Search Strategy

Search date: July 21, 2017
Databases searched: Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946-Present, Embase Classic+Embase 1947 to 2017 July 20; Wiley Cochrane Library

Ovid MEDLINE(R), Embase

#	Searches	Results
1	exp Colitis, Ulcerative/ use ppez	31384
2	exp ulcerative colitis/ use emczd	63427
3	(ulcerative adj2 colitis).ti,ab.	84200
4	exp Proctitis/	8719
5	proctitis.ti,ab.	6262
6	or/1-5	118527
7	exp Mesalamine/ use ppez	3194
8	exp mesalazine/ use emczd	15415
9	(Mesalazine or mesalamine or 5-aminosalicylic acid or 5-ASA or Asacol or Pentasa or Salofalk or Mezavant or mesasal or Canasa or Rowasa or Delzicol or Lialda or Apriso).mp.	21711
10	exp Sulfasalazine/ use ppez	4019
11	exp salazosulfapyridine/ use emczd	22776
12	(Sulfasalazine or Azulfidine or Salazopyrin or sulfazine).mp.	11184
13	exp balsalazide/ use emczd	862
14	(olsalazine or olsalazide or Dipentum or balsalazide or Colazol or Giazo).mp.	2160
15	exp Aminosalicylic Acids/ use ppez	9245
16	exp aminosalicylic acid/ use emczd	9872
17	(5-aminosalicylate or 5-asa).mp.	4571
18	exp Budesonide/	22394
19	(Cortiment or Uceris or cortifoam or budesonide).mp.	25644
20	exp Adrenal Cortex Hormones/ use ppez	378164
21	exp corticosteroid/ use emczd	902714
22	(Entocort or dexamethasone or hydrocortisone or Cortef or Cortenema or Proctofoam or methylprednisolone or prednisolone or Orapred or prednisone or Colocort).mp.	797408
23	exp Probiotics/ use ppez	12861
24	exp probiotic agent/ use emczd	25723
25	(probiotic* or lactobacill* or bifidobacteri* or streptococc* or Saccharomyces or Escherichia coli or e coli or VSL#3).mp.	1354448
26	exp Curcumin/	25621
27	(curcumin or tumeric).mp.	29836

28	exp Fecal Microbiota Transplantation/	1336
29	bacteriotherap*.ti,ab.	382
30	((fecal or stool) adj3 transplant*).ti,ab.	2311
31	or/7-30	2748464
32	6 and 31	27971
33	animals/ not (humans/ and animals/)	5708458
34	32 not 33	27544
35	(Meta Analysis or Controlled Clinical Trial).pt.	177710
36	Meta - Analysis/ use ppez or Meta - Analysis as Topic/ use ppez or exp Technology Assessment, Biomedical/ use ppez	108619
37	Meta Analysis/ use emczd or "Meta Analysis (Topic)"/ use emczd or Biomedical Technology Assessment/ use emczd	175201
38	(meta analy* or metaanaly* or health technolog* assess*).mp.	367924
39	exp Randomized Controlled Trial/	933715
40	exp Random Allocation/ use ppez or exp Double - Blind Method/ use ppez or exp Control Groups/ use ppez or exp Placebos/ use ppez	254933
41	exp Randomization/ use emczd or exp RANDOM SAMPLE/ use emczd or Double Blind Procedure/ use emczd or exp Triple Blind Procedure/ use emczd or exp Control Group/ use emczd or exp PLACEBO/ use emczd	588123
42	(random* or RCT or RCTs or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	2542362
43	(((systematic* or methodologic*) adj3 (review* or overview*)) or pooled analysis or published studies or published literature or hand search* or handsearch* or medline or pub med or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	567921
44	or/35-41	1906409
45	34 and 44	3731
46	remove duplicates from 45	3087

Wiley Cochrane Library

ID Search Hits
#1 MeSH descriptor: [Colitis, Ulcerative] explode all trees 1074
#2 (ulcerative near/2 colitis):ti,ab 2214
#3 MeSH descriptor: [Proctitis] explode all trees 125
#4 proctitis:ti,ab 247
#5 #1 or #2 or #3 or #4 2547
#6 MeSH descriptor: [Mesalamine] explode all trees 441
#7 (Mesalazine or mesalamine or 5-aminosalicylic acid or 5-ASA or Asacol or Pentasa or Salofalk or Mezavant or mesasal or Canasa or Rowasa or Delzicol or Lialda or Apriso):ti,ab 853

#8 MeSH descriptor: [Sulfasalazine] explode all trees 416
#9 (Sulfasalazine or Azulfidine or Salazopyrin or sulfazine):ti,ab 501
#10 (olsalazine or olsalazide or Dipentum or balsalazide or Colazol or Giazo):ti,ab 112
#11 MeSH descriptor: [Aminosalicylic Acids] explode all trees 577
#12 (5-aminosalicylate or 5-asa):ti,ab 280
#13 MeSH descriptor: [Budesonide] explode all trees 1317
#14 (Cortiment or Uceris or cortifoam or budesonide):ti,ab 3145
#15 MeSH descriptor: [Adrenal Cortex Hormones] explode all trees 13030
#16 (Entocort or dexamethasone or hydrocortisone or Cortef or Cortenema or Proctofoam or methylprednisolone or prednisolone or Orapred or prednisone or Colocort):ti,ab 16552
#17 MeSH descriptor: [Probiotics] explode all trees 1632
#18 (probiotic* or lactobacill* or bifidobacteri* or streptococc* or Saccharomyces or Escherichia coli or e coli or VSL #3):ti,ab 8778
#19 MeSH descriptor: [Curcumin] explode all trees 114
#20 (curcumin or tumeric):ti,ab 249
#21 MeSH descriptor: [Fecal Microbiota Transplantation] explode all trees 5
#22 bacteriotherap*:ti,ab 18
#23 ((fecal or stool) near/3 transplant*):ti,ab 56
#24 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 39563
#25 #5 and #24 1009

Ulcerative Colitis – Patient Preferences – Final Search

Search date: July 24, 2017
Databases searched: Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946-Present, Embase Classic+Embase 1947 to 2017 July 21

Ovid MEDLINE(R), Embase

#	Searches	Results
1	*Colitis, Ulcerative/ use ppez	24697
2	*ulcerative colitis/ use emczd	34245
3	(ulcerative adj2 colitis).ti.	40386
4	*Proctitis/	3330
5	proctitis.ti,ab.	6262
6	or/1-5	67709
7	exp Mesalamine/ use ppez	3194
8	exp mesalazine/ use emczd	15420
9	(Mesalazine or mesalamine or 5-aminosalicylic acid or 5-ASA or Asacol or Pentasa or Salofalk or Mezavant or mesasal or Canasa or Rowasa or Delzicol or Lialda or Apriso).mp.	21719
10	exp Sulfasalazine/ use ppez	4019
11	exp salazosulfapyridine/ use emczd	22782

12	(Sulfasalazine or Azulfidine or Salazopyrin or sulfazine).mp.	11181
13	exp balsalazide/ use emczd	862
14	(olsalazine or olsalazide or Dipentum or balsalazide or Colazol or Giazo).mp.	2160
15	exp Aminosalicylic Acids/ use ppez	9245
16	exp aminosalicylic acid/ use emczd	9872
17	(5-aminosalicylate or 5-asa).mp.	4574
18	exp Budesonide/	22397
19	(Cortiment or Uceris or cortifoam or budesonide).mp.	25648
20	exp Adrenal Cortex Hormones/ use ppez	378186
21	exp corticosteroid/ use emczd	902699
22	(Entocort or dexamethasone or hydrocortisone or Cortef or Cortenema or Proctofoam or methylprednisolone or prednisolone or Orapred or prednisone or Colocort).mp.	797450
23	exp Probiotics/ use ppez	12864
24	exp probiotic agent/ use emczd	25696
25	(probiotic* or lactobacill* or bifidobacteri* or streptococc* or Saccharomyces or Escherichia coli or e coli or VSL#3).mp.	1354430
26	exp Curcumin/	25614
27	(curcumin or tumeric).mp.	29837
28	exp Fecal Microbiota Transplantation/	1334
29	bacteriotherap*.ti,ab.	383
30	((fecal or stool) adj3 transplant*).ti,ab.	2313
31	or/7-30	2748465
32	6 and 31	17055
33	animals/ not (humans/ and animals/)	5709061
34	32 not 33	16802
35	exp *Patient Satisfaction/	48921
36	exp *patient participation/	20405
37	exp *Attitude to health/ use ppez	189488
38	exp *patient attitude/ use emczd	78030
39	exp *patient decision making/ use emczd	1717
40	exp *"patient acceptance of health care"/ use ppez	100137
41	*"Activities of Daily Living"/ use ppez	18355
42	*daily life activity/ use emczd	11552
43	*"Quality of Life"/	151895
44	exp *Questionnaires/ use ppez	173572
45	exp *questionnaire/ use emczd	29606

46	(euroqol or EQ5D or EQ-5D or short form* or QWB or Quality of Well-Being or health utilit* index).ti,ab.	80533
47	(health utilit* or utility index or utility indices).ti,ab.	4671
48	(patient* adj2 (value* or preference* or participation or satisfaction or decision* or attitude* or view* or perception or perceive* or perspective* or accept*)).ti,ab.	266539
49	(standard gambl* or VAS or time trade off or willingness to pay or (visual analog adj2 scale) or probability trade-off or best-worst scal*).ti,ab.	132728
50	or/35-49	997303
51	34 and 50	459
52	remove duplicates from 51	356

Ulcerative Colitis – Economics – Final Search

Search date: July 24, 2017
Databases searched: Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946-Present, Embase Classic+Embase 1947 to 2017 July 21

