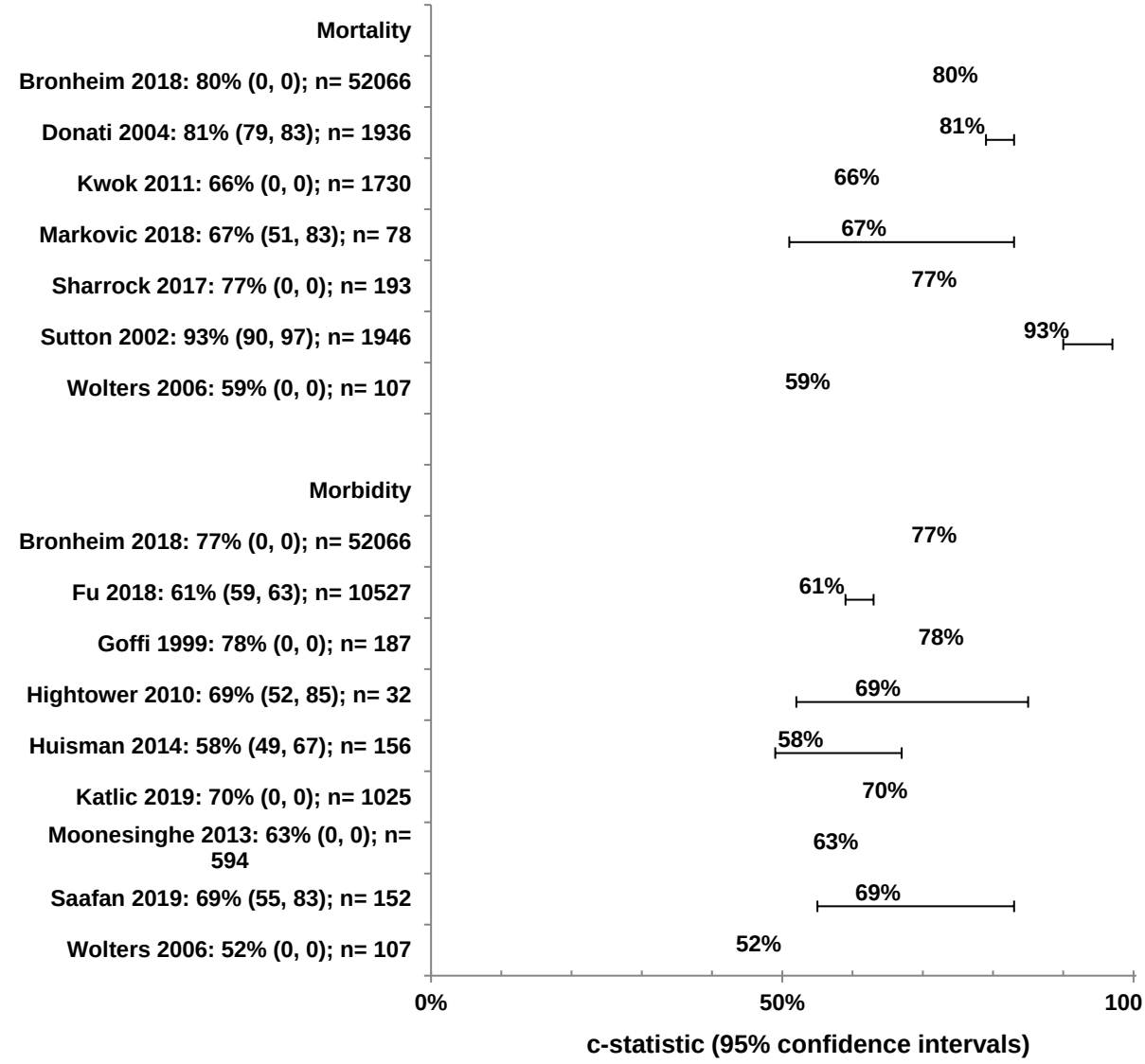


Figure 7: SORT

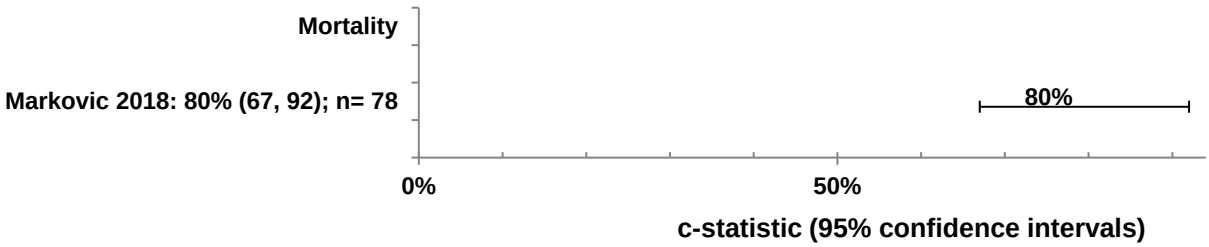


