

Supplementary information

Effectiveness and Tolerability of Different Recommended Doses of PPIs and H₂RAs in GERD: Network Meta-Analysis and GRADE System

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Supplementary Appendix S1

Appendix S1. Search strategies

Supplementary Appendix S1

Search strategies

We will search the electronic database included the PubMed, Embase, Scopus, and the Cochrane Library published up to 1 Sep 2016, then addition to search the ClinicalTrials.gov and FDA website as supplement. Follow, we will provide the search strategies of PubMed electronic database.

PubMed:

#1 Gastroesophageal Reflux[mh]

#2 Gastric Acid Reflux

#3 Esophageal Reflux

#4 GERD

#5 Gastro-oesophageal Reflux

#6 Acid reflux

#7 Reflux

#8 RE

#9 Nonerosive reflux oesophagitis

#10 NERD

#11 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

#12 Proton pump inhibitors

#13 Esomeprazole

#14 Nexium

#15 #13 OR #14

#16 Lansoprazole

#17 2-(((3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl)methyl)sulfinyl)benzimidazole

#18 Bamalite

#19 Lansol

#20 Lanzor

#21 Prezal

#22 Monolitum

#23 Opiren

#24 Prevacid

#25 Ogastro

#26 Pro Ulco

#27 Promeco

#28 Takepron

#29 Ulpax

#30 Zoton

#31 AG 1749

#32 AG-1749

#33 AG1749

#34 Agopton

#35 Ogast

#36 #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR
#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35

#37 Omeprazole

#38 Prilosec

#39 H 168-68

#40 H 168 68

#41 H 16868

#42 #37 OR #38 OR #39 OR #40 OR #41

#43 Pantoprazole

#44 SK and F 96022

#45 SKF-96022

#46 SK and F-96022

#47 Protonix

#48 BY 1023

#49 BY-1023

#50 #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49

#51 Rabeprazole

#52 2-((4-(3-methoxypropoxy)-3-methylpyridin-2-yl)methylsulfinyl)-1H-benzimidazole

#53 Dexrabeprazole

#54 E 3810

#55 E3810

#56 Pariet

#57 Aciphex

58 LY-307640

#59 LY 307640

#60 LY307640

#61 #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60

#62 Histamine H2 antagonists

#63 Receptor Blockaders, H2

#64 Blockaders, Histamine H2 Receptor

#65 Histamine H2 Receptor Blockaders

#66 Histamine H2 Blockers

#67 Blockers, Histamine H2

#68 H2 Blockers, Histamine

#69 Receptor Antagonists, Histamine H2

#70 Histamine H2 Receptor Antagonists

#71 Antagonists, Histamine H2

#72 H2 Antagonists, Histamine

#73 H2 Receptor Blockaders

#74 Blockaders, H2 Receptor

#75 Antihistaminics, H2

#76 H2 Antihistaminics

#77 H2RAs

#78 #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR

#73 OR #74 OR #75 OR #76 OR #77
#79 Cimetidine
#80 Eureceptor
#81 Altramet
#82 SK and F-92334
#83 SK and F 92334
#84 SK and F92334
#85 SKF-92334
#86 SKF 92334
#87 SKF92334
#88 Tagamet
#89 Biomet
#90 Histodil
#91 Biomet400
#92 N-Cyano-N'-methyl-N''-(2-(((5-methyl-1H-imidazol-4-yl)methyl)thio)ethyl) guanidine
#93 #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR
#90 OR #91 OR #92
#94 Famotidine
#95 YM-11170
#96 YM 11170
#97 YM11170
#98 Pepcid
#99 Famotidine Hydrochloride
#100 MK-208
#101 MK 208
#102 MK208
#103 #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102
#104 Nizatidine
#105
N-(2-(((2-((Dimethylamino)methyl)-4-thiazolyl)methyl)thio)ethyl)-N'-methyl-2-nitro-1,1-ethene#10
0 nediamine
#106 LY-139037
#107 LY 139037
#108 LY139037
#109 Axid
#110 #104 OR #105 OR #106 OR #107 OR #108 OR #109
#111 Ranitidine
#112
N(2-(((5-((Dimethylamino)methyl)-2-furanyl)methyl)thio)ethyl)-N'-methyl-2-nitro-1,1-ethenedia
mine
#113 Ranitidin
#114 Biotidin
#115 Ranisen
#116 Sostril

#117 Zantac
#118 Zantic
#119 AH-19065
#120 AH 19065
#121 AH19065
#121 #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120
OR #121
#122 #12 OR #15 OR #36 OR #42 OR #50 OR #61 OR #78 OR #93 OR #103 OR #110 OR #121
#123 randomized controlled trial [pt]
#124 controlled clinical trial [pt]
#125 randomized controlled trials [mh]
#126 random allocation [mh]
#127 double-blind method [mh]
#128 single-blind method [mh]
#129 clinical trial [pt]
#130 clinical trials [mh]
#131 "clinical trial" [tw]
#132 #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40
#134 singl* [tw]
#135 doubl* [tw]
#136 trebl* [tw]
#137 tripl* [tw]
#138 #134 OR #135 OR #136 OR #137
#139 mask* [tw]
#140 blind* [tw]
#141 #139 OR #140
#142 #138 AND #141
#143 -placebos [mh]
#144 placebo* [tw]
#145 random* [tw]
#146 research design [mh:noexp]
#147 comparative study [pt]
#148 evaluation studies [mh]
#149 follow-up studies [mh]
#150 prospective studies [mh]
#151 control* [tw]
#152 prospective* [tw]
#153 volunteer* [tw]
#154 #143 OR #144 OR #145 OR #146 OR #147 OR #148 OR #149 OR #150 OR #151 OR #152
OR #153
#155 #132 OR #142 OR #154
#156 #11 AND #122 AND #155

Supplementary eTables Legends

Supplementary Table S1. Summary of included clinical trials and patient characteristics

Supplementary Table S2. Adjusting the confounding factors in all outcomes

Supplementary Table S3. Adjusting four selective design biases and model parameters for all outcomes

Supplementary Table S4. The results of compare models in all outcomes

Supplementary Table S5. The network results and the pairwise comparison results for healing
(Separate Excel documents)

Supplementary Table S6. The network results and the pairwise comparison results for relief of symptoms (Separate Excel documents)

Supplementary Table S7. The network results and the pairwise comparison results for tolerance
(Separate Excel documents)

Supplementary Table S8. The baseline results for the network analysis comprising sensitivity analyses

Supplementary Table S9. Estimates of effects and quality ratings for comparison of recommended doses of different drugs from the main outcome (healing) based on the GRADE system

Supplementary Table S1 Summary of included clinical trials and patient characteristics