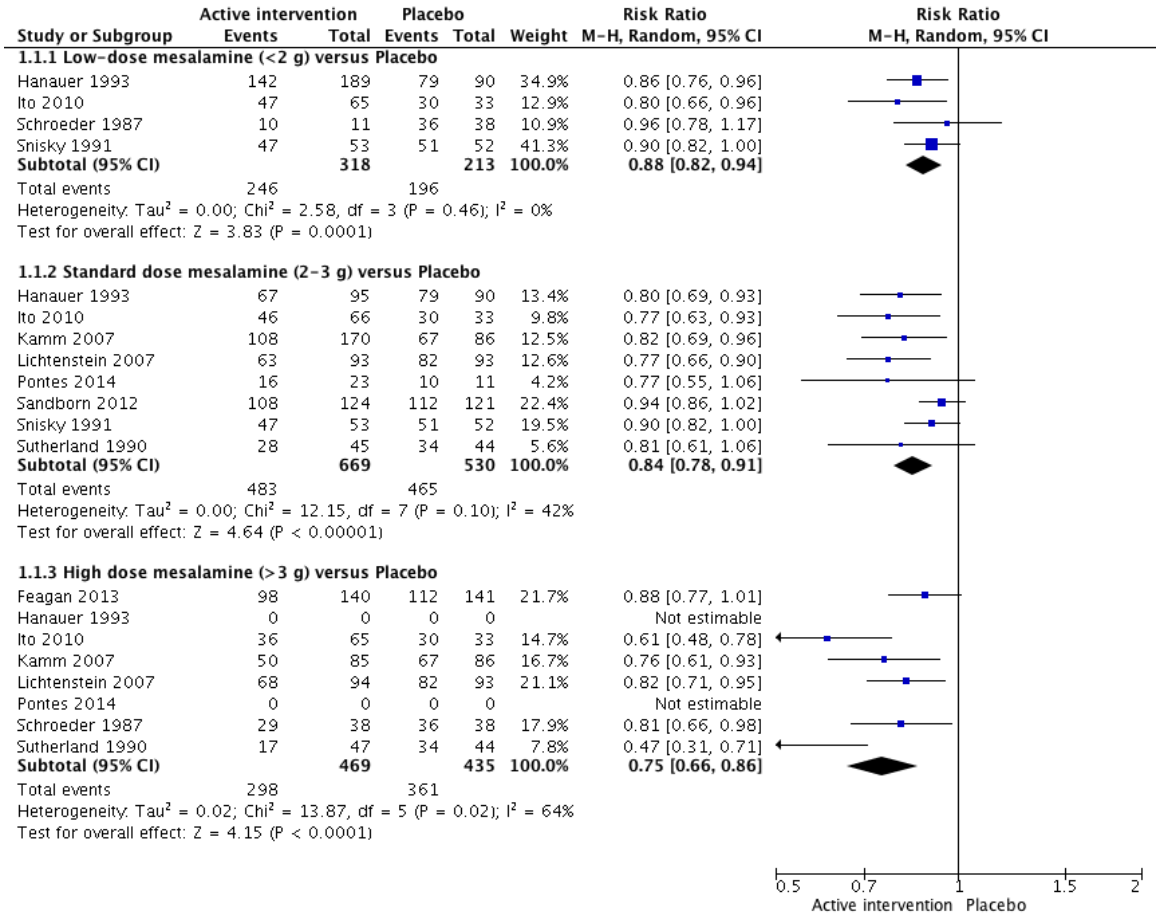
Ovid MEDLINE(R), Embase

#	Searches	Results
1	*Colitis, Ulcerative/ use ppez	24697
2	*ulcerative colitis/ use emczd	34245
3	(ulcerative adj2 colitis).ti.	40386
4	*Proctitis/	3330
5	proctitis.ti.	2034
6	or/1-5	64661
7	exp Mesalamine/ use ppez	3194
8	exp mesalazine/ use emczd	15420
9	(Mesalazine or mesalamine or 5-aminosalicylic acid or 5-ASA or Asacol or Pentasa or Salofalk or Mezavant or mesasal or Canasa or Rowasa or Delzicol or Lialda or Apriso).mp.	21719
10	exp Sulfasalazine/ use ppez	4019
11	exp salazosulfapyridine/ use emczd	22782
12	(Sulfasalazine or Azulfidine or Salazopyrin or sulfazine).mp.	11181
13	exp balsalazide/ use emczd	862
14	(olsalazine or olsalazide or Dipentum or balsalazide or Colazol or Giazo).mp.	2160
15	exp Aminosalicylic Acids/ use ppez	9245
16	exp aminosalicylic acid/ use emczd	9872

17	(5-aminosalicylate or 5-asa).mp.	4574
18	exp Budesonide/	22397
19	(Cortiment or Uceris or cortifoam or budesonide).mp.	25648
20	exp Adrenal Cortex Hormones/ use ppez	378186
21	exp corticosteroid/ use emczd	902699
22	(Entocort or dexamethasone or hydrocortisone or Cortef or Cortenema or Proctofoam or methylprednisolone or prednisolone or Orapred or prednisone or Colocort).mp.	797450
23	exp Probiotics/ use ppez	12864
24	exp probiotic agent/ use emczd	25696
25	(probiotic* or lactobacill* or bifidobacteri* or streptococc* or Saccharomyces or Escherichia coli or e coli or VSL#3).mp.	1354430
26	exp Curcumin/	25614
27	(curcumin or tumeric).mp.	29837
28	exp Fecal Microbiota Transplantation/	1334
29	bacteriotherap*.ti,ab.	383
30	((fecal or stool) adj3 transplant*).ti,ab.	2313
31	or/7-30	2748465
32	6 and 31	16813
33	animals/ not (humans/ and animals/)	5709061
34	32 not 33	16563
35	exp *Economics/	322902
36	exp *"Costs and Cost Analysis"/ use ppez	59533
37	exp *Cost/ use emczd	71709
38	exp *Health Economics/ use emczd	226544
39	exp *Pharmacoeconomics/ use emczd	26542
40	exp *Models, Economic/ use ppez	4387
41	exp *monte carlo method/	9129
42	exp *Statistical Model/ use emczd	20461
43	exp *markov chains/ use ppez	2021
44	exp Economic Aspect/ use emczd or exp Economic Evaluation/ use emczd	1459676
45	exp Quality-Adjusted Life Years/	29074
46	(econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic* or cost*).ti.	392411
47	(QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).ti.	1998
48	((adjusted adj (quality or life)) or (willing* adj2 pay) or sensitivity	170627

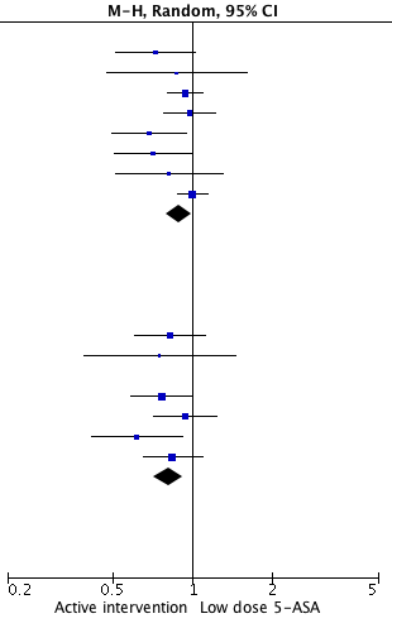
	analys*).mp.	
49	(markov or markow or monte carlo).mp.	131508
50	(decision adj1 (tree* or analy* or model*)).mp.	45652
51	(value adj2 (money or monetary)).mp.	4536
52	or/35-51	2192949
53	34 and 52	491
54	remove duplicates from 53	449

eFigures



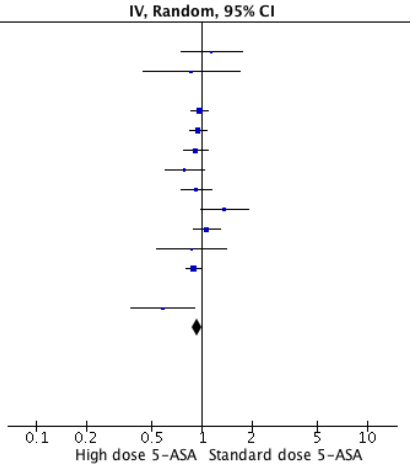
eFigure 1. PICO#1 – Efficacy of low-, standard- and high-dose mesalamine vs. placebo for INDUCTION of remission in patients with mild-moderate UC.

Study or Subgroup	Active intervention Events	Total	Low dose 5-ASA Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 Standard dose 5-ASA (2-3 g) versus Low dose 5-ASA (<2 g)						
D'Haens 2006	10	14	13	13	8.3%	0.73 [0.51, 1.03]
Good 1992	12	31	12	27	3.1%	0.87 [0.47, 1.61]
Hanauer 1993	67	95	142	189	23.7%	0.94 [0.80, 1.09]
Ito 2010	46	66	45	63	15.8%	0.98 [0.78, 1.22]
Kruis 2003	37	108	52	104	9.2%	0.69 [0.50, 0.95]
Miglioli 1990	15	24	22	25	8.5%	0.71 [0.50, 1.00]
Riley 1988	12	21	14	20	5.0%	0.82 [0.51, 1.30]
Snisky 1991	47	53	47	53	26.3%	1.00 [0.87, 1.15]
Subtotal (95% CI)		**412**		**494**	**100.0%**	**0.88 [0.79, 0.99]**
Total events	246		347			
Heterogeneity: Tau² = 0.01; Chi² = 10.24, df = 7 (P = 0.18); I² = 32%						
Test for overall effect: Z = 2.19 (P = 0.03)						
2.1.2 High dose 5-ASA (>3 g) versus Low dose 5-ASA (<2 g)						
D'Haens 2006	9	11	13	13	17.4%	0.82 [0.60, 1.12]
Good 1992	10	30	12	27	3.8%	0.75 [0.39, 1.45]
Hanauer 1993	0	0	0	0		Not estimable
Ito 2010	35	64	45	63	22.2%	0.77 [0.58, 1.01]
Kruis 2003	51	109	52	104	21.3%	0.94 [0.71, 1.24]
Miglioli 1990	13	24	22	25	10.5%	0.62 [0.41, 0.91]
Schroeder 1987	29	38	10	11	24.8%	0.84 [0.65, 1.09]
Subtotal (95% CI)		**276**		**243**	**100.0%**	**0.81 [0.71, 0.92]**
Total events	147		154			
Heterogeneity: Tau² = 0.00; Chi² = 3.19, df = 5 (P = 0.67); I² = 0%						
Test for overall effect: Z = 3.26 (P = 0.001)						

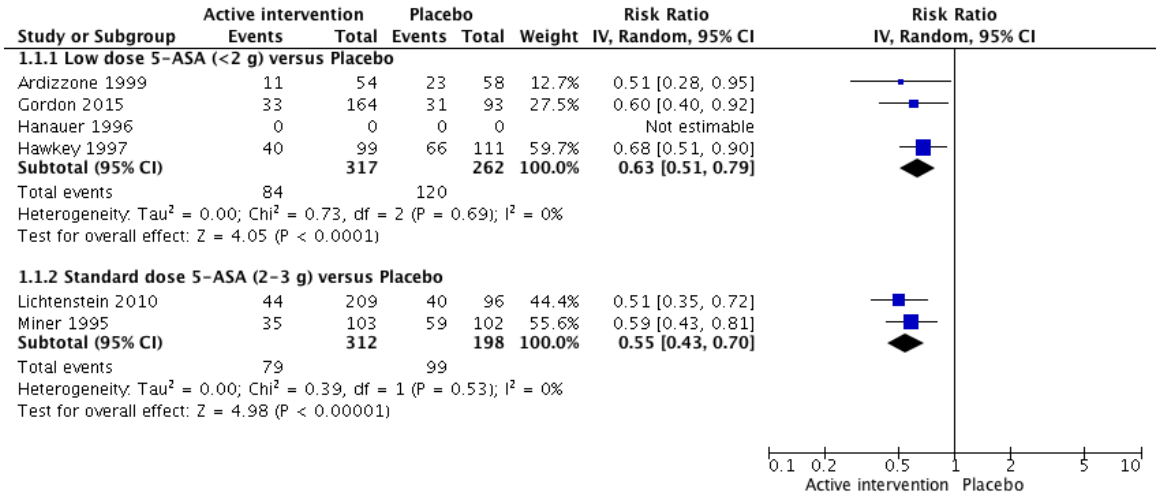


eFigure 2. PICO#1 – Efficacy of high- and standard-dose vs. low-dose mesalamine for INDUCTION of remission in patients with mild-moderate UC.