Figure 8: SRS

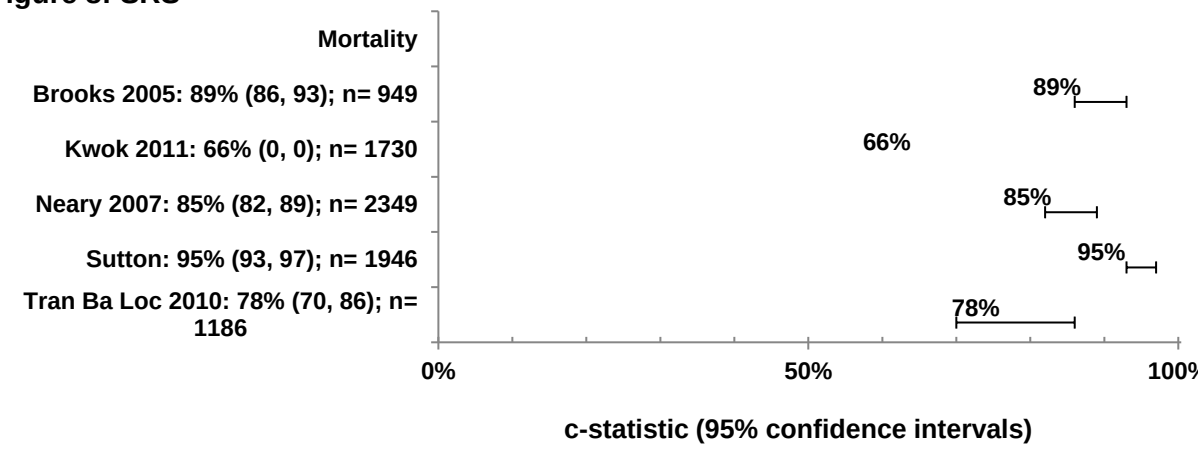
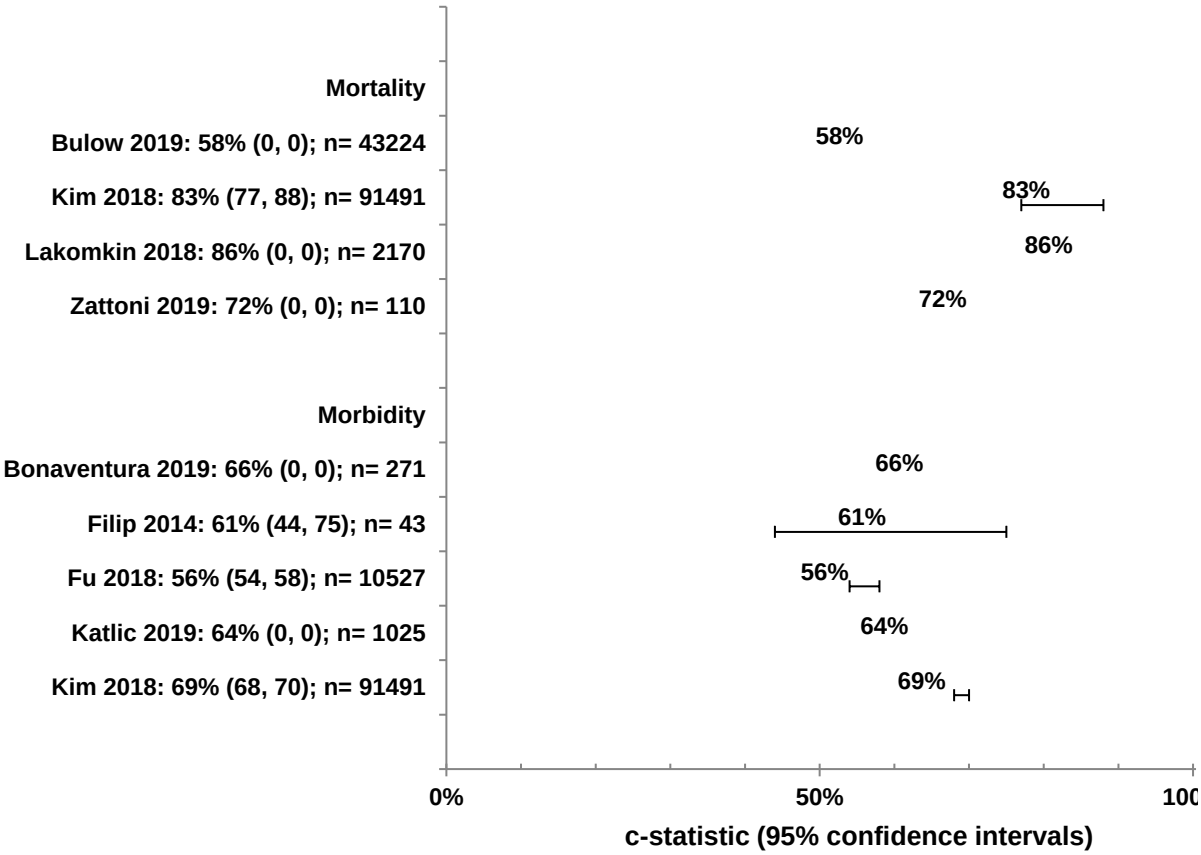