Study	Year	County	Drugs, dose, usage	Total (female)	Age (Mean \pm SD or range)	Level of disease from endoscopy or symptoms	Mean courses of disease	Follow-up from start of treatment (weeks)	Might be sponsor drugs	ITT/PP	Healing	Relief of symptoms	Tolerance
Kim ¹	2015	Korea	Omeprazole 20mg QD; Famotidine 20mg BID	167(46); 162(48)	50(20-74); 53(24-74)	Reflux esophagitis grade:A-D	≥ 2 weeks	8	Omeprazole	ITT	126/147; 92/145	87/147; 58/144	10/147; 10/147
Peura a ²	2014	USA	Placebo; Esomeprazole 20mg QD	163(95); 168(104)	45.9 \pm 12.6; 43.6 \pm 12.2	Heartburn: Mild; Moderate; Severe	≥ 4 weeks	2	Esomeprazole	ITT	NA	54/163; 77/168	11/169; 8/171
Peura b ²	2014	USA	Placebo; Esomeprazole 20mg QD	158(82); 162(86)	42.8 \pm 13.2; 41.6 \pm 14.0	Heartburn: Mild; Moderate; Severe	≥ 4 weeks	2	Esomeprazole	ITT	NA	52/158; 78/162	19/171; 19/170
Moraes-Filho ³	2014	Brazil	Esomeprazole 40mg QD; Pantoprazole 40mg QD	288(144); 290(162)	42.3 \pm 12.6; 43.1 \pm 11.5	LA: A-D	NA	8	Esomeprazole; Pantoprazole	ITT	253/279; 246/284	227/264; 252/275	85/288; 71/290
Cho ⁴	2012	Korea	Pantoprazole 20mg QD; Pantoprazole 40mg QD	67(22); 62(13)	51.2 \pm 12.6; 49.5 \pm 13.3	LA: A-C	NA	8	None	PP	63/67; 60/62	NA	8/75; 12/74
Kobeissy ⁵	2012	USA	Ranitidine 150mg BID; Rabeprazole 10mg BID	39(23); 44(28)	45.1 \pm 15.3; 45.4 \pm 15.2	NA	3.9(4.2); 4.7(7.8) years	4	None	ITT	NA	17/39; 20/44	3/39; 4/44
Tan ⁶	2011	Hong Kong	Placebo; Esomeprazole 40mg QD	175(123)	48.5; 48.3	A Chinese GerdQ reflux score \geq 12	NA	8	Esomeprazole	ITT	NA	29/78; 44/77	12/90; 8/85
Laine a ⁷	2011	Mix	Rabeprazole 50mg QD; Esomeprazole 40mg QD	524(202); 531(206)	48.0 \pm 13.4; 49.0 \pm 13.1	LA: C,D	≥ 3 months	8	Rabeprazole	ITT	419/524; 398/531	253/524; 256/531	45/524; 40/531
Laine b ⁷	2011	Mix	Rabeprazole 50mg QD; Esomeprazole 40mg QD	528(179); 537(195)	51.0 \pm 12.8; 49.1 \pm 13.4	LA: C,D	≥ 3 months	8	Rabeprazole	ITT	409/528; 421/537	281/528; 282/537	43/528; 42/537
Kinoshita ⁸	2011	Japan	Placebo; Rabeprazole 5mg QD; Rabeprazole 10mg QD	91(51); 93(55); 101(51)	49.7 \pm 17.0; 46.3 \pm 15.3; 46.8 \pm 15.7	Heartburn: Mild; Moderate; Severe	NA	4	Rabeprazole	ITT	NA	31/91; 44/93; 56/101	5/93; 5/93; 4/102
Ohara ⁹	2010	Japan	Placebo; Famotidine 20mg BID;	158(32); 150(38)	52.9; 52.6	LA: A,B	NA	8	None	PP	14/145; 86/140	NA	24/169; 23/163
Johnson ¹⁰	2010	USA	Placebo; Esomeprazole 20mg QD	125(85); 137(89)	46.8 \pm 12.9; 47.0 \pm 11.7	NA	≥ 3 months	4	Esomeprazole	ITT	NA	9/125; 45/137	8/133; 6/143

Zheng ¹¹	2009	China	Omeprazole 20mg QD; Pantoprazole 40mg QD;	68(35); 69(35);	57.9±14.1; 57.8±13.2;	LA: A-D	NA	8	None	PP	57/65; 60/67;	NA	3/68; 2/69; 2/69;
			Lansoprazole 30mg QD; Esomeprazole 40mg QD	69(34); 68(35)	58.1±13.0; 57.4±12.8						61/67; 62/65		3/68
Peura ¹²	2009	USA	Placebo; Lansoprazole 15mg QD; Lansoprazole	277(181); 291(173);	47.4±13.7; 48.2±14.5;	Heartburn: Mild;	NA	2	Lansoprazole	ITT	NA	82/277; 145/291;	12/277; 13/291;
			30mg QD	284(183)	48.8±14.1								Moderate; Severe
Kushner a ¹³	2009	USA	Placebo; Lansoprazole 15mg QD	282(182); 282(178)	48.1(13.8); 46.3(13.8)	Heartburn: Mild;	4.0(1.6);	2	Lansoprazole	ITT	NA	NA	11/282; 13/282
Kushner b ¹³	2009	USA	Placebo; Lansoprazole 15mg QD	282(190); 288(190)	47.6(13.2); 49.5(14.1)								Moderate; Severe
Eggleston ¹⁴	2009	Australia	Rabeprazole 20mg QD; Esomeprazole 20mg QD;	464(264); 459(208);	45.8±0.68; 46.2±0.69;	NA	≥ 3 months	4	Rabeprazole;	ITT	NA	405/464; 414/459;	69/464; 59/459;
			Esomeprazole 40mg QD	469(208)	48±0.68								Esomeprazole
Uemura ¹⁵	2008	Japan	Placebo; Omeprazole 10mg QD; Omeprazole	92(19); 96(49);	42.4±15.4; 44.4±16.2;	Heartburn: Mild;	NA	4	Omeprazole	ITT	NA	22/95; 44/96; 43/93	7/95; 3/96; 3/93
		20mg QD	93(40)	43.8±16.4	Moderate; Severe								
Hongo ¹⁶	2008	Japan	Placebo; Famotidine 20mg QD; Famotidine 40mg	177(97); 177(97);	47.3; 47.4; 46.3	Heartburn: Mild	NA	8	Famotidine	ITT	NA	106/177; 120/177;	11/177; 9/177;
		QD	174(87)		132/174								9/174
Pilotto ¹⁷	2007	Italy	Omeprazole 20mg QD; Pantoprazole 40mg QD;	80(36); 80(41);	77.9±6.4; 76.8±6.1;	SM: 1-4	NA	8	None	ITT	60/80; 68/80;	64/80; 62/80;	6/80; 3/80; 5/80;
			Lansoprazole 30mg QD; Rabeprazole 20mg QD	80(44); 80(43)	77.8±9.2; 77.0±9.5								72/80; 71/80
Männikes ¹⁸	2007	Germany	Pantoprazole 20mg QD; Esomeprazole 20mg QD	263(159); 266(167)	51.2±14.2; 52.6±15.4	LA: A-D	NA	4	Pantoprazole;	ITT	NA	211/263; 211/266	41/263; 37/266
Glatzel ¹⁹	2007	Germany	Pantoprazole 40mg QD; Esomeprazole 40mg QD	284(125); 277(136)	52.6±14.5; 54.0±14.3	LA: A-D	NA	4	Pantoprazole;	ITT	NA	NA	40/284; 45/277
										Esomeprazole			
Bardhan ²⁰	2007	Germany	Pantoprazole 40mg QD; Esomeprazole 40mg QD	288(139); 293(139)	53±14; 54±14	LA: A-D	NA	8	Pantoprazole;	ITT	248/288;	222/288; 220/293	NA
Bytzer ²¹	2006	Europe	Omeprazole 20mg QD; Rabeprazole 20mg QD	359(162); 358(181)	51.7(19-81);	LA: A-D	84.2(3.3-729.3);	1	Omeprazole;	ITT	NA	NA	178/359;
					50.6(18-87)								73.7(3.1-626.4)
Lightdale ²²	2006	USA	Esomeprazole 20mg QD; Omeprazole 20mg QD	588(216); 588(212)	44.7(13.2); 45.3(13.0)	LA: A-D	NA	8	Esomeprazole;	PP	508/588;	NA	9/588; 10/588