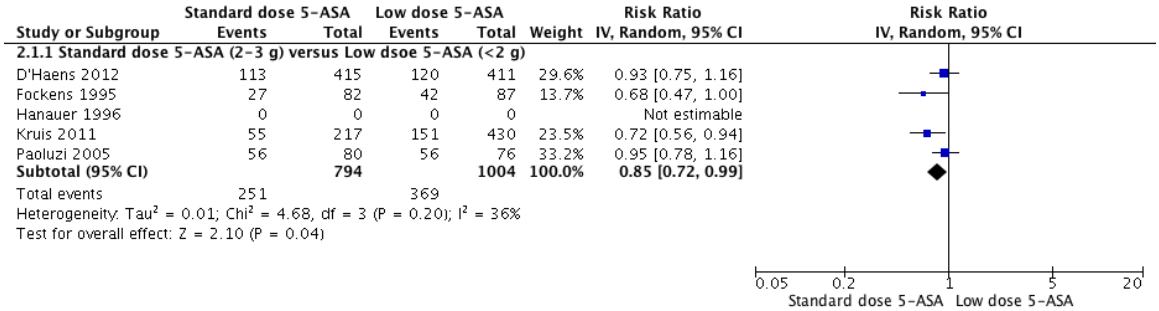
Study or Subgroup	High dose 5-ASA Events	Total	Standard dose 5-ASA Events	Total	Weight	Risk Ratio IV, Random, 95% CI
3.1.1 High dose 5-ASA (>3 g) versus Standard dose 5-ASA (2-3 g)						
D'Haens 2006	9	11	10	14	2.3%	1.15 [0.74, 1.77]
Good 1992	10	30	12	31	1.0%	0.86 [0.44, 1.69]
Hanauer 1993	0	0	0	0		Not estimable
Hanauer 2005	104	129	116	139	18.0%	0.97 [0.86, 1.08]
Hanauer 2007	112	147	124	154	17.0%	0.95 [0.84, 1.07]
Hiwatashi 2011	47	60	54	63	11.4%	0.91 [0.77, 1.08]
Ito 2010	35	64	46	66	5.3%	0.78 [0.60, 1.03]
Kamm 2007	50	85	108	170	8.1%	0.93 [0.75, 1.14]
Kruis 2003	51	109	37	108	3.9%	1.37 [0.98, 1.90]
Lichtenstein 2007	68	94	63	93	9.6%	1.07 [0.88, 1.29]
Miglioli 1990	13	24	15	24	1.9%	0.87 [0.54, 1.40]
Sandborn 2009	240	392	262	383	19.3%	0.89 [0.81, 0.99]
Schroeder 1987	0	0	0	0		Not estimable
Sutherland 1990	17	47	28	45	2.2%	0.58 [0.37, 0.91]
Subtotal (95% CI)		**1192**		**1290**	**100.0%**	**0.94 [0.88, 1.01]**
Total events	756		875			
Heterogeneity: Tau² = 0.00; Chi² = 15.11, df = 11 (P = 0.18); I² = 27%						
Test for overall effect: Z = 1.75 (P = 0.08)						



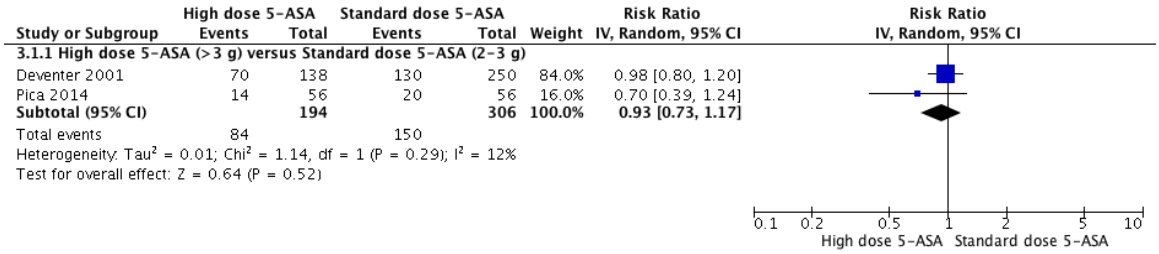
eFigure 3. PICO#1 – Efficacy of high- vs. standard-dose mesalamine for INDUCTION of remission in patients with mild-moderate UC.



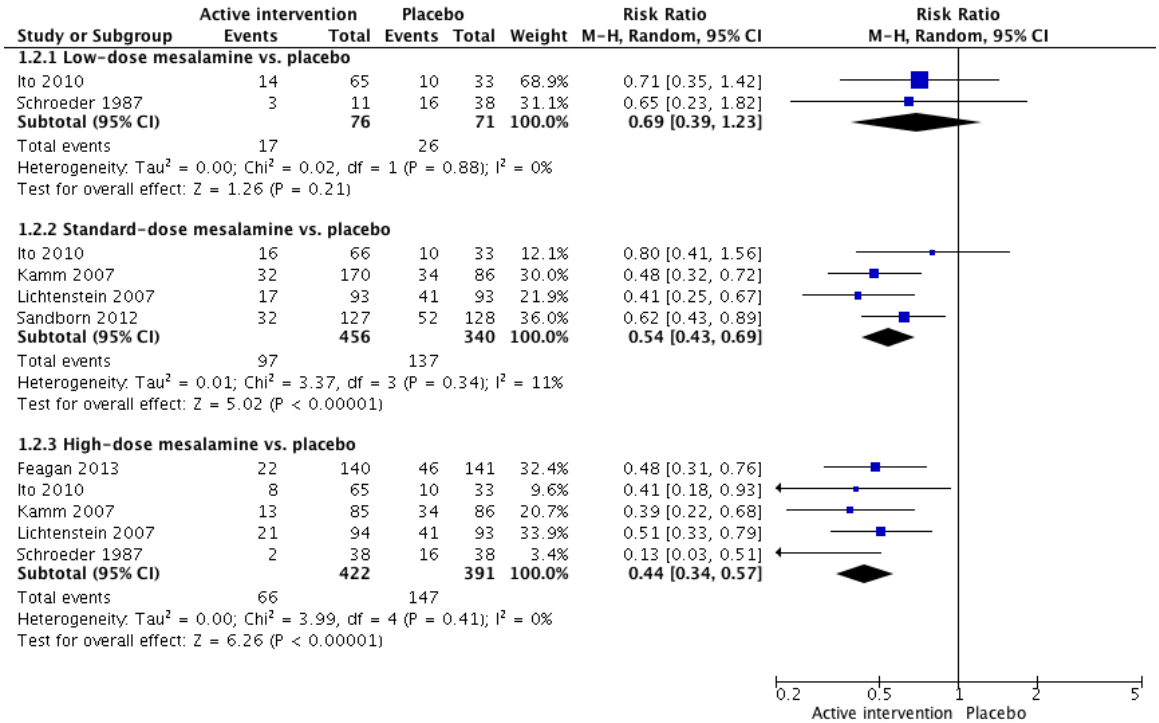
eFigure 4. PICO#1 – Efficacy of low-, standard- and high-dose mesalamine vs. placebo for MAINTENANCE of remission in patients with mild-moderate UC.



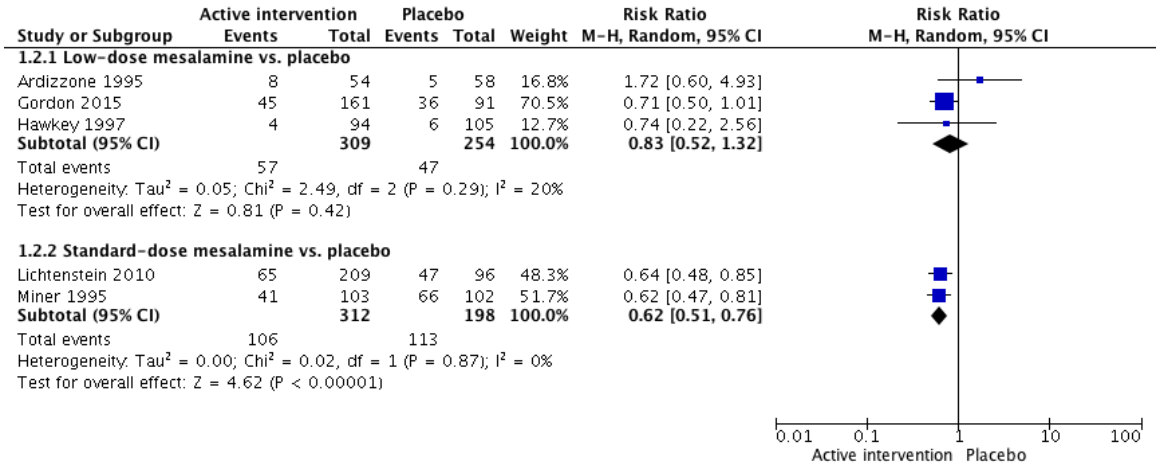
eFigure 5. PICO#1 – Efficacy of standard-dose vs. low-dose mesalamine for MAINTENANCE of remission in patients with mild-moderate UC.



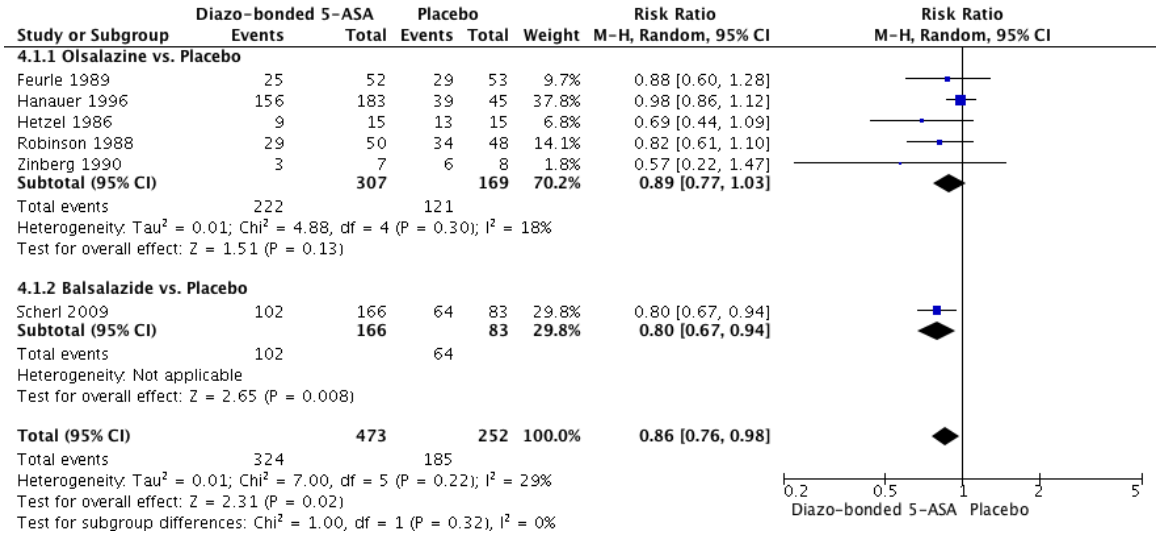
eFigure 6. PICO#1 – Efficacy of high-dose vs. standard-dose mesalamine for MAINTENANCE of remission in patients with mild-moderate UC.