Figure 9: Charlson comorbidity index



Appendix G: Calibration plots

Figure 10: POSSUM

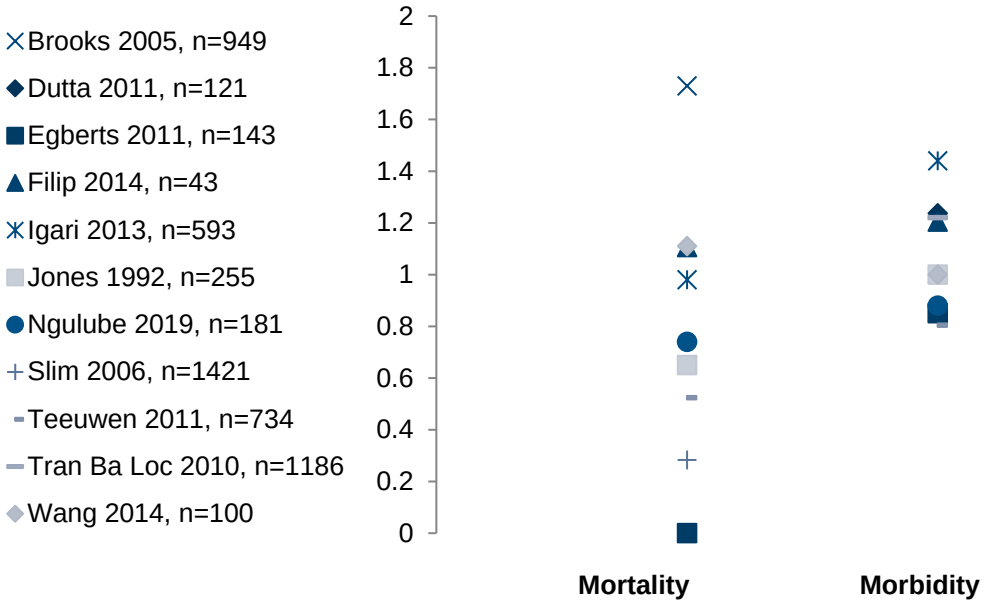


Figure 11: P-POSSUM