										Omeprazole		484/588		
Schmitt ²³	2006	USA	Esomeprazole 40mg QD; Omeprazole 20mg QD	576(230); 572(237)	47.1(13.3); 46.2(13.6)	LA: A-D	NA	8		Esomeprazole; Omeprazole	PP	501/576; 491/572	NA	18/576; 10/572
Pace ²⁴	2005	Italy	Omeprazole 20mg QD; Rabeprazole 20mg QD	272(88); 277(87)	47.1±14.9; 47.4±14.2	SM: 0-3	56.6(67.2); 51.5(59.0)	8		None	PP	231/237; 228/237	NA	22/277; 25/283
Kahrilas ²⁵	2005	USA	Placebo; Rabeprazole 20mg QD	126(86); 126(89)	44.0±0.99; 43.1±1.04	Modified HD: 0,1	7.8(0.63)	4		None	ITT	NA	24/126; 66/126	15/132; 14/129
Johnson ²⁶	2005	USA	Placebo; Esomeprazole 20mg QD; Esomeprazole 40mg QD	221(131); 220(132); 209(125)	46.5±13.6; 46.8±14.0; 46.3±14.6	Heartburn: Mild; Moderate; Severe	≥ 3 months	4		Esomeprazole	ITT	NA	18/221; 102/220; 98/209	17/229; 8/226; 8/220
Fock ²⁷	2005	Asia	Rabeprazole 10mg QD; Esomeprazole 20mg QD	63(25); 64(37)	39.3±11.2; 38.4±10.0	NA	3.2(4.2); 3.9(4.7) years	4		None	ITT	NA	37/63; 27/64	23/63; 30/64
Fennerty ²⁸	2005	USA	Esomeprazole 40mg QD; Lansoprazole 30mg QD	498(171); 501(168)	47.3±13.2; 47.1±12.9	LA: C,D	NA	8		Esomeprazole	ITT	386/498; 367/501	344/478; 307/483	32/499; 30/502
Van Zyl ²⁹	2004	Germany and South Africa	Ranitidine 300mg QD; Pantoprazole 20mg QD	171(86); 167(81)	49.7±14.2; 48.1±15.0	NA	≥ 3 months	4		Pantoprazole	ITT	NA	114/167; 74/171	14/171; 18/167
Gillessen ³⁰	2004	Germany	Pantoprazole 40mg QD; Esomeprazole 40mg QD	113(49); 114(57)	53±15; 54±14	NA	NA	8		None	ITT	69/113; 70/114	57/113; 54/114	19/113; 11/114
Armstrong a ³¹	2004	Canada, England and Ireland	Omeprazole 20mg QD; Esomeprazole 20mg QD; Esomeprazole 40mg QD	434(247); 423(240); 425(242)	48.3(19-78); 48.0(18-80); 48.4(19-79)	NA	≥ 6 months	4		Omeprazole; Esomeprazole	ITT	NA	252/434; 256/423; 241/425	NA
Armstrong b ³¹	2004	France, Germany and	Omeprazole 20mg QD; Esomeprazole 40mg QD	346(190); 347(193)	50.0(19-83); 50.6(21-77)	NA	≥ 6 months	4		Omeprazole; Esomeprazole	ITT	NA	235/346; 244/347	NA

Armstrong c ³¹	2004	Switzerland	Omeprazole 20mg QD; Esomeprazole 20mg QD	334(166); 336(161)	48.5(19-79);	NA	≥ 6 months	4	Omeprazole;	ITT	NA	199/334; 208/336	NA
		Denmark, Finland, Norway and Sweden			48.5(20-79)				Esomeprazole				
Scholten ³²	2003	Germany	Pantoprazole 40mg QD; Esomeprazole 40mg QD	112(43); 105(48)	54.7±15.1; 52.6±13.8	LA: B,C	NA	5	Pantoprazole; Esomeprazole	ITT	NA	80/112; 74/105 *	13/112; 10/105
Katz a ³³	2003	USA	Placebo; Esomeprazole 20mg QD; Esomeprazole 40mg QD	124(62.9); 121(59.5); 123(61.0)	46(19-82); 47(21-75); 47(20-78)	Heartburn: Mild; Moderate; Severe	≥ 6 months	4	None	ITT	NA	17/123; 41/121; 41/124 *	6/123; 9/121; 9/124
Katz b ³³	2003	USA	Placebo; Esomeprazole 20mg QD; Esomeprazole 40mg QD	118(57.6); 113(69.9); 118(64.4)	47(21-77); 46(19-75); 45(19-77)	Heartburn: Mild; Moderate; Severe	≥ 6 months	4	None	ITT	NA	14/118; 47/113; 43/118 *	12/118; 11/113; 4/118
Kürner ³⁴	2003	Europe	Omeprazole 40mg QD; Pantoprazole 40mg QD	332(146); 337(121)	53.8±14.6; 53.7±14.3	SM: 2,3	NA	8	Omeprazole, Pantoprazole	ITT	220/332; 220/337	250/270; 257/282	4/332; 3/337
Kao ³⁵	2003	Taiwan	Omeprazole 40mg QD; Esomeprazole 20mg QD	50(15); 50(16)	49.2; 49.8	LA: A,B	NA	4	None	ITT	NA	34/50; 23/50	4/50; 5/50
Adachi ³⁶	2003	Japan	Omeprazole 20mg QD; Rabeprazole 20mg QD	30(15); 30(15)	67.3±11.7; 65.3±13.0	LA: A-D	NA	8	None	ITT	NA	NA	2/30; 2/30
Mulder ³⁷	2002	Netherland	Omeprazole 20mg QD; Pantoprazole 40mg QD; Lansoprazole 30mg QD	151(63); 154(60); 156(66)	51.6±15.0; 51.2±14.4; 50.8±14.5	Modified SM: 1-4	NA	8	None	ITT	NA	131/151; 125/154; 139/156 *	7/151; 5/154; 11/156
Miner ³⁸	2002	USA	Placebo; Rabeprazole 10mg QD; Rabeprazole 20mg QD	70(46); 65(37); 68(43)	46.1±1.2; 44.4±1.5; 45.5±1.3	HD: 0,1	NA	4	Rabeprazole	ITT	NA	22/68; 36/64; 38/67	NA
Meneghelli ³⁹	2002	Brazil	Ranitidine 150mg BID; Pantoprazole 40mg QD	128(40); 128(48)	47.0(21-74); 46.5(19-82)	SM: 2,3	NA	8	Ranitidine, Pantoprazole	ITT	52/128; 96/128	60/113; 99/109 *	18/128; 21/128
Kovacs ⁴⁰	2002	USA	Nizatidine 150mg BID; Pantoprazole 20mg BID; Pantoprazole 40mg BID	221(66)	50.1±13.4; 47.8±12.9; 49.4±13.8	HD 2-4	NA	8	Nizatidine, Pantoprazole	ITT	29/70; 57/72; 58/70	NA	NA
Holtmann ⁴¹	2002	Europe	Omeprazole 40mg QD; Rabeprazole 20mg QD	116(36); 118(44)	51.0(18-79);	SM: 2,3	2.51(0-19);	8	Omeprazole,	ITT	NA	NA	9/126; 12/125