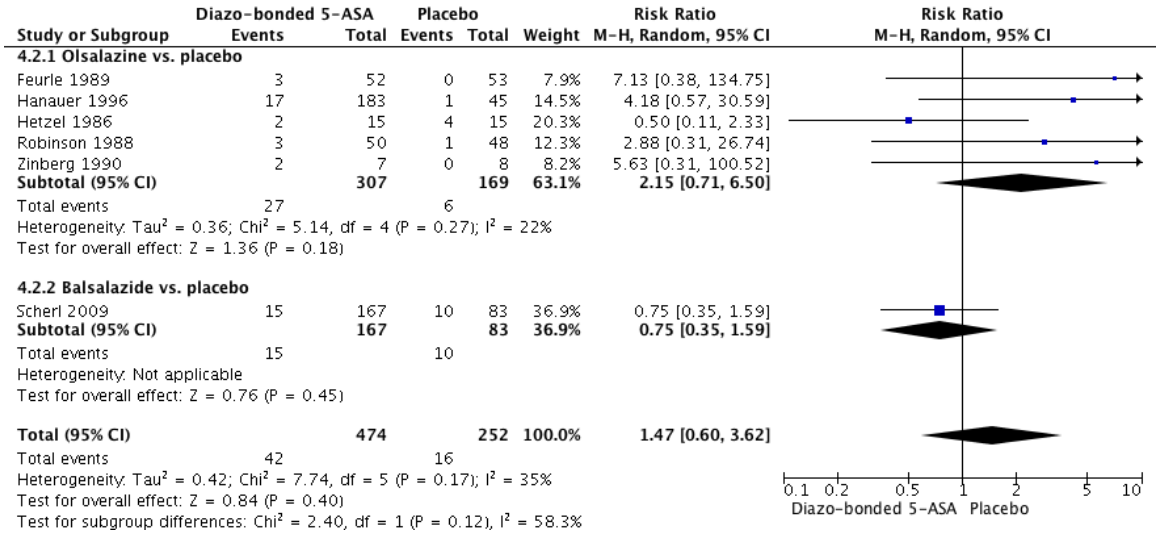
eFigure 7. PICO#1 – Tolerability of low-, standard- and high-dose mesalamine vs. placebo for INDUCTION of remission in patients with mild-moderate UC.



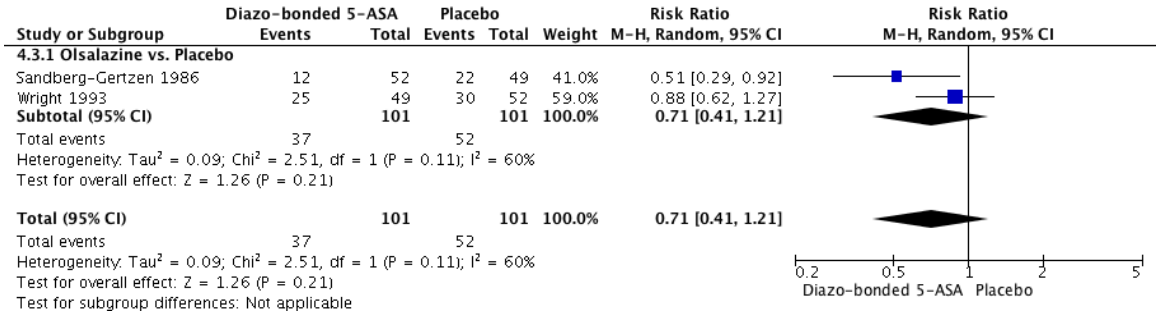
eFigure 8. PICO#1 – Tolerability of low-, standard- and high-dose mesalamine vs. placebo for MAINTENANCE of remission in patients with mild-moderate UC.



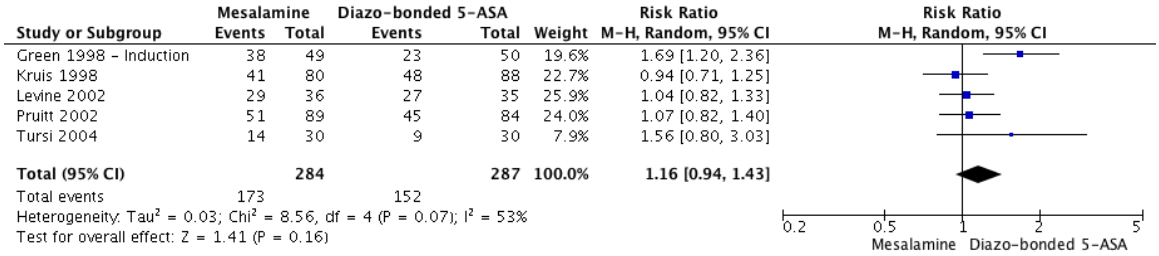
eFigure 9. PICO#2 – Efficacy of diazo-bonded vs. placebo for INDUCTION of remission in patients with mild-moderate UC.



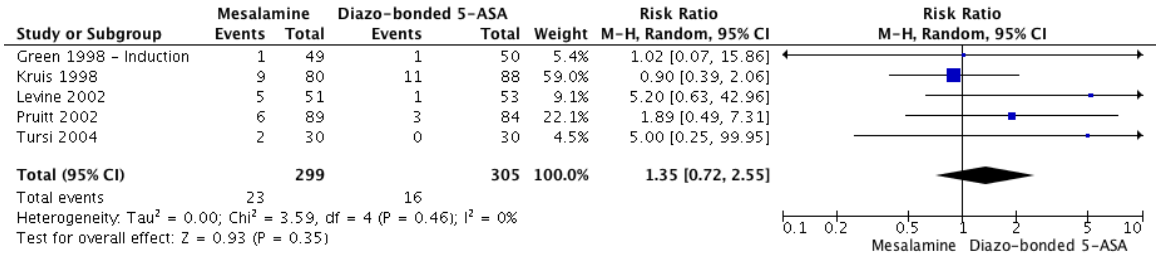
eFigure 10. PICO#2 – Tolerability of diazo-bonded vs. placebo for INDUCTION of remission in patients with mild-moderate UC.



eFigure 11. PICO#2 – Efficacy of diazo-bonded 5-ASA vs. placebo for MAINTENANCE of remission in patients with mild-moderate UC.



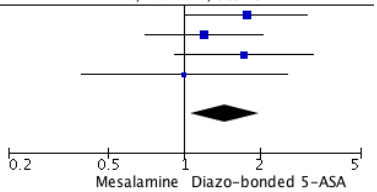
eFigure 12. PICO#2 – Efficacy of mesalamine vs. diazo-bonded 5-ASA for INDUCTION of remission in patients with mild-moderate UC (Note: Kruis 1998 studied olsalazine and all other trials studied balsalazide)



eFigure 13. PICO#2 – Tolerability of mesalamine vs. diazo-bonded 5-ASA for INDUCTION of remission in patients with mild-moderate UC (Note: Kruis 1998 studied olsalazine and all other trials studied balsalazide)

Study or Subgroup	Mesalamine Events	Mesalamine Total	Diazo-bonded 5-ASA Events	Diazo-bonded 5-ASA Total	Weight	Risk Ratio M-H, Random, 95% CI
Courtney 1992	23	50	13	50	31.5%	1.77 [1.01, 3.08]
Green 1998 - Maintenance	18	46	16	49	33.4%	1.20 [0.70, 2.06]
Kruis 2001	19	44	10	40	24.2%	1.73 [0.92, 3.26]
Mahmud 2002	6	20	6	20	10.9%	1.00 [0.39, 2.58]
Total (95% CI)		**160**		**159**	**100.0%**	**1.45 [1.06, 1.98]**
Total events	66		45			

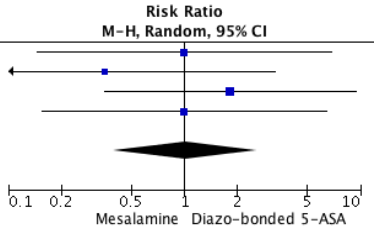
Heterogeneity: Tau² = 0.00; Chi² = 1.86, df = 3 (P = 0.60); I² = 0%
Test for overall effect: Z = 2.34 (P = 0.02)



eFigure 14. PICO#2 – Efficacy of mesalamine vs. diazo-bonded 5-ASA for MAINTENANCE of remission in patients with mild-moderate UC

Study or Subgroup	Mesalamine Events	Mesalamine Total	Diazo-bonded 5-ASA Events	Diazo-bonded 5-ASA Total	Weight	Risk Ratio M-H, Random, 95% CI
Courtney 1992	2	50	2	50	23.9%	1.00 [0.15, 6.82]
Green 1998 - Maintenance	1	46	3	49	17.8%	0.36 [0.04, 3.29]
Kruis 2001	4	44	2	40	32.7%	1.82 [0.35, 9.40]
Mahmud 2002	2	20	2	20	25.5%	1.00 [0.16, 6.42]
Total (95% CI)		**160**		**159**	**100.0%**	**1.01 [0.40, 2.59]**
Total events	9		9			

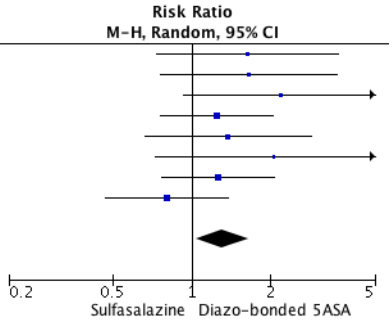
Heterogeneity: Tau² = 0.00; Chi² = 1.34, df = 3 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.02 (P = 0.98)



eFigure 15. PICO#2 – Tolerability of mesalamine vs. diazo-bonded 5-ASA for MAINTENANCE of remission in patients with mild-moderate UC

Study or Subgroup	Sulfasalazine Events	Sulfasalazine Total	Diazo-bonded 5-ASA Events	Diazo-bonded 5-ASA Total	Weight	Risk Ratio M-H, Random, 95% CI
Cai 2001	7	30	15	105	8.2%	1.63 [0.73, 3.64]
Green 2002	12	29	7	28	8.8%	1.66 [0.76, 3.59]
Jiang 2004	11	21	5	21	7.0%	2.20 [0.92, 5.24]
Mansfield 2002	15	24	13	26	21.6%	1.25 [0.76, 2.05]
Qian 2004	10	25	9	31	9.9%	1.38 [0.66, 2.86]
Rao 1989	7	17	4	20	4.8%	2.06 [0.72, 5.85]
Rijk 1991	17	28	13	27	21.8%	1.26 [0.77, 2.06]
Willoughby 1988	13	30	14	26	17.9%	0.80 [0.47, 1.38]
Total (95% CI)		**204**		**284**	**100.0%**	**1.30 [1.04, 1.64]**
Total events	92		80			