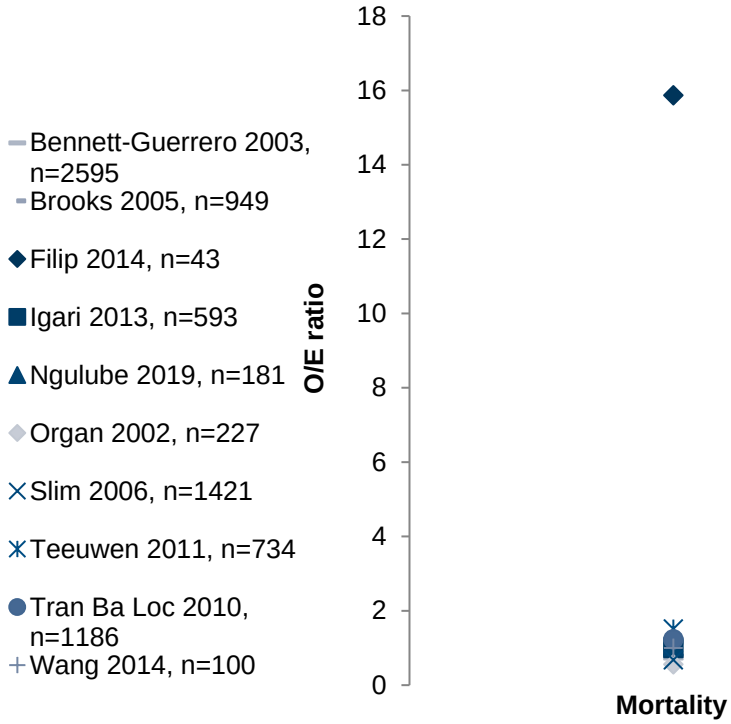


Figure 12: ACS NSQIP risk calculator

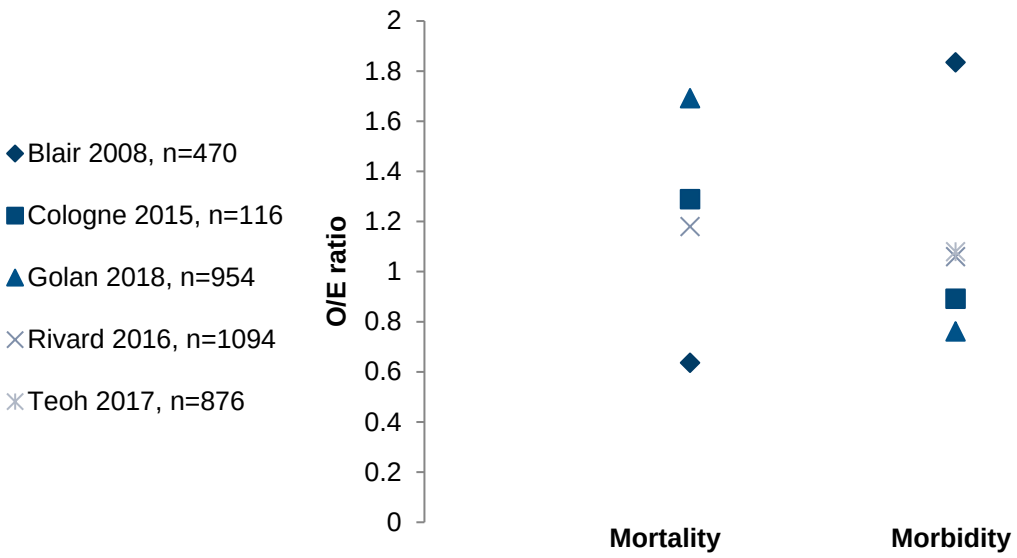


Figure 13: E-PASS

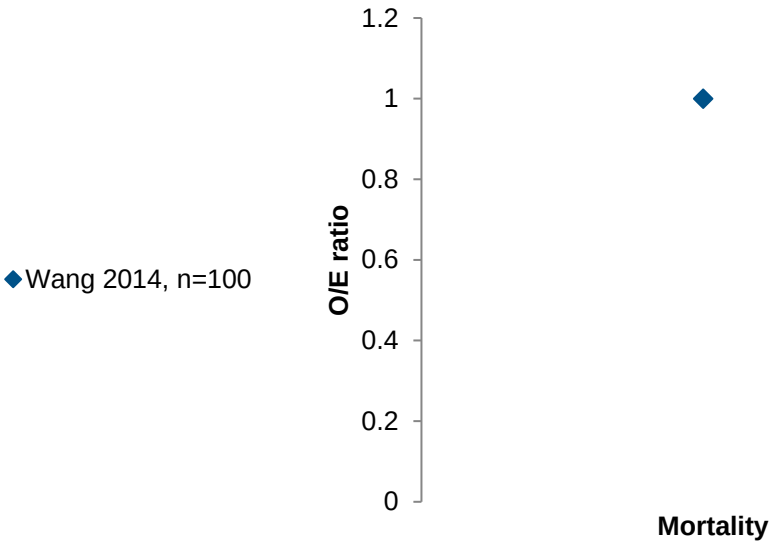