Author	Year	Country	Intervention	Control	Primary Outcome (Mean ± SD)	Secondary Outcome (Mean ± SD)	Study Design	Duration (months)	Intervention	Control	Primary Outcome (n/N)	Secondary Outcome (n/N)	Other Outcomes
					52.9(20-80)	2.55(0-21)			Rabeprazole				
								years					
Castell ⁴²	2002	USA	Lansoprazole 30mg QD; Esomeprazole 40mg QD	2627(1116); 2624(1120)	47.4±13.1; 47.0±13.0	LA: A-D	NA	4	None	ITT	2324/2617; 2430/2624	1575/2627; 1650/2624 *	NA
Richter ⁴³	2001	USA	Omeprazole 20mg QD; Lansoprazole 30 mg QD	1756(772); 1754 (747)	46.9±13.6; 47.8±13.8	SM: 1-4	NA	8	Omeprazole, Lansoprazole	ITT	NA	1457/1756; 1479/1754	78/1756; 75/1754
Richter ⁴⁴	2001	USA	Omeprazole 20mg QD; Esomeprazole 40mg QD	1209(449); 1216(496)	NA	LA: A-D	NA	8	Omeprazole, Esomeprazole	ITT	1018/1209; 1139/1216	929/1209; 1036/1216	54/1209; 55/1216
Paul ⁴⁵	2001	USA	Placebo; Nizatidine 75mg BID	496(262); 498(277)	43.5(16-81); 42.3(16-81)	NA	≥ 3 months	2	None	ITT	NA	119/496; 184/498 *	NA
Kaspari ⁴⁶	2001	Germany	Ranitidine 150mg BID; Pantoprazole 20mg QD	175(88); 181(97)	48.8±13.2; 48.5±13.8	SM: 0,1	≥ 3 months	4	Ranitidine, Pantoprazole	ITT	NA	91/132; 124/141	42/175; 37/181
Bardhan ⁴⁷	2001	Europe	Omeprazole 20mg QD; Pantoprazole 20mg QD	161(58); 166(79)	45.2±14.4; 44.6±13.3	SM: 1	NA	8	None	ITT	142/161; 134/166	140/161; 138/166	30/161; 33/166
Armstrong ⁴⁸	2001	Canada	Nizatidine 150mg BID; Pantoprazole 40 mg QD	102(51); 106(49)	47.6±14.1; 47.1±14.0	SM: 0-3	≥ 6 months	4	Nizatidine	ITT	73/109; 95/111	37/109; 67/111 *	15/109; 10/111
Van Zyl ⁴⁹	2000	South Africa	Ranitidine 300mg QD; Pantoprazole 20mg QD	100(44); 101(40)	18-82	NA	NA	8	Ranitidine, Pantoprazole	ITT	69/100; 84/101	45/89; 74/88	16/100; 13/101
Richter ⁵⁰	2000	USA	Placebo; Omeprazole 10mg QD; Omeprazole 20mg QD	123(56); 118(53); 118(57)	49.7; 50.0; 49.5	NA	≥ 12 months	4	Omeprazole	ITT	NA	28/123; 58/118; 87/118 *	NA
Richter ⁵¹	2000	USA	Placebo; Pantoprazole 10mg QD; Pantoprazole 20mg QD; Pantoprazole 40mg QD	82(29); 174(63); 174(59); 173(52)	48.3±14.0; 49.6±13.9; 48.7±12.4; 49.3±13.6	HD: 1-4	NA	8	Omeprazole, Pantoprazole	ITT	102/174; 135/174; 152/173	NA	NA
Kahrilas ⁵²	2000	USA	Omeprazole 20mg QD; Esomeprazole 20mg QD; Esomeprazole 40mg QD	650(251); 656(265); 654(270)	46.5±13.5; 45.3±13.3; 44.8±13.0	LA: A-D	NA	8	Omeprazole, Esomeprazole	ITT	565/650; 590/656;	357/624; 382/626; 402/621	51/650; 60/654; 48/656

Author	Year	Country	Intervention	Control	Primary Outcome	Secondary Outcome	Duration	Sample Size	Comparator	Design	Number of Events	Relative Risk (95% CI)	Number of Events
Fass ⁵³	2000	USA	Omeprazole 40 mg QD; Lansoprazole 30mg BID	46(2); 44(4)	57.8±14.7; 57.8±12.1	NA	≥ 3 months	6	Omeprazole, Lansoprazole	ITT	NA	8/46; 10/44 *	4/50; 2/46
Farley ⁵⁴	2000	UK	Ranitidine 150mg QID; Rabeprazole 20mg QD	169(56); 169(51)	50.4±14.2; 51.4±14.9	Modified HD: 2-4	NA	8	Ranitidine, Rabeprazole	ITT	112/169; 146/167	108/158; 127/161	12/169; 15/167
Delchier ⁵⁵	2000	Europe	Omeprazole 20mg QD; Rabeprazole 10mg QD; Rabeprazole 20mg BID	103(63); 103(72); 104(57)	53±15.1; 52±14.3; 55±15.7	HD: 2-4	NA	8	Omeprazole, Rabeprazole	ITT	97/103; 94/103; 95/104	NA	17/104; 21/103; 25/104
Richter ⁵⁶	1999	USA	Placebo; Lansoprazole 15mg QD; Lansoprazole 30mg QD	43(25); 80(41); 86(47)	46.4±12.5; 44.9±14.9; 43.4±13.5	NA	NA	4-8	Lansoprazole	ITT	NA	NA	7/43; 5/80; 8/86
Pappa ⁵⁷	1999	USA	Placebo; Ranitidine 25mg QID; Ranitidine 75mg QID	494(177); 504(178); 491(156)	47.3(18-83); 46.7(18-84); 47.4(18-87)	NA	≥ 3 months	2	Ranitidine	ITT	NA	197/470; 245/480; 275/482	24/494; 24/504; 9/491
Pappa ⁵⁸	1999	USA	Placebo; Ranitidine 25mg QD; Ranitidine 75mg QD; Ranitidine 125mg QD	143(48); 144(49); 143(47); 147(58)	41.0±1.06; 42.0±1.09; 39.5±1.09; 40.8±1.02	NA	≥ 3 months	4	Ranitidine	ITT	NA	72/143; 97/144; 102/143; 104/147	3/143; 3/144; 4/143; 5/147
Maton ⁵⁹	1999	USA	Ranitidine 150mg BID; Omeprazole 20mg QD	161(90); 156(91)	45.8; 44.7	NA	≥ 6 months	8	Ranitidine, Omeprazole	ITT	NA	71/144; 104/148	15/161; 8/156
Jones ⁶⁰	1999	UK	Omeprazole 10mg QD; Lansoprazole 15mg QD	279(143); 283(143)	46; 47	NA	NA	4	Omeprazole, Lansoprazole	ITT	NA	142/279; 167/283 *	50/279; 48/283
Jansen ⁶¹	1999	Netherland	Ranitidine 300mg BID; Lansoprazole 30mg QD	65(24); 68(26)	53.3±13.7; 53.7±14.8	NA	NA	8	None	ITT	43/65; 62/68	43/65; 60/68	2/65; 7/68
Festen ⁶²	1999	Netherland	Ranitidine 300mg BID; Omeprazole 20mg QD	224(109); 222(104)	49.8±13.9; 51.1±14.5	SM: 1,2	NA	8	Ranitidine, Omeprazole	ITT	NA	112/224; 165/222	29/224; 28/222
Galmiche ⁶³	1998	France and Germany	Placebo; Cimetidine 200mg QD; Ranitidine 75mg QD	270(161); 515(306); 504(285)	49.9±0.9; 50.6±0.7; 48.0±0.6	SM: 0,1	5.5±0.4; 5.6±0.3; 5.1±0.3 years	2	Cimetidine, Ranitidine	ITT	NA	208/270; 417/515; 423/504	52/270; 83/515; 64/504
Earnest ⁶⁴	1998	USA	Placebo; Lansoprazole 15mg QD; Lansoprazole	NA	NA	NA	NA	8	Lansoprazole	ITT	31/66; 60/72;	NA	7/66; 6/72; 6/71;