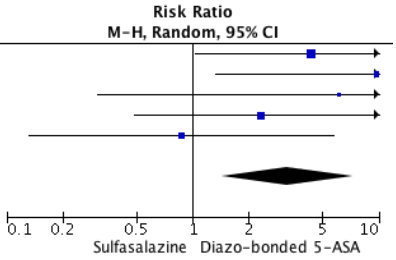
Heterogeneity: Tau² = 0.00; Chi² = 6.03, df = 7 (P = 0.54); I² = 0%
Test for overall effect: Z = 2.27 (P = 0.02)



eFigure 16. PICO#2 – Efficacy of sulfasalazine vs. diazo-bonded 5-ASA for INDUCTION of remission in patients with mild-moderate UC

Study or Subgroup	Sulfasalazine Events	Sulfasalazine Total	Diazo-bonded 5-ASA Events	Diazo-bonded 5-ASA Total	Weight	Risk Ratio M-H, Random, 95% CI
Green 2002	9	29	2	28	31.5%	4.34 [1.03, 18.37]
Mansfield 2002	9	24	1	26	16.5%	9.75 [1.33, 71.33]
Qian 2004	2	25	0	31	7.3%	6.15 [0.31, 122.61]
Rao 1989	4	18	2	21	26.3%	2.33 [0.48, 11.29]
Willoughby 1988	2	30	2	26	18.3%	0.87 [0.13, 5.73]
Total (95% CI)		**126**		**132**	**100.0%**	**3.22 [1.43, 7.22]**
Total events	26		7			

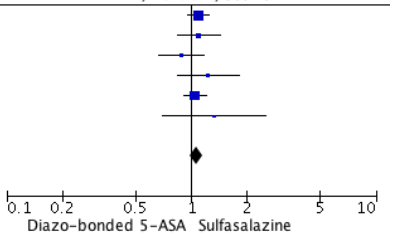
Heterogeneity: Tau² = 0.00; Chi² = 3.65, df = 4 (P = 0.46); I² = 0%
Test for overall effect: Z = 2.83 (P = 0.005)



eFigure 17. PICO#2 – Tolerability of sulfasalazine vs. diazo-bonded 5-ASA for INDUCTION of remission in patients with mild-moderate UC

Study or Subgroup	Sulfasalazine Events	Sulfasalazine Total	Diazo-bonded 5-ASA Events	Diazo-bonded 5-ASA Total	Weight	Risk Ratio (Non-event) M-H, Random, 95% CI
Ireland 1988	10	82	16	82	40.4%	1.09 [0.95, 1.25]
Kiilerich 1992	55	112	61	114	10.0%	1.09 [0.84, 1.43]
Kruis 1995	13	40	8	34	8.9%	0.88 [0.66, 1.17]
McIntyre 1988	14	38	20	41	4.9%	1.23 [0.84, 1.81]
Nilsson 1995	47	161	52	161	34.0%	1.05 [0.90, 1.21]
Rijk 1992	11	23	14	23	1.7%	1.33 [0.70, 2.54]
Total (95% CI)		**456**		**455**	**100.0%**	**1.07 [0.98, 1.16]**
Total events	150		171			

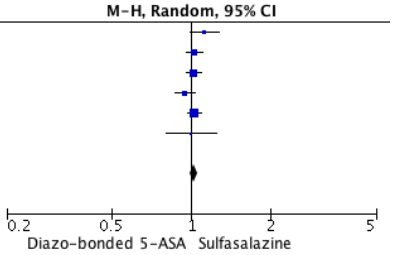
Heterogeneity: Tau² = 0.00; Chi² = 2.94, df = 5 (P = 0.71); I² = 0%
Test for overall effect: Z = 1.47 (P = 0.14)



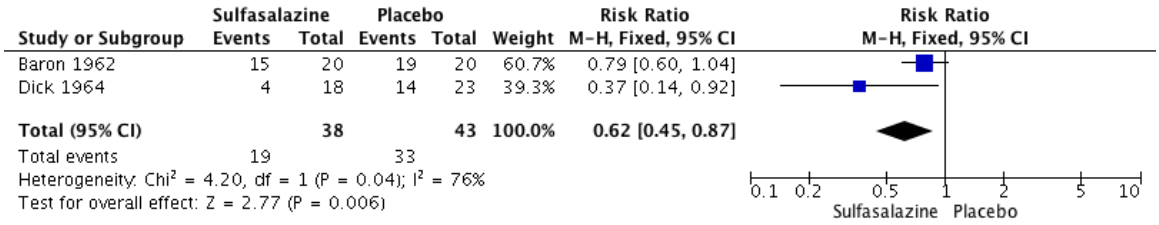
eFigure 18. PICO#2 – Efficacy of sulfasalazine vs. diazo-bonded 5-ASA for MAINTENANCE of remission in patients with mild-moderate UC

Study or Subgroup	Sulfasalazine Events	Sulfasalazine Total	Diazo-bonded 5-ASA Events	Diazo-bonded 5-ASA Total	Weight	Risk Ratio (Non-event) M-H, Random, 95% CI
Ireland 1988	8	82	16	82	6.8%	1.12 [0.99, 1.27]
Kiilerich 1992	6	112	9	114	21.5%	1.03 [0.96, 1.10]
Kruis 1995	1	40	5	108	24.4%	1.02 [0.96, 1.09]
McIntyre 1988	2	38	0	41	13.8%	0.95 [0.87, 1.03]
Nilsson 1995	8	161	12	161	31.1%	1.03 [0.97, 1.09]
Rijk 1992	3	23	3	23	2.3%	1.00 [0.80, 1.25]
Total (95% CI)		**456**		**529**	**100.0%**	**1.02 [0.99, 1.06]**
Total events	28		45			

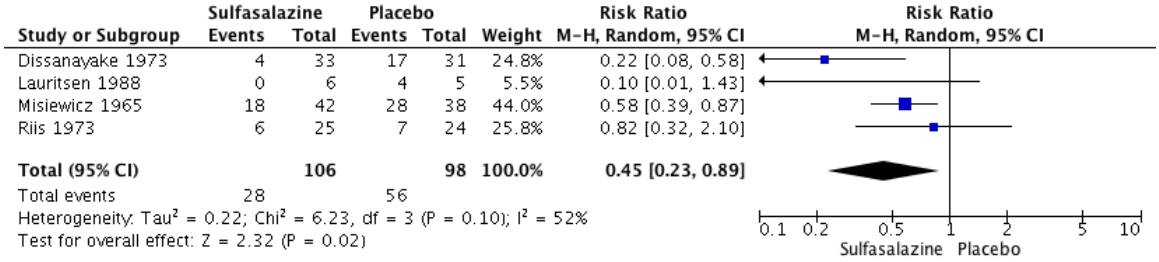
Heterogeneity: Tau² = 0.00; Chi² = 5.43, df = 5 (P = 0.37); I² = 8%
Test for overall effect: Z = 1.14 (P = 0.26)



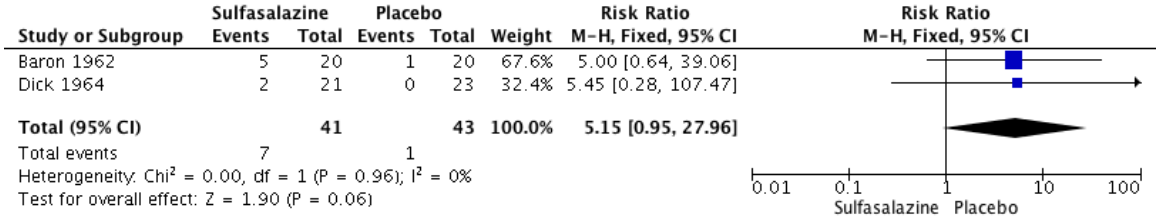
eFigure 19. PICO#2 – Tolerability of sulfasalazine vs. diazo-bonded 5-ASA for MAINTENANCE of remission in patients with mild-moderate UC



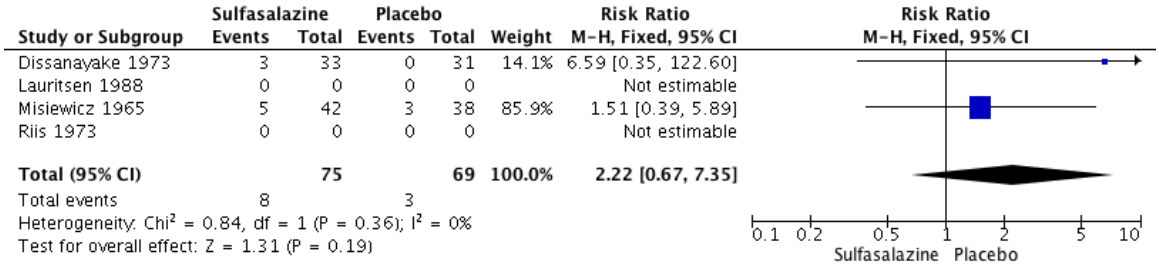
eFigure 20. PICO#3 – Efficacy of sulfasalazine vs. placebo for INDUCTION of remission in patients with mild-moderate UC.



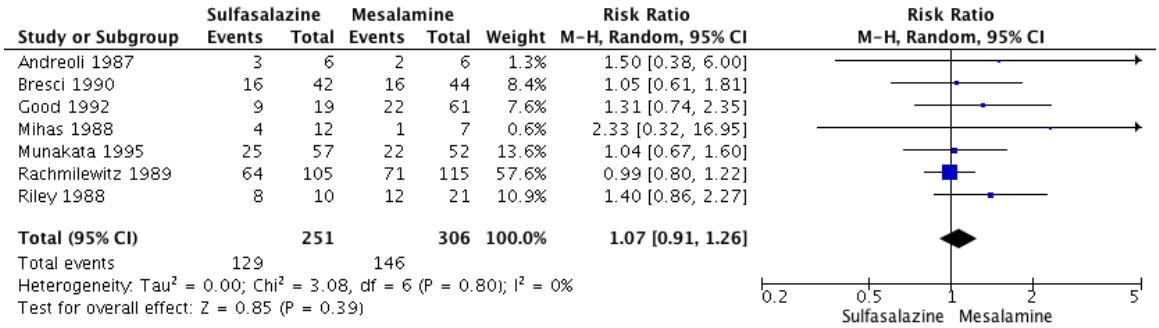
eFigure 21. PICO#3 – Efficacy of sulfasalazine vs. placebo for MAINTENANCE of remission in patients with mild-moderate UC.



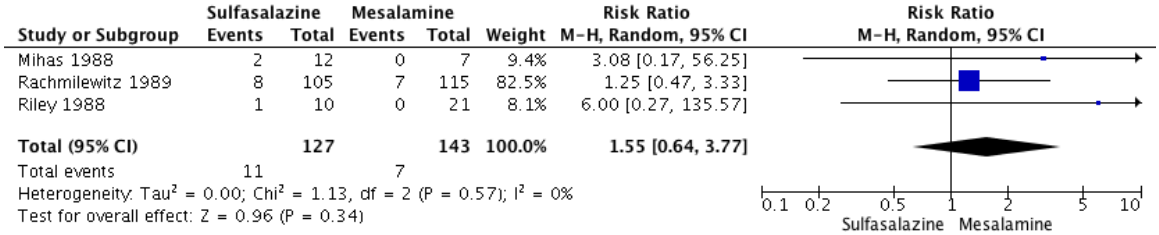
eFigure 22. PICO#3 – Tolerability of sulfasalazine vs. placebo for INDUCTION of remission in patients with mild-moderate UC.