Figure 14: ASA

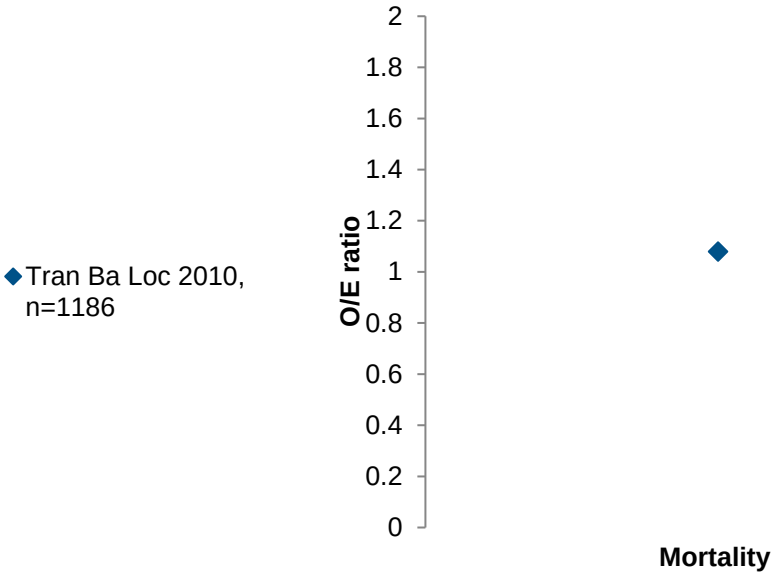
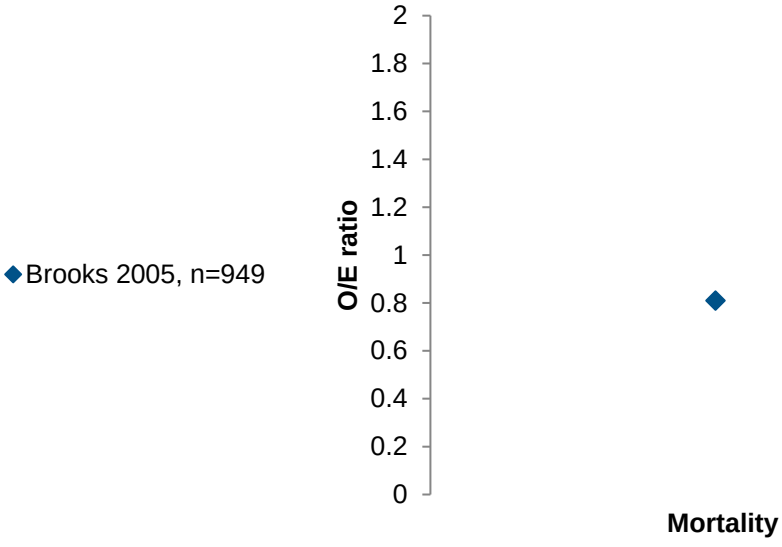
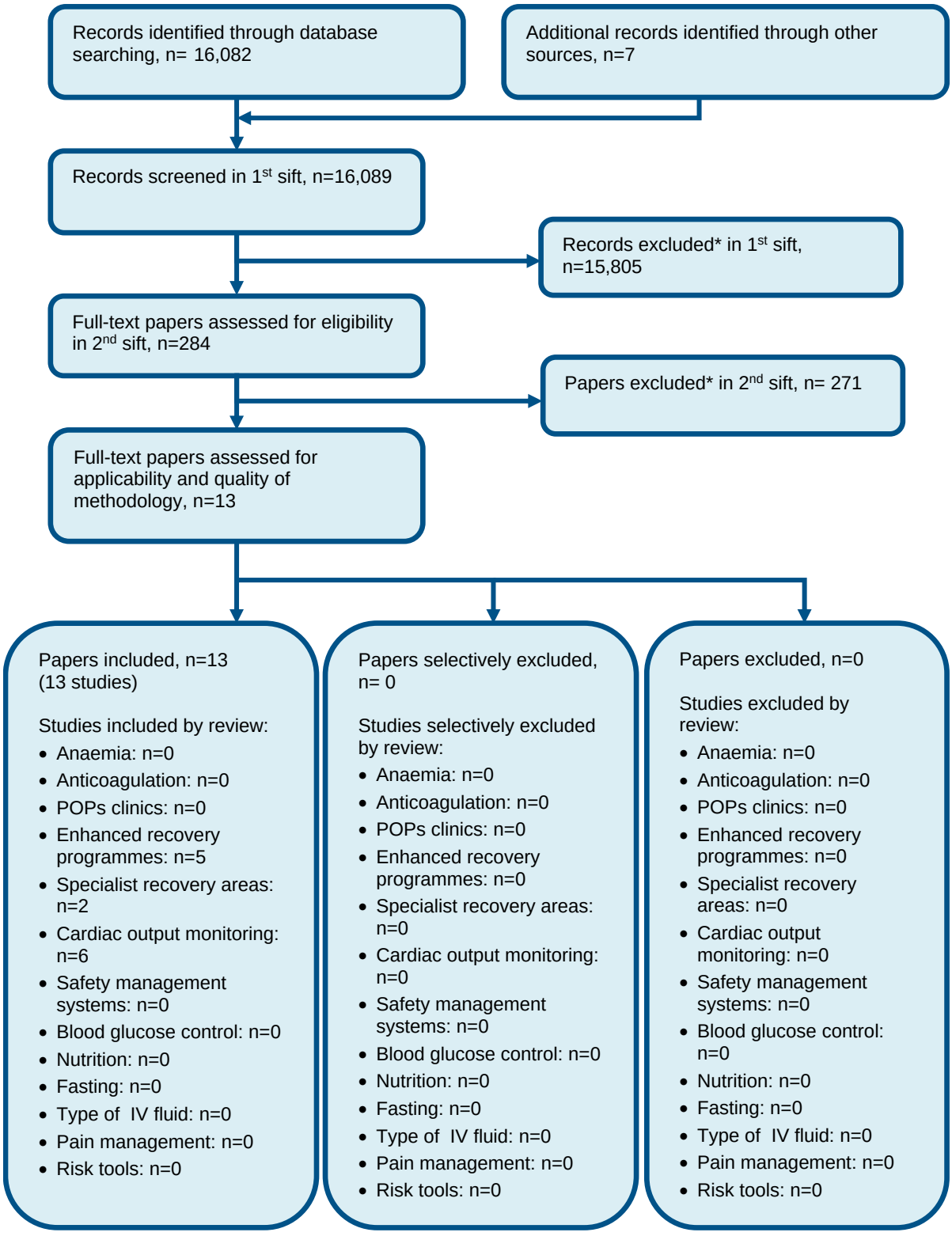


Figure 15: SRS



Appendix H: Health economic evidence selection

Figure 16: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix I: Health economic evidence tables

None.