			30mg QD; Lansoprazole 60mg QD								62/71; 70/79	8/79	
Detmer ⁶⁵	1998	Germany	Ranitidine 300mg QD; Pantoprazole 20mg QD	104(39); 105(41)	54(21-82); 47(19-80)	SM: 1	NA	8	Pantoprazole	ITT	63/104; 78/105	55/84; 68/85	18/104; 18/105
Venables ⁶⁶	1997	UK	Ranitidine 150mg BID; Omeprazole 10mg QD; Omeprazole 20mg QD	326(50); 338(51); 320(48)	50±14; 51±15; 51±14	Modified SM: 0-1	NA	4	Ranitidine, Omeprazole	ITT	NA	131/326; 167/338; 200/330	NA
Galmiche ⁶⁷	1997	Europe	Omeprazole 10mg QD; Omeprazole 20mg QD	144(89); 141(78)	51±15; 50±16	Heartburn: Mild; Moderate; Severe	≥ 3 months	8	Omeprazole	ITT	NA	102/144; 112/141	NA
Bate ⁶⁸	1997	UK	Cimetidine 400mg QD; Omeprazole 20mg QD	109(37); 112(48)	46±14; 49±13	SM: 0-3	NA	4	Cimetidine, Omeprazole	ITT	NA	34/109; 74/112	22/109; 14/112
Silver ⁶⁹	1996	USA	Placebo; Ranitidine 300 mg BID; Ranitidine 150mg QID	251(81); 260(83); 261(91)	47.9; 48.6; 48.8	HD: 2-4	NA	8	Ranitidine	ITT	79/217; 118/230; 145/235	NA	51/251; 38/260; 40/261
Rensburg ⁷⁰	1996	Germany	Pantoprazole 40mg QD; Pantoprazole 80mg QD	97(40); 95(38)	46(18-88); 46(21-89)	SM: 2,3	NA	8	Pantoprazole	ITT	82/97; 82/95	83/86; 85/87	NA
Mee ⁷¹	1996	UK, Ireland	Lansoprazole 30mg QD; Omeprazole 20mg QD	NA	18-80	SM: 1-4	NA	8	None	ITT	226/300; 216/304	NA	75/300; 75/304
Mccarty-Dawson 72	1996	USA	Cimetidine 800mg BID; Ranitidine 150mg BID; Ranitidine 150mg QID	231(89); 236(99); 229(84)	46.8; 48.4; 46.5	HD: 2-4	NA	8	Cimetidine, Ranitidine	ITT	120/231; 132/236; 153/229	NA	43/231; 32/236; 20/229
Castell ⁷³	1996	UK	Placebo; Omeprazole 20mg QD; Lansoprazole 15mg QD; Lansoprazole 30mg QD	213(71); 431(171); 218(73); 421(133)	47.6(18-80); 47.5(19-78); 45.8(20-82); 48.6(18-84)	HD: 2-4	NA	8	None	ITT	68/213; 375/431; 164/218; 367/421	NA	15/213; 13/431; 10/218; 20/422
Bate ⁷⁴	1996	Europe	Placebo; Omeprazole 20mg QD	111(69); 98(56)	51±14; 47±14	SM: 0,1	NA	4	Omeprazole	ITT	NA	21/111; 56/98 *	22/111; 18/98
Robinson ⁷⁵	1995	USA	Ranitidine 150mg BID; Lansoprazole 30mg QD	127(48); 115(43)	NA	HD: 2-4	NA	8	None	ITT	83/127; 102/115	NA	4/127; 1/115
Mossner ⁷⁶	1995	Germany	Omeprazole 20mg QD; Pantoprazole 40mg QD	95(29); 191(58)	55(21-81); 53(19-89)	SM: 2,3	NA	8	None	PP	81/86;	81/86; 149/165	1/95; 2/191

											153/170		
Koop ⁷⁷	1995	USA	Ranitidine 150mg BID; Pantoprazole 40mg QD	83(17); 166(97)	53; 53	SM: 2,3	NA	8	None	ITT	46/83; 122/166	35/83; 104/166	NA
Bardhan ⁷⁸	1995	UK	Ranitidine 150mg BID; Lansoprazole 30mg QD; Lansoprazole 60mg QD	77(22); 77 (27); 75(25)	49.3(19-74); 48(19-78); 47.9(18-74)	Reflux grades: 1-3	NA	8	None	ITT	37/77; 70/77; 59/75	30/77; 61/77; 54/75 *	20/77; 20/77; 16/75
Simon ⁷⁹	1993	USA	Ranitidine 150mg BID; Famotidine 20mg BID; Famotidine 40mg BID	172(65); 93(31); 175(61)	48.9; 52.2; 50.5	Modified SM: 2-4	NA	6	None	ITT	76/172; 48/93; 81/175	117/172; 56/93; 119/175 *	NA
Euler ⁸⁰	1993	USA	Placebo; Ranitidine 150mg QID; Ranitidine 300mg QID	116(34); 106(28); 106(23)	48.6±1.4; 46.3±1.5; 49.7±1.5	HD: 2-4	NA	8	Ranitidine	ITT	33/116; 73/106; 66/106	NA	37/116; 8/106; 12/106
Roufail ⁸¹	1992	USA	Placebo; Ranitidine 150mg QID; Ranitidine 300mg QID	113(28); 109(34); 120(38)	48.6±1.3; 49.3±1.4; 48.4±1.3	HD: 2-4	NA	8	None	ITT	30/113; 68/109; 73/120	NA	33/113; 15/109; 18/120
Cloud ⁸²	1992	USA and Canada	Placebo; Nizatidine 150mg BID; Nizatidine 300mg BID	178(67); 168(81); 169(77)	44.78; 44.78; 45.83	Endoscopically Grade: 1-4	NA	6	None	ITT	46/178; 69/168; 65/169	NA	45/178; 19/168; 26/169
Sabesin ⁸³	1991	USA	Placebo; Famotidine 20mg BID; Famotidine 40mg QD	66(27); 137(63); 135(56)	46.9±15.9; 47.3±13.7; 47.9±14.6	HD: 0-4	NA	6	None	ITT	4/66; 47/137; 39/135	26/66; 88/137; 99/135	22/66; 33/137; 37/135
Robinson ⁸⁴	1991	USA	Placebo; Famotidine 20mg BID; Famotidine 40mg QD	76(31); 158(85); 155(81)	44.5±13.0; 45.2±14.2; 44.2±14.7	HD: 0,1	NA	6	Famotidine	ITT	NA	29/76; 95/158; 71/155 *	NA
Riemann ⁸⁵	1991	Germany	Placebo; Cimetidine 200mg QID	60(35); 60(26)	47.1(18-73); 48.9(18-69)	Heartburn: Mild	≥ 30 months	2	None	ITT	NA	12/65; 22/60	0/65; 0/60
Quik ⁸⁶	1990	Europe	Placebo; Nizatidine 300mg QD; Nizatidine 300mg BID	107(40); 109(40); 109(37)	52±17; 53±16; 53±16	NA	≥ 3 months	6	None	ITT	28/107; 33/109; 44/109	NA	10/107; 11/109; 7/109

Palmer ⁸⁷	1990	USA	Placebo; Cimetidine 800mg BID	86(28); 93(26)	51±15; 50±16	NA	NA	6	None	ITT	17/86; 47/93	NA	27/86; 16/93
Lundell ⁸⁸	1990	Sweden	Ranitidine 300mg BID; Omeprazole 40mg QD	47(11); 51(15)	59.8±16.0; 58.1±16.2	SM: 2-4	NA	8	None	ITT	18/47; 44/51	15/47; 44/51 *	NA
Dehn ⁸⁹	1990	UK	Cimetidine 400mg QID; Omeprazole 40mg QD	36(8); 31(10)	39.6(24-78); 54(21-74)	Endoscopically Grade: 2-4	NA	8	None	PP	7/31; 20/31	16/30; 23/31	5/36; 3/31
Vantrappen ⁹⁰	1988	Europe	Ranitidine 150mg BID; Omeprazole 40mg QD	30(21); 31(23)	52.3(24-79); 55.4(26-79)	Endoscopically Grade: 2,3	NA	8	None	ITT	15/30; 25/31	11/30; 27/31	5/30; 6/31
Havelund ⁹¹	1988	Denmark	Ranitidine 150mg BID; Omeprazole 40mg QD	82(26); 80(32)	54.9(22-79); 53.7(24-79)	Endoscopically Grade: 1-3	NA	8	Ranitidine, Omeprazole	ITT	44/82; 69/80	NA	9/82; 5/80
Sontag ⁹²	1987	USA	Placebo; Ranitidine 150mg BID	118(42); 119(39)	48.2±1.40; 49.5±1.33	Endoscopy grade: Normal, Moderate, Severe	NA	6	Ranitidine	PP	29/71; 41/73	NA	32/150; 15/134

QD: Quaque die; BID: Bis in die; TID: Ter in die; QID: Quaque in die; A Chinese GerdQ reflux score⁹³: A 20-item GERD questionnaire in the Chinese language; LA⁹⁴: The Los Angeles grade; SM⁹⁵: The Savary-Miller criteria; HD⁹⁶: The Hetzel-Dent scale; ITT: Intention-to-treat data; PP: Per-protocol data; NA: Not available; *: Complete relief of symptoms.