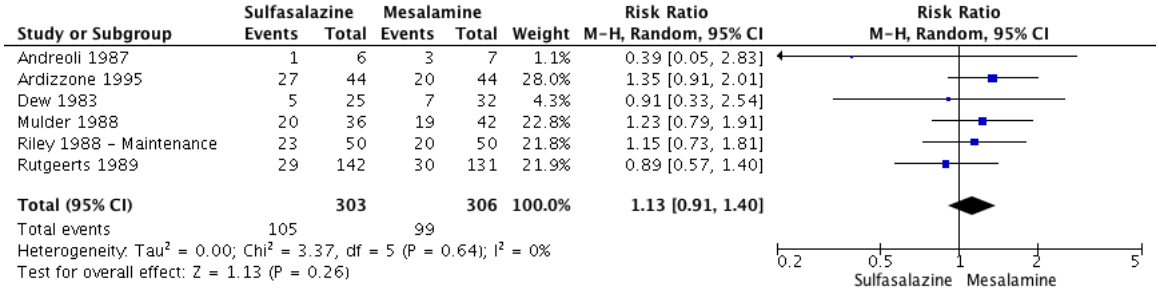
eFigure 23. PICO#3 – Tolerability of sulfasalazine vs. placebo for MAINTENANCE of remission in patients with mild-moderate UC.



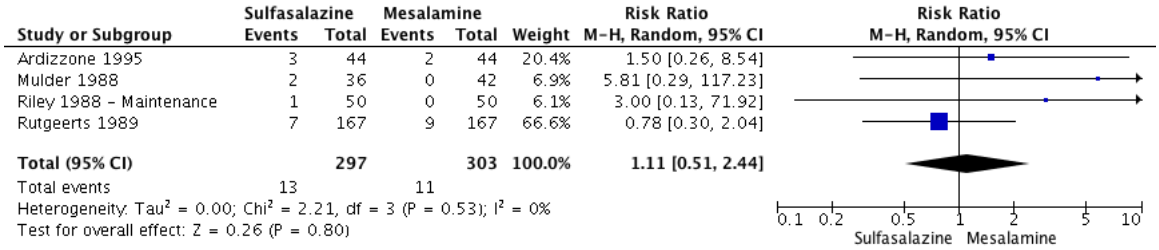
eFigure 24. PICO#3 – Efficacy of sulfasalazine vs. mesalamine for INDUCTION of remission in patients with mild-moderate UC.



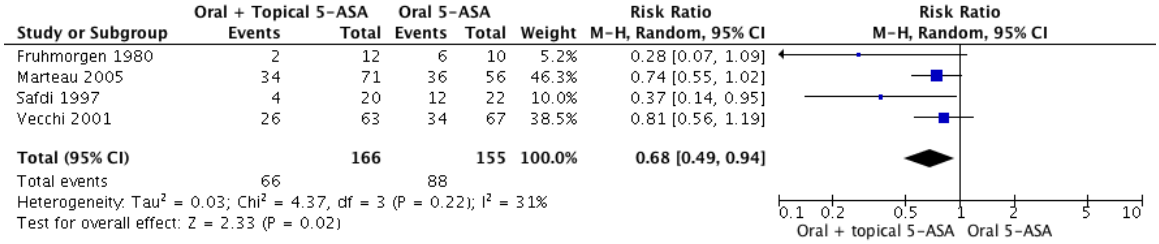
eFigure 25. PICO#3 – Tolerability of sulfasalazine vs. mesalamine for INDUCTION of remission in patients with mild-moderate UC.



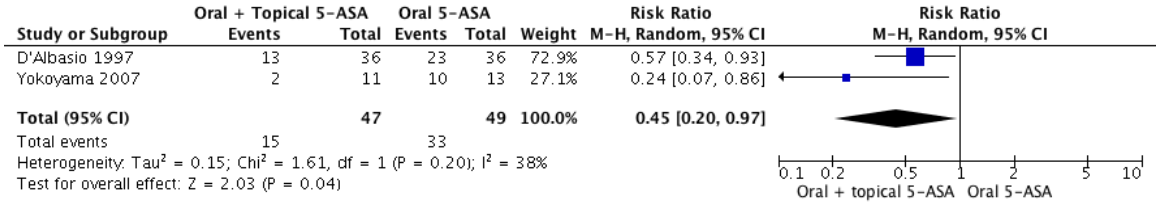
eFigure 26. PICO#3 – Efficacy of sulfasalazine vs. mesalamine for MAINTENANCE of remission in patients with mild-moderate UC.



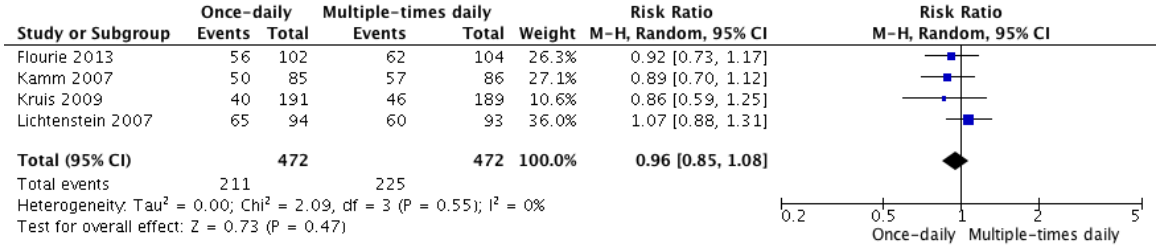
eFigure 27. PICO#3 – Tolerability of sulfasalazine vs. mesalamine for MAINTENANCE of remission in patients with mild-moderate UC.



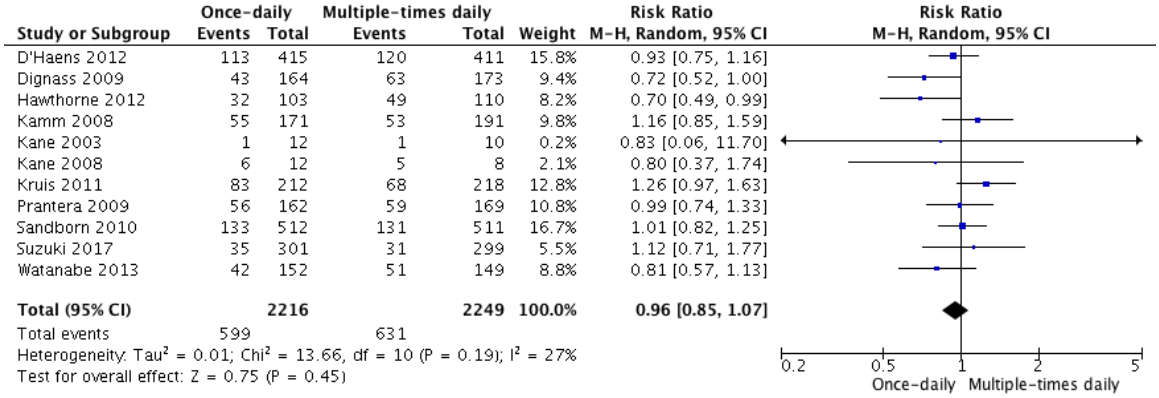
eFigure 28. PICO#4 – Efficacy of oral + topical 5-ASA vs. oral 5-ASA for INDUCTION of remission in patients with mild-moderate UC.



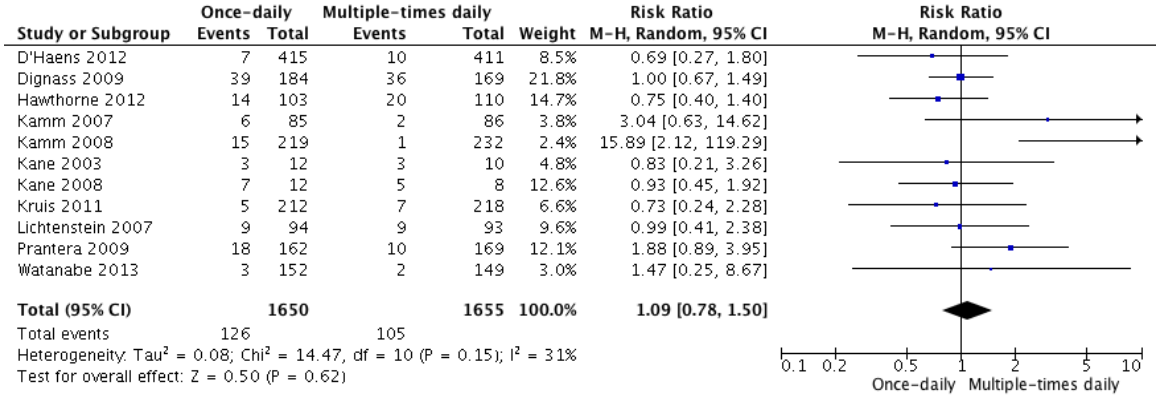
eFigure 29. PICO#4 – Efficacy of oral + topical 5-ASA vs. oral 5-ASA for MAINTENANCE of remission in patients with mild-moderate UC.



eFigure 30. PICO#5 – Efficacy of once-daily vs. multiple-times daily equivalent doses of mesalamine for INDUCTION of remission in patients with mild-moderate UC.



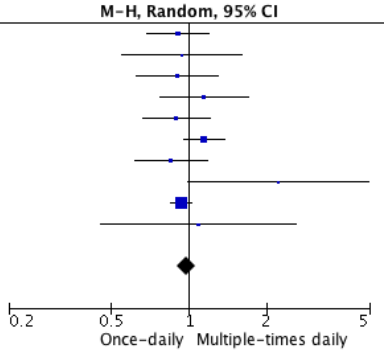
eFigure 31. PICO#5 – Efficacy of once-daily vs. multiple-times daily equivalent doses of mesalamine for MAINTENANCE of remission in patients with mild-moderate UC.



eFigure 32. PICO#5 – Adherence of once-daily vs. multiple-times daily equivalent doses of mesalamine in patients with mild-moderate UC.

Study or Subgroup	Once-daily Events	Once-daily Total	Multiple-times daily Events	Multiple-times daily Total	Weight	Risk Ratio M-H, Random, 95% CI
D'Haens 2012	76	415	83	411	8.6%	0.91 [0.69, 1.20]
Dignass 2009	22	175	25	187	2.5%	0.94 [0.55, 1.60]
Flourie 2013	35	102	38	100	5.2%	0.90 [0.63, 1.30]
Kamm 2008	43	225	39	234	4.6%	1.15 [0.77, 1.70]
Kruis 2009	55	191	61	189	7.4%	0.89 [0.66, 1.21]
Kruis 2011	117	212	105	218	18.0%	1.15 [0.95, 1.38]
Lichtenstein 2007	38	94	44	93	6.5%	0.85 [0.62, 1.18]
Prantera 2009	17	162	8	169	1.1%	2.22 [0.98, 4.99]
Suzuki 2017	215	302	229	301	45.1%	0.94 [0.85, 1.03]
Watanabe 2013	10	152	9	149	1.0%	1.09 [0.46, 2.60]
Total (95% CI)		**2030**		**2051**	**100.0%**	**0.98 [0.90, 1.06]**
Total events	628		641			

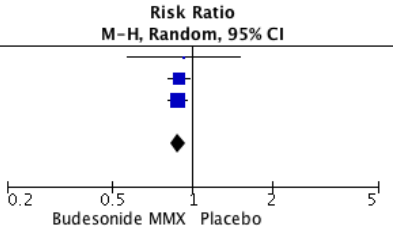
Heterogeneity: Tau² = 0.00; Chi² = 9.88, df = 9 (P = 0.36); I² = 9%
Test for overall effect: Z = 0.54 (P = 0.59)



eFigure 33. PICO#5 – Tolerability of once-daily vs. multiple-times daily equivalent doses of mesalamine in patients with mild-moderate UC.