Appendix J: Excluded studies

J.1 Excluded clinical studies

Table 8: Studies excluded from the clinical review

Reference	Reason for exclusion
Ahle 2019[1]	Inappropriate intervention
Al-Homoud 2004[2]	Inappropriate outcome data
Ali 2016[3]	Inappropriate outcome data
Amrock 201[44]	Inappropriate study design (internal validation)
Anderson 2012[5]	Inappropriate intervention
Anonymous 2018[6]	No usable data
Anonymous 2018[7]	Inappropriate intervention
Arakkal 2018[8]	Abstract only
Armstrong 2019[9]	Inappropriate outcome data
Arshad 2014[10]	Abstract only
Bartlett 2014[12]	Inappropriate intervention
Bekelis 2014[13]	Inappropriate intervention
Bihorac 2019[15]	Inappropriate intervention
Blair 2016[16]	Citation only
Bollschweiler 2005[19]	Inappropriate outcome data
Borja-Cacho 2010[21]	Inappropriate intervention
Brennan 2019[23]	Inappropriate intervention
Bryce 2012[26]	Inappropriate intervention
Burg 2019[28]	Inappropriate outcome data
Burgess 2017[29]	Inappropriate outcome data
Butterfield 2015[30]	Inappropriate intervention
Cao 2018[31]	Inappropriate outcome data
Chung 2017[34]	Inappropriate intervention
Cohen 2009[35]	Inappropriate intervention
Collard 2018[36]	Inappropriate outcome data
Cote 2019[38]	Inappropriate review population
de Castro 2009[40]	Inappropriate outcome data
Debinska 2011[41]	Inappropriate outcome data
DeLuzio 2016[42]	Inappropriate outcome data
Dunn 2019[44]	Inappropriate outcome data
Easterlin 2013[46]	Inappropriate intervention
Engin 2018[49]	Inappropriate outcome data
Farhat 2012[50]	Inappropriate outcome data
Ford 2015[52]	Abstract only
Fryer 2018[53]	Citation only
Gentry 2018[55]	Systematic review: references screened
Hacohen Solovitz 2018[58]	Inappropriate outcome data
Harris 2019[60]	Inappropriate intervention
Hirpara 2019[64]	Inappropriate outcome data

Reference	Reason for exclusion
Hoeks 2009[66]	Inappropriate intervention
Hoftman 2013[67]	Inappropriate outcome data
Huang 2017[68]	Inappropriate outcome data
Inoue 2019[71]	Inappropriate intervention
Jean 2016[72]	Inappropriate outcome data
Jensen 2019[73]	Inappropriate intervention
Kalender 2014[75]	Inappropriate intervention
Kapma 2017[76]	Inappropriate intervention
Karabulut 2003[77]	Inappropriate intervention
Kavanagh 2016[79]	Citation only
Kelly 2011[80]	Inappropriate intervention
Kertai 2003[81]	Inappropriate intervention
Khalfallah 2016[82]	Inappropriate intervention
Khene 2018[83]	Inappropriate outcome data
Klausing 2019[85]	Inappropriate outcome data
Klinceva 2006[86]	Inappropriate intervention
Knight 2009[87]	Citation only
Kong 2015[89]	Inappropriate Intervention
Kongkaewpaisan 2019[90]	Inappropriate outcome data
Kongwibulwut 2019[91]	Inappropriate outcome data
Kurki 2002[92]	Inappropriate intervention
Lam 2004[95]	Inappropriate outcome data
Laurent 2013[96]	Inappropriate intervention
Lazarides 1997[97]	Inappropriate outcome data
Le Manach 2016[98]	Inappropriate intervention
Lee 1999[100]	Inappropriate intervention
Lee 2019[99]	Systematic review: references screened
Lindroth 2019[102]	Inappropriate intervention
Malik 2019[103]	Inappropriate outcome data
Marconi 2018[104]	Inappropriate intervention
Marufu 2015[106]	Inappropriate outcome data
Mayhew 2019[107]	Systematic review: references screened
Meguid 2016[108]	Inappropriate intervention
Meguid 2016[109]	Inappropriate intervention
Moonesinghe 2013[110]	Systematic review: references screened
Nag 2015[111]	Inappropriate study design
Nagashima 2005[112]	Inappropriate outcome data
Nashef 1999[114]	Inappropriate intervention
Nashef 2002[113]	Inappropriate intervention
Nesi 2004[117]	Inappropriate intervention
O'Brien 2009[119]	Inappropriate intervention
Parmar 2010[121]	Inappropriate outcome data
Patila 2006[122]	Inappropriate intervention
Patterson 2008[123]	Systematic review: references screened
Paul 2007[124]	Inappropriate intervention