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Supplementary Table S2 Adjusting the confounding factors in all outcomes

Confounding factors	Healing	Relief of symptoms	Tolerance
Area			
Europe	Ref	Ref	Ref
North America	0.674 (-0.324, 1.031)	-0.101(-0.886, 0.635)	-0.02(-0.371, 0.319)
Asia	1.244(-0.875, 3.954)	-0.448(-1.390, 0.432)	0.091(-0.500, 0.672)
Other/mix	-12.87(-66.25, 25.47)	-2.801(-3.157, 12.10)	-1.398(-20.7, 15.32)
σ	0.832	0.469	0.084
Gender			
Coefficient	-0.127(-0.225, -0.026)	-0.014(-0.036, 0.009)	0.010(-0.004, 0.021)
σ	0.941	0.462	0.076
Mean age			
Coefficient	-0.130(-0.372, 0.107)	0.029(-0.067, 0.131)	0.001(-0.060, 0.058)
σ	0.996	0.469	0.080
Level of disease from endoscopy			
Coefficient	-0.348(-4.953, 4.284)	NA	-0.006(-0.015, 0.005)
σ	1.013	NA	0.090
Level of disease from symptoms			
Coefficient	NA	1.275(-1.144, 3.741)	-0.008(-0.041, 0.240)
σ	NA	0.467	0.079
Degree of relieve symptoms			
Complete relief	NA	Ref	NA
Relief	NA	0.012(-0.517, 0.543)	NA
σ	NA	0.471	NA
Methodological quality score			
Coefficient	-1.006(-1.808, -0.213)	-0.048(-0.233, 0.141)	0.085(-0.049, 0.218)
σ	0.943	0.469	0.081
Year of publication			
Coefficient	-0.046(-0.156, 0.062)	-0.051(-0.088, 0.012)	0.028(0.008, 0.049)
σ	1.005	0.433	0.064
Pharmaceutical industry sponsorship			
None	Ref	Ref	Ref
Sponsorship	0.811(-0.341, 1.955)	-0.240(-0.808, 0.353)	0.100(-0.215, 0.408)
σ	0.990	0.464	0.075
ITT/PP			
ITT	Ref	Ref	Ref
PP	1.249(-0.063, 2.565)	-0.698(-1.847, 0.460)	-0.087(-0.626, 0.440)
σ	0.972	0.464	0.076
Withdrawal rate			
Coefficient	-0.023(-0.002, 0.119)	0.021(-0.022, 0.064)	NA
σ	1.008	0.465	NA

Coefficient of posterior median, and 95% credible interval (CrIs) of the between-trial heterogeneity (σ) in ln(OR) scale for all outcomes using the random effects models; Ref, Reference; NA, Not available. If the coefficient was positive value, the effect was expanded by

corresponding confounding factor in corresponding outcome; Otherwise, the opposite.

Supplementary Table S3 Adjusting selective design biases and model parameters in all outcomes

Model	Healing	Relief of symptoms	Tolerance
Model: No adjustment			
PD	98.7	139.8	107.9
D	117.1	162.3	172.7
DIC	215.8	302.1	280.6
σ	0.383	0.461	0.077
Model 1.1: New favored - Fixed coefficient			
Coefficient	0.42(-0.91, 1.78)	-0.17(-1.24, 0.90)	-0.02(-0.49, 0.43)
PD	96.6	140.5	108.9
D	117.6	162.3	174.5
DIC	214.2	302.8	283.4
σ	0.327	0.464	0.078
Model 1.2: New favored - Exchangeable coefficients			
Coefficient	1.40(-3.00, 5.84)	4.27(-2.84, 11.2)	-0.21(-1.36, 0.96)
PD	96.3	140.2	109.5
D	118.0	162.4	174.1
DIC	214.3	302.6	283.6
σ	0.317	0.460	0.082
Model 1.3: New favored - Consistent coefficients			
PD	104.2	143.3	129.2
D	121.0	161.0	184.0
DIC	225.2	304.3	313.2
σ	0.314	0.428	0.093
Model 2.1: Sponsored favored - Fixed coefficient			
Coefficient	0.72(-2.84, 4.21)	-0.74(-5.39, 4.20)	-0.21(-1.36, 0.96)
PD	96.4	140.4	109.3
D	117.9	162.4	173.9
DIC	214.3	302.8	283.2
σ	0.326	0.466	0.081
Model 2.2: Sponsored favored - Exchangeable coefficients			
Coefficient	-2.12(-6.38, 2.33)	0.87(-4.92, 7.53)	0.19(-1.02, 1.47)
PD	96.6	140.7	110.7
D	117.7	162.3	175.2
DIC	214.3	303.0	285.9
σ	0.324	0.467	0.081
Model 2.3: Sponsored favored - Consistent coefficients			
PD	101.1	144.3	123.8
D	117.0	161.5	178.8
DIC	218.1	305.8	302.6
σ	0.318	0.503	0.085
Model 3.1: High-dose favored - Fixed coefficient			
Coefficient	-1.06(-2.79, 0.67)	0.37(-3.84, 4.79)	0.51(-0.60, 1.60)
PD	96.3	140.3	109.7

D	117.9	162.0	173.3
DIC	214.2	302.3	283.0
σ	0.321	0.464	0.084
Model 3.2: High-dose favored - Exchangeable coefficients			
Coefficient	-1.33(-6.40, 3.32)	-0.33(-4.94, 4.28)	0.25(-1.04, 1.69)
PD	96.7	140.4	110.1
D	117.4	162.4	174.1
DIC	214.1	302.8	284.2
σ	0.327	0.465	0.080
Model 3.3: High-dose favored - Consistent coefficients			
PD	102.4	142.0	119.2
D	118.8	161.2	179.3
DIC	220.2	303.2	298.5
σ	0.322	0.475	0.084
Model 4.1: PPIs favored - Fixed coefficient			
Coefficient	1.14(-1.36, 3.64)	4.49(1.26, 7.85)	0.35(-0.72, 1.45)
PD	96.2	138.3	109.7
D	118.1	163.1	174.0
DIC	214.3	301.4	283.7
σ	0.323	0.422	0.083
Model 4.2: PPIs favored - Exchangeable coefficients			
Coefficient	1.98(-3.10, 6.98)	2.29(1.32, 7.55)	0.41(-0.71, 1.62)
PD	96.1	139.8	108.3
D	118.6	162.1	173.6
DIC	214.7	301.9	281.9
σ	0.316	0.459	0.078
Model 4.3: PPIs favored - Consistent coefficients			
PD	100.9	140.3	111.8
D	118.7	162.8	174.6
DIC	219.6	303.1	286.4
σ	0.302	0.442	0.080
Model 5.1: Supplementary merger favored - Fixed coefficient			
Coefficient	1.14(-1.36, 3.64)	3.98(-1.04, 6.89)	0.10(-0.67, 0.89)
PD	96.2	138.3	109.7
D	118.1	163.6	174.6
DIC	214.3	301.9	284.3
σ	0.323	0.421	0.083
Model 5.2: Supplementary merger favored - Exchangeable coefficients			
Coefficient	1.98(-3.10, 6.98)	0.87(-4.92, 7.53)	0.19(-1.00, 1.47)
PD	96.1	140.7	110.7
D	118.6	162.3	175.2
DIC	214.7	303.0	285.9
σ	0.316	0.467	0.08
Model 5.3: Supplementary merger favored - Consistent coefficients			

PD	100.9	143.4	124.3
D	118.7	162.3	181.0
DIC	219.6	305.7	305.3
σ	0.302	0.470	0.097

Medians and 95% credible intervals from the posterior distributions of the heterogeneity (σ), two small-study effects coefficients in $\ln(\text{OR})$ scale for all outcomes. Deviance information criterion (DIC) and posterior mean of the residual deviance (D) are also reported. Model 5 provide different merger favored in different outcomes, sponsored favored and high-dose favored for the healing rate, PPIs favored and sponsored favored for relief of symptoms, sponsored and PPIs favored for tolerance. If coefficient is found positive, it means that there are small-study effects in the direction of design bias, otherwise the opposite.