Study or Subgroup	Budesonide MMX Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
D'Haens 2010 (1)	13	21	10	15	1.5%	0.93 [0.57, 1.52]
Sandborn 2012	105	127	119	128	41.6%	0.89 [0.81, 0.98]
Travis 2014	108	127	124	128	56.9%	0.88 [0.81, 0.95]
Total (95% CI)		**275**		**271**	**100.0%**	**0.88 [0.83, 0.94]**
Total events	226		253			

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 2 (P = 0.96); I² = 0%
Test for overall effect: Z = 4.06 (P < 0.0001)

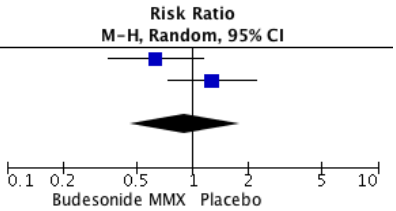


Footnotes
(1) Data is from 4 week

eFigure 34. PICO#6 – Efficacy of budesonide MMX vs. placebo for INDUCTION of remission in patients with mild-moderate UC.

Study or Subgroup	Budesonide MMX Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Sandborn 2012	15	127	24	129	48.6%	0.63 [0.35, 1.15]
Travis 2014	24	128	19	129	51.4%	1.27 [0.73, 2.21]
Total (95% CI)		**255**		**258**	**100.0%**	**0.91 [0.46, 1.80]**
Total events	39		43			

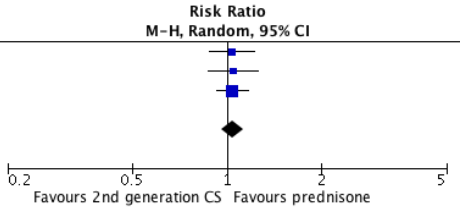
Heterogeneity: Tau² = 0.16; Chi² = 2.83, df = 1 (P = 0.09); I² = 65%
Test for overall effect: Z = 0.28 (P = 0.78)



eFigure 35. PICO#6 – Tolerabiliy of budesonide MMX vs. placebo in patients with mild-moderate UC.

Study or Subgroup	2nd generation CS Events	Total	Prednisone Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Hawthorne 1993	75	100	76	105	26.5%	1.04 [0.88, 1.22]
Lofberg 1996	30	34	32	38	20.8%	1.05 [0.87, 1.26]
Van Assche 2015	112	137	114	145	52.7%	1.04 [0.93, 1.17]
Total (95% CI)		**271**		**288**	**100.0%**	**1.04 [0.96, 1.13]**
Total events	217		222			

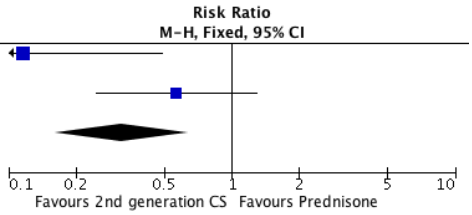
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 2 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.92 (P = 0.36)



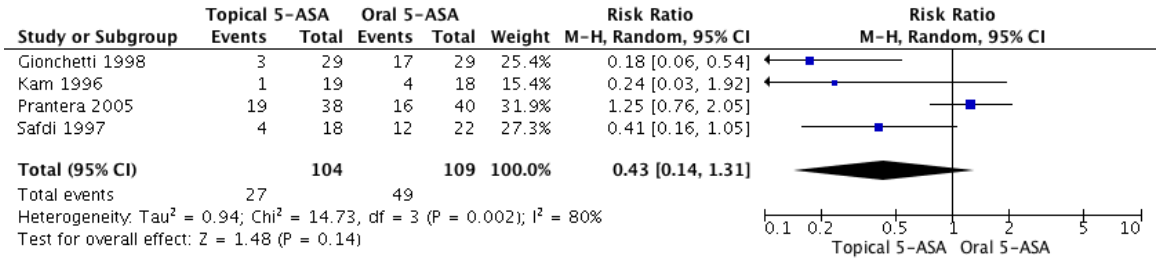
eFigure 36. PICO#6 – Efficacy of 2nd-generation corticosteroids vs. oral prednisone/prednisolone for INDUCTION of remission in patients with mild-moderate UC.

Study or Subgroup	2nd generation CS Events	Total	Prednisone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hawthorne 1993	2	100	18	105	54.6%	0.12 [0.03, 0.49]
Lofberg 1996	0	0	0	0	0.0%	2.24 [0.21, 23.57]
Van Assche 2015	8	137	15	145	45.4%	0.56 [0.25, 1.29]
Total (95% CI)		**237**		**250**	**100.0%**	**0.32 [0.16, 0.64]**
Total events	10		33			

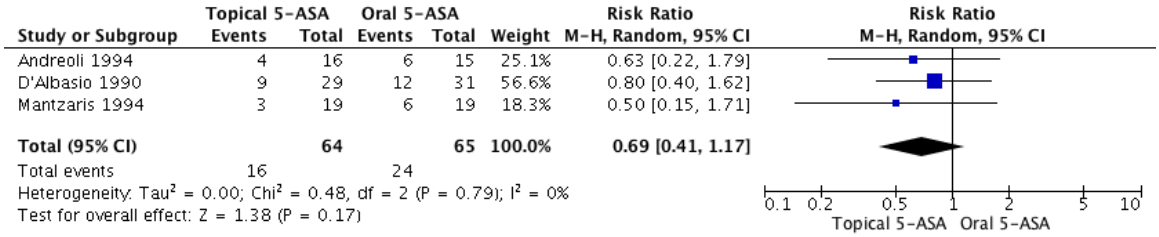
Heterogeneity: Chi² = 3.72, df = 1 (P = 0.05); I² = 73%
Test for overall effect: Z = 3.25 (P = 0.001)



eFigure 37. PICO#6 – Risk of steroid-related adverse events with 2nd-generation corticosteroids vs. oral prednisone/prednisolone for INDUCTION of remission in patients with mild-moderate UC.



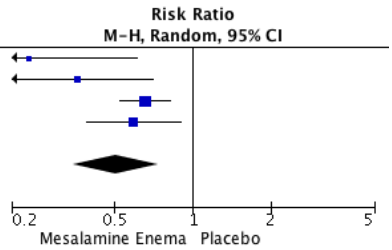
eFigure 38. PICO#7 – Efficacy of topical 5-ASA vs. oral 5-ASA for INDUCTION of remission in patients with mild-moderate UC.



eFigure 39. PICO#7 – Efficacy of topical 5-ASA vs. oral 5-ASA for MAINTENANCE of remission in patients with mild-moderate UC.

Study or Subgroup	Mesalamine enema Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Campieri 1991 (1)	4	29	16	27	11.5%	0.23 [0.09, 0.61]
Campieri 1991b	6	18	13	14	18.8%	0.36 [0.18, 0.70]
Hanauer 1998 (2)	41	73	60	70	40.2%	0.66 [0.52, 0.82]
Pokrotnieks 2000 (3)	19	54	34	57	29.5%	0.59 [0.39, 0.90]
Total (95% CI)		**174**		**168**	**100.0%**	**0.50 [0.35, 0.73]**
Total events	70		123			

Heterogeneity: Tau² = 0.08; Chi² = 7.15, df = 3 (P = 0.07); I² = 58%
Test for overall effect: Z = 3.58 (P = 0.0003)

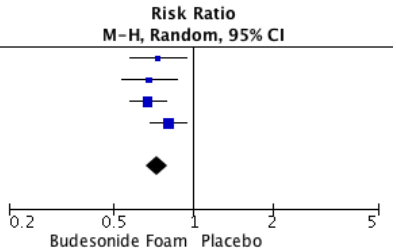


Footnotes
(1) Includes patients with left sided disease n=32 (37% of data)
(2) combined 3 different doses for mesalamine
(3) Includes patients with left sided disease

eFigure 40. PICO#8 – Efficacy of 5-ASA enemas vs. placebo for INDUCTION of remission in patients with mild-moderate left-sided UC.

Study or Subgroup	Budesonide Foam Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Hanauer 1998 (1)	33	56	48	60	14.1%	0.74 [0.57, 0.95]
Naganuma 2016	56	111	40	54	15.3%	0.68 [0.53, 0.87]
Sandborn 2015a	77	133	114	132	35.2%	0.67 [0.57, 0.79]
Sandborn 2015b	83	134	113	147	35.4%	0.81 [0.69, 0.95]
Total (95% CI)		**434**		**393**	**100.0%**	**0.73 [0.66, 0.80]**
Total events	249		315			

Heterogeneity: Tau² = 0.00; Chi² = 2.87, df = 3 (P = 0.41); I² = 0%
Test for overall effect: Z = 6.59 (P < 0.00001)

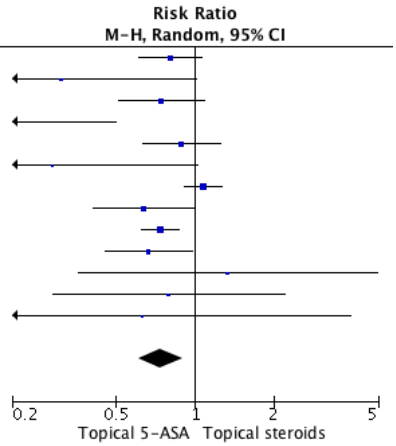


Footnotes
(1) Used enema not foam

eFigure 41. PICO#8 – Efficacy of budesonide enemas vs. placebo for INDUCTION of remission in patients with mild-moderate left-sided UC.

Study or Subgroup	Topical 5-ASA Events	Total	Topical steroids Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Anonymous 1987	34	61	43	62	13.1%	0.80 [0.61, 1.06]
Bianchi Porro 1995	3	27	9	25	2.4%	0.31 [0.09, 1.01]
Biancone 2007	20	42	32	50	10.7%	0.74 [0.51, 1.09]
Campieri 1981	3	44	18	42	2.5%	0.16 [0.05, 0.50]
Farup 1995	24	41	25	38	11.5%	0.89 [0.63, 1.26]
Friedman 1986	2	9	7	9	2.1%	0.29 [0.08, 1.02]
Gionchetti 2005	80	106	78	111	15.9%	1.07 [0.91, 1.26]
Hartmann 2010	24	106	36	101	9.4%	0.64 [0.41, 0.99]
Lee 1996	90	167	122	167	15.8%	0.74 [0.62, 0.87]
Lemann 1995	21	49	31	48	10.6%	0.66 [0.45, 0.98]
Mulder 1988	4	15	3	15	2.0%	1.33 [0.36, 4.97]
Mulder 1996	5	21	6	20	3.1%	0.79 [0.29, 2.19]
Senagore 1992	2	19	2	12	1.1%	0.63 [0.10, 3.91]
Total (95% CI)		**707**		**700**	**100.0%**	**0.74 [0.61, 0.90]**
Total events	312		412			

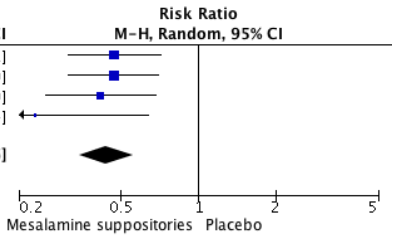
Heterogeneity: Tau² = 0.06; Chi² = 31.65, df = 12 (P = 0.002); I² = 62%
Test for overall effect: Z = 3.03 (P = 0.002)



eFigure 42. PICO#8 – Efficacy of topical 5-ASA vs. topical steroids for INDUCTION of remission in patients with mild-moderate left-sided UC.