Reference	Reason for exclusion
Pavone 2018[125]	Inappropriate outcome data
Perkins 2004[127]	Inappropriate intervention
Perkins 2006[126]	Inappropriate intervention
Pillai 2015[128]	Inappropriate intervention
Pinna-Pintor 2002[129]	Inappropriate intervention
Pliam 1997[130]	Inappropriate intervention
Prabakaran 2019[131]	Inappropriate intervention
Ranucci 2010[132]	Inappropriate intervention
Ranucci 2016[133]	Inappropriate intervention
Ranucci 2018[134]	Inappropriate intervention
Rasmussen 2018[135]	Inappropriate outcome data
Raymond 2019[136]	Inappropriate outcome data
Rix 2007[139]	Systematic review: references screened
Roxas 2017[140]	Abstract only
Ryan 2018[141]	Inappropriate outcome data
Sankar 2019[143]	Inappropriate outcome data
Saunders 2015[144]	Citation only
Schneider 2016[145]	Inappropriate outcome data
Sfoungaristos 2015[147]	Inappropriate intervention
Sfoungaristos 2016[146]	Inappropriate intervention
Shah 2012[148]	Inappropriate intervention
Sharma 2019[150]	Inappropriate intervention
Shiba 2013[152]	Inappropriate outcome data
Silaschi 2015[153]	Inappropriate intervention
Silva Junior 2010[154]	Inappropriate review population
Singh 2018[156]	Inappropriate intervention
Sobotka 2018[158]	Inappropriate intervention
Srilata 2015[159]	Inappropriate intervention
Strilchuk 2018[160]	Inappropriate outcome data
Suzuki 2018[163]	Inappropriate outcome data
Tambyraja 2008[164]	Systematic review: references screened
ter Horst 2012[167]	Inappropriate Intervention
Thiels 2017[168]	Inappropriate intervention
Tian 2014[169]	Inappropriate intervention
Traven 2019[172]	Inappropriate intervention
Tsaousi 2015[173]	Inappropriate intervention
Tyritzis 2012[174]	Inappropriate intervention
Vaid 2012[175]	Inappropriate intervention
Varela Barca 2019[176]	Inappropriate intervention
Veeravagu 2017[178]	Inappropriate intervention
Wang 2015[181]	Inappropriate intervention
Wang 2015[180]	Inappropriate intervention
Wendt 2014[184]	Inappropriate intervention
Wingert 2016[185]	Inappropriate outcome data
Ye 2019[188]	Inappropriate outcome data

Reference	Reason for exclusion
Zhang 2014[190]	Inappropriate intervention
Zheng 2013[191]	Inappropriate intervention
Zugel 2011[192]	Inappropriate intervention

J.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 9: Studies excluded from the health economic review

Reference	Reason for exclusion
None.	