Supplementary Table S4 The results of compare models in all outcomes

	Healing				Relief of symptoms			Tolerance		
	NM0	HM1	HM2	HM3	NM0	HM1	HM4	NM0	HM1	HM5
PD	98.7	91.7	90.1	92.0	139.8	132.1	132.7	107.9	91.6	89.5
D	117.1	117.0	116.6	116.7	162.3	165.1	165.2	172.7	171.3	164.2
DIC	215.8	208.7	206.7	208.7	302.1	297.2	297.9	280.6	262.9	253.7
σ	0.383	0.334	0.306	0.332	0.461	0.418	0.410*; 0.107#	0.077	0.066	0.055

NM0: No-adjustment model;

HM1: The hierarchical modeling approach incorporating dose-related and PPI favored constraints;

HM2: The hierarchical modeling approach incorporating dose-related and PPI favored constraints with gender;

HM3: The hierarchical modeling approach incorporating dose-related and PPI favored constraints with methodological quality score;

HM4: The hierarchical modeling approach incorporating dose-related and PPI favored constraints with inconsistency;

HM5: The hierarchical modeling approach incorporating dose-related and PPI favored constraints with year of publication.

PD: number of parameters, D: posterior mean of the residual deviance, DIC: deviance information criterion, σ : Heterogeneity/Inconsistency, * indicates heterogeneity, # indicates inconsistency.

		Relief of symptoms	3.42(2.31, 4.65)	14	3.40(2.37, 4.71)	14	NA	NA	NA	NA	NA	3.37(2.17, 4.77)	14	
		Tolerance	0.66(0.54, 0.83)	15	0.67(0.55, 0.81)	15	0.67(0.59, 0.81)	15	0.65(0.52, 0.80)	16	0.67(0.58, 0.74)	15	0.66(0.54, 0.78)	12
	20mg/day	Healing	10.18(6.93, 14.48)	10	10.02(5.96,13.84)	10	9.87(5.92, 13.91)	10	NA	NA	9.51(6.04, 12.54)	11	11.41(5.81,13.87)	10
		Relief of symptoms	4.21(3.22, 5.46)	7	4.31(3.37, 5.63)	8	NA	NA	NA	NA	NA	NA	4.17(3.19, 5.47)	7
		Tolerance	0.61(0.51, 0.72)	6	0.62(0.54, 0.71)	7	0.63(0.59, 0.72)	6	0.62(0.57, 0.73)	6	0.62(0.51, 0.70)	5	0.63(0.53, 0.71)	6
	40mg/day	Healing	14.93(9.56, 23.12)	3	13.73(9.48, 21.46)	4	13.77(8.56, 22.9)	4	NA	NA	11.69(8.2141, 23.4)	4	13.71(8.65, 24.6)	5
		Relief of symptoms	5.70(3.74, 9.52)	1	5.72(3.91, 9.78)	1	NA	NA	NA	NA	NA	NA	5.54(3.58, 8.43)	1
		Tolerance	0.57(0.44, 0.69)	1	0.57(0.52, 0.70)	1	0.55(0.53, 0.68)	1	0.57(0.47, 0.70)	1	0.60(0.46, 0.67)	1	0.62(0.51, 0.71)	1
Pantoprazole	10-20mg/day	Healing	6.88(4.23, 10.82)	13	6.84(4.32, 9.75)	13	5.78(4.32, 9.57)	13	NA	NA	5.96(2.89, 8.73)	12	5.23(3.79, 8.95)	13
		Relief of symptoms	3.54(2.40, 4.76)	13	3.58(2.41, 4.89)	12	NA	NA	NA	NA	NA	NA	3.43(2.43, 4.98)	13
		Tolerance	0.64(0.53, 0.78)	12	0.65(0.59, 0.76)	12	0.67(0.60, 0.78)	12	0.64(0.58, 0.77)	12	0.65(0.52, 0.76)	11	0.65(0.59, 0.73)	10
	40mg/day	Healing	11.64(8.16, 16.05)	9	10.20(7.98, 15.7)	9	11.77(6.91, 17.31)	9	NA	NA	10.96(7.65, 16.97)	7	9.98(6.78,15.20)	9
		Relief of symptoms	4.19(3.10, 5.58)	8	4.32(3.27, 6.04)	6	NA	NA	NA	NA	NA	NA	4.14(3.24, 5.63)	8
		Tolerance	0.59(0.48, 0.70)	2	0.60(0.51, 0.71)	2	0.61(0.52, 0.70)	2	0.60(0.51, 0.73)	3	0.58(0.50, 0.70)	3	0.61(0.54, 0.69)	3
	80mg/day	Healing	14.74(9.42, 23.30)	4	14.31(8.29, 21.91)	3	13.86(9.33, 21.70)	3	NA	NA	13.54(9.14, 20.15)	3	12.21(7.82,19.7)	3
		Relief of symptoms	4.95(3.43, 7.71)	3	5.14(3.67, 7.73)	2	NA	NA	NA	NA	NA	NA	4.64(3.51, 7.79)	3
		Tolerance	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Rabeprazole	5-10mg/day	Healing	9.56(5.63, 14.62)	11	9.54(5.31, 13.12)	11	8.97(5.32, 12.84)	11	NA	NA	8.63(3.54, 12.91)	10	8.49(4.32,12.97)	11
		Relief of symptoms	3.61(2.50, 4.83)	12	3.47(2.64, 4.74)	13	NA	NA	NA	NA	NA	NA	3.53(2.37, 4.78)	12
		Tolerance	0.67(0.55, 0.84)	17	0.67(0.58, 0.79)	17	0.68(0.58, 0.81)	17	0.67(0.59, 0.81)	17	0.66(0.54, 0.78)	18	0.67(0.59, 0.81)	11

Cimetidine	20mg/day	Healing	12.04(7.78, 17.95)	7	11.42(7.94, 17.32)	7	12.45(6.36, 16.97)	7	NA	NA	11.72(4.77, 17.20)	6	11.79(5.93, 17.94)	7	
		Relief of symptoms	4.09(3.01, 5.39)	9	4.06(3.07, 5.47)	9	NA	NA	NA	NA	NA	NA	NA	3.91(2.90, 5.43)	9
		Tolerance	0.64(0.53, 0.76)	11	0.65(0.55, 0.72)	11	0.62(0.53, 0.74)	11	0.64(0.54, 0.72)	11	0.63(0.50, 0.71)	8	0.64(0.57, 0.72)	8	
	40-50mg/day	Healing	15.07(9.58, 23.51)	2	15.24(9.23, 22.41)	2	15.51(8.35, 20.4)	2	NA	NA	14.88(7.78, 22.41)	2	15.32(7.35, 22.95)	2	
		Relief of symptoms	4.74(3.39, 6.93)	4	4.72(3.45, 7.02)	4	NA	NA	NA	NA	NA	NA	4.47(3.72, 6.82)	4	
		Tolerance	0.60(0.49, 0.72)	5	0.62(0.52, 0.71)	4	0.63(0.51, 0.72)	7	0.62(0.52, 0.74)	4	0.62(0.50, 0.71)	4	0.62(0.51, 0.72)	4	
	200-400mg/day	Healing	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Relief of symptoms	1.40(0.92, 1.93)	24	1.38(0.91, 1.92)	24	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Tolerance	0.75(0.61, 0.97)	23	0.75(0.62, 0.95)	23	0.77(0.66, 0.97)	23	0.76(0.64, 0.94)	22	0.74(0.65, 0.93)	22	NA	NA	
	600-800mg/day	Healing	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Relief of symptoms	1.65(1.17, 2.38)	20	1.60(1.12, 2.32)	20	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Tolerance	0.69(0.58, 0.86)	21	0.72(0.60, 0.85)	20	0.72(0.61, 0.86)	21	NA	NA	0.72(0.62, 0.84)	20	NA	NA	
	1600mg/day	Healing	2.87(1.81, 4.28)	19	2.54(1.57, 4.14)	18	2.57(1.83, 4.52)	19	NA	NA	1.57(1.01, 2.72)	18	NA	NA	
		Relief of symptoms	1.89(1.31, 2.95)	16	1.82(1.31, 3.41)	16	NA	NA	NA	NA	NA	NA	NA	NA	
		Tolerance	0.65(0.54, 0.81)	13	0.71(0.54, 0.82)	13	0.68(0.60, 0.83)	13	0.67(0.58, 0.79)	13	0.70(0.58, 0.82)	12	NA	NA	
Famotidine	20mg/day	Healing	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
		Relief of symptoms	1.46(0.97, 2.00)	23	1.43(0.90, 2.01)	23	NA	NA	NA	NA	NA	NA	1.44(0.97, 2.18)	21	
		Tolerance	0.72(0.58, 0.94)	22	0.75(0.62, 0.91)	22	0.74(0.63, 0.92)	22	0.72(0.60, 0.90)	21	0.73(0.62, 0.88)	21	0.72(0.62, 0.89)	16	
	40mg/day	Healing	4.15(2.57, 6.42)	16	3.84(2.18, 5.47)	16	4.95(1.78, 6.64)	16	NA	NA	NA	NA	3.97(1.98, 5.78)	16	
		Relief of symptoms	1.71(1.25, 2.36)	19	1.65(1.20, 2.33)	19	NA	NA	NA	NA	NA	NA	1.69(1.32, 2.24)	18	