Study or Subgroup	Mesalamine suppositories Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Campieri 1990a (1)	21	63	22	31	34.2%	0.47 [0.31, 0.71]
Campieri 1990b (2)	14	32	28	30	36.1%	0.47 [0.31, 0.70]
Watanabe 2013 (3)	12	37	28	36	23.9%	0.42 [0.25, 0.69]
Williams 1987 (4)	3	14	12	13	5.7%	0.23 [0.08, 0.64]
Total (95% CI)		**146**		**110**	**100.0%**	**0.44 [0.34, 0.56]**
Total events	50		90			

Heterogeneity: Tau² = 0.00; Chi² = 1.82, df = 3 (P = 0.61); I² = 0%
Test for overall effect: Z = 6.66 (P < 0.00001)

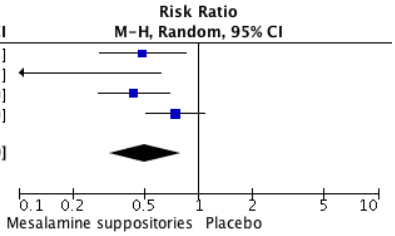


Footnotes
(1) disease is up to 20cm
(2) disease is < 20cm
(3) Watanabe study included patients with all different extents of disease this is a subgroup
(4) Disease is < 15cm

eFigure 43. PICO#9 – Efficacy of 5-ASA suppositories vs. placebo for INDUCTION of remission in patients with mild-moderate ulcerative proctitis.

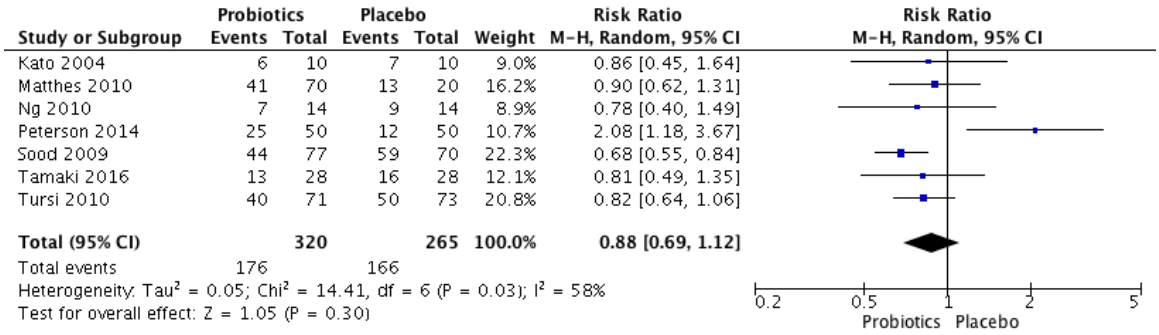
Study or Subgroup	Mesalamine suppositories Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
D'albasio 1998 (1)	17	76	16	35	27.8%	0.49 [0.28, 0.85]
D'arienzo 1990 (2)	1	15	11	15	5.1%	0.09 [0.01, 0.62]
Hanauer 2000	12	31	31	35	31.8%	0.44 [0.28, 0.69]
Marteau 1998	22	48	29	47	35.3%	0.74 [0.51, 1.09]
Total (95% CI)		**170**		**132**	**100.0%**	**0.50 [0.32, 0.79]**
Total events	52		87			

Heterogeneity: Tau² = 0.12; Chi² = 7.38, df = 3 (P = 0.06); I² = 59%
Test for overall effect: Z = 2.96 (P = 0.003)

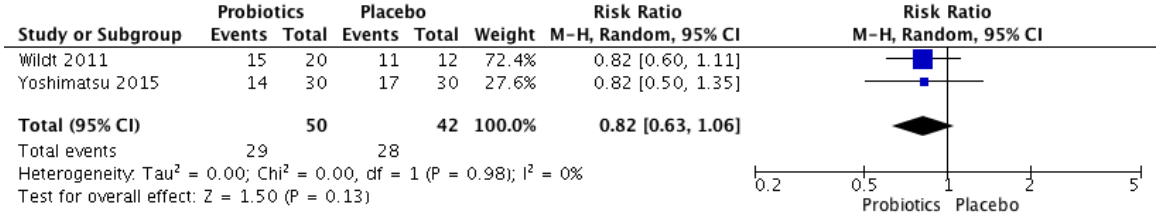


Footnotes
(1) Combined the two doses of 1g and 0.5g suppositories
(2) Includes proctitis n=17 and ps n=13

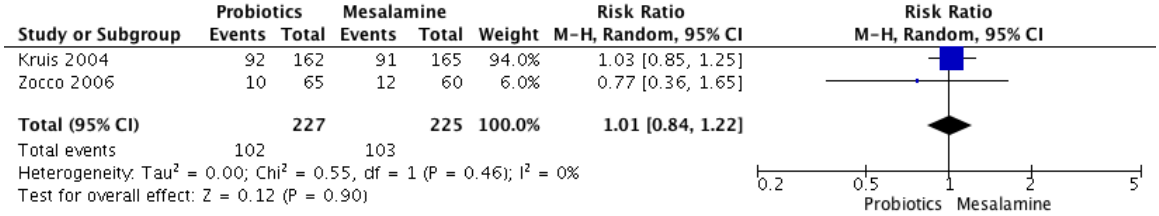
eFigure 44. PICO#9 – Efficacy of 5-ASA suppositories vs. placebo for MAINTENANCE of remission in patients with mild-moderate ulcerative proctitis.



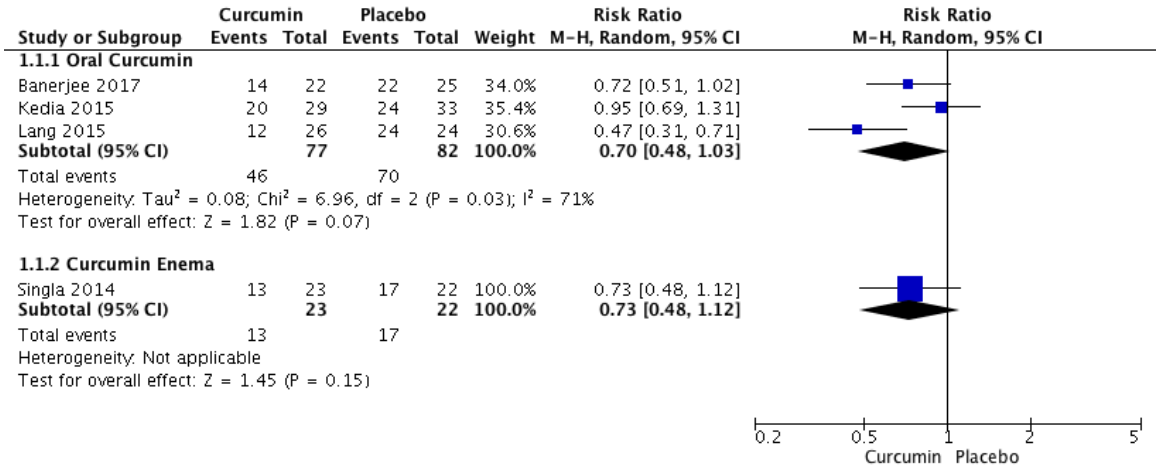
eFigure 45. PICO#10 – Efficacy of probiotics vs. placebo for INDUCTION of remission in patients with mild-moderate ulcerative colitis.



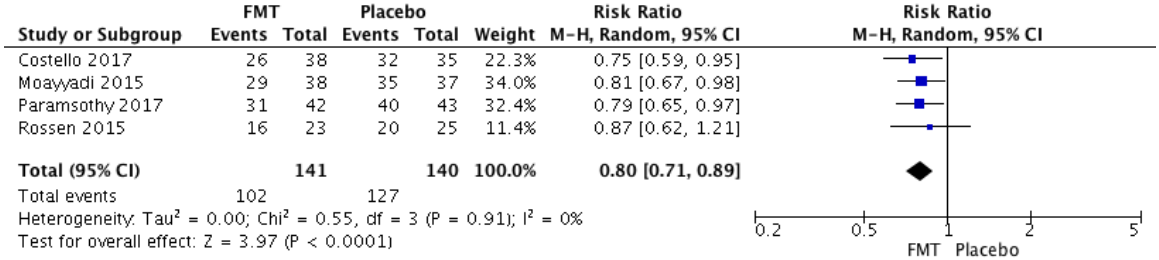
eFigure 46. PICO#10 – Efficacy of probiotics vs. placebo for MAINTENANCE of remission in patients with mild-moderate ulcerative colitis.



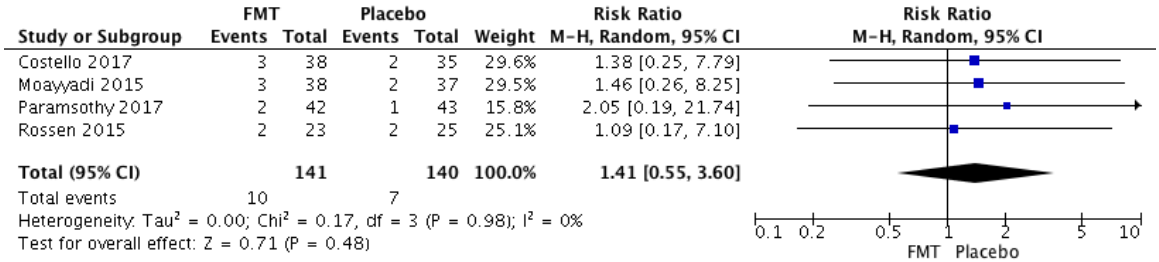
eFigure 47. PICO#10 – Efficacy of probiotics vs. mesalamine for MAINTENANCE of remission in patients with mild-moderate ulcerative colitis.



eFigure 48. PICO#11 – Efficacy of curcumin vs. placebo for INDUCTION of remission in patients with mild-moderate ulcerative colitis.



eFigure 49. PICO#12 – Efficacy of fecal microbiota transplantation vs. placebo for INDUCTION of remission in patients with mild-moderate ulcerative colitis.



eFigure 50. PICO#12 – Safety of fecal microbiota transplantation vs. placebo for INDUCTION of remission in patients with mild-moderate ulcerative colitis.