Nizatidine	80mg/day	Tolerance	0.66(0.55, 0.80)	14	0.70(0.60, 0.82)	14	0.71(0.61, 0.80)	14	0.67(0.57, 0.79)	14	0.68(0.56, 0.81)	16	0.69(0.57, 0.75)	13	
		Healing	4.71(2.87, 7.38)	14	4.26(2.65, 6.24)	14	3.92(2.84, 6.21)	14	NA	NA	NA	NA	3.70(2.91, 5.97)	14	
		Relief of symptoms	1.96(1.38, 2.95)	15	1.91(1.37, 3.00)	15	NA	NA	NA	NA	NA	NA	1.90(1.37, 3.08)	15	
	150mg/day	Tolerance	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Healing	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Relief of symptoms	1.53(1.02, 2.18)	22	1.50(1.04, 2.26)	22	NA	NA	NA	NA	NA	NA	1.52(1.07, 2.13)	20	
	300mg/day	Tolerance	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Healing	2.46(1.66, 3.52)	21	2.72(1.65, 3.34)	20	2.75(1.70, 3.32)	21	NA	NA	2.80(1.73, 3.47)	17	2.93(1.71, 3.68)	19	
		Relief of symptoms	1.82(1.25, 2.82)	17	1.86(1.27, 2.74)	17	NA	NA	NA	NA	NA	NA	1.79(1.23, 2.72)	16	
	600mg/day	Tolerance	0.69(0.56, 0.87)	20	0.71(0.64, 0.85)	21	0.73(0.63, 0.91)	20	0.72(0.61, 0.87)	20	0.71(0.59, 0.89)	17	0.72(0.59, 0.82)	18	
		Healing	3.01(1.99, 4.44)	18	3.72(1.78, 3.78)	17	3.58(1.79, 3.54)	17	NA	NA	3.03(1.94, 3.66)	14	2.78(1.86, 3.65)	17	
		Relief of symptoms	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Ranitidine	≤300mg/day	Tolerance	0.63(0.51, 0.77)	9	0.65(0.56, 0.79)	9	0.67(0.58, 0.80)	9	0.68(0.57, 0.78)	10	NA	NA	0.68(0.59, 0.75)	9	
		Healing	2.90(2.06, 3.83)	20	2.77(1.99, 3.82)	21	2.29(1.76, 3.18)	20	NA	NA	2.57(2.26, 2.84)	16	2.19(1.52, 3.48)	20	
		Relief of symptoms	1.56(1.18, 2.03)	21	1.54(1.17, 2.09)	21	NA	NA	NA	NA	NA	NA	1.54(1.17, 2.14)	19	
	600mg/day	Tolerance	0.67(0.57, 0.78)	18	0.71(0.54, 0.90)	19	0.68(0.58, 0.80)	19	0.71(0.60, 0.81)	18	0.68(0.61, 0.78)	14	0.68(0.63, 0.76)	17	
		Healing	3.44(2.54, 4.64)	17	3.64(2.73, 4.45)	19	2.99(1.65, 4.76)	18	NA	NA	2.89(2.45, 3.46)	15	2.97(1.56, 3.62)	18	
		Relief of symptoms	1.75(1.28, 2.47)	18	1.70(1.29, 2.41)	18	NA	NA	NA	NA	NA	NA	1.71(1.22, 2.31)	17	
1200mg/day	Tolerance	0.61(0.49, 0.73)	8	0.64(0.51, 0.81)	8	0.63(0.53, 0.77)	8	0.61(0.51, 0.72)	8	0.62(0.49, 0.73)	7	0.64(0.50, 0.70)	20		
Healing	4.05(2.86, 5.85)	15	3.78(2.92, 5.17)	15	3.97(2.13, 5.32)	15	NA	NA	3.96(2.21, 4.98)	13	3.87(2.34, 5.27)	15			

	Relief of symptoms	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Tolerance	0.58(0.44, 0.71)	4	0.61(0.49, 0.75)	5	0.57(0.51, 0.73)	4	0.61(0.57, 0.73)	7	0.61(0.53, 0.75)	10	0.59(0.54, 0.72)	19
Placebo	Healing	Ref	22	Ref	22	Ref	22	NA	NA	Ref	19	Ref	21
	Relief of symptoms	Ref	25	Ref	25	NA	NA	NA	NA	NA	NA	Ref	22
	Tolerance	Ref	24	Ref	24	Ref	24	Ref	23	Ref	23	Ref	21
Heterogeneity	Healing	0.33(0.22, 0.47)		0.33(0.28, 0.43)		0.34(0.23, 0.42)		NA		0.34(0.16, 0.46)		0.33(0.22, 0.41)	
	Relief of symptoms	0.41(0.31, 0.41)*; 0.11(0.004, 0.29)#		0.38(0.30, 0.42)*; 0.11(0.006, 0.28)#		NA		NA		NA		0.43(0.33, 0.53)*; 0.11(0.006, 0.28)#	
	Tolerance	0.07(0.002, 0.17)		0.06(0.002, 0.13)		0.07(0.003, 0.14)		0.07(0.003, 0.14)		0.08(0.005, 0.16)		0.06(0.003, 0.18)	
Heterogeneity change	Healing	Ref		0%		↑3.0%		NA		↑3.0%		0%	
	Relief of symptoms	Ref		↓7.3%; 0%		NA		NA		NA		↑4.9%; 0%	
	Tolerance	Ref		↓14.3%		0%		0%		↑14.3%		↓14.3%	

Ref: Reference, NA: Not available, * indicates heterogeneity, # indicates inconsistency.

Supplementary Table S9 Estimates of effects and quality ratings for comparison of recommended doses of different drugs from the main outcome (healing) based on the GRADE system

Comparisons	Direct evidence		Indirect evidence		Network meta-analysis	
	OR 95%CrIs	Quality of evidence	OR 95%CrIs	Quality of evidence	OR 95%CrIs	Quality of evidence
Esomeprazole 20mg VS. Placebo	—	—	11.67(7.33, 17.66)	LOW**	11.67(7.33, 17.66)	LOW
Esomeprazole 40mg VS. Placebo	—	—	15.45(10.24, 21.96)	LOW**	15.45(10.24, 21.96)	LOW
Lansoprazole 15mg VS. Placebo	6.28 (4.33, 9.11)	MODERATE※	12.14(3.13, 26.43)	LOW**	8.23(4.87, 12.79)	LOW‡‡
Lansoprazole 30mg VS. Placebo	11.9 (6.78, 21.0)	LOW†,※	12.53(8.18, 19.21)	VERY LOW**	12.30(8.60, 17.03)	LOW
Lansoprazole 60mg VS. Placebo	8.78 (3.77, 20.5)	MODERATE※	16.15(10.26, 25.42)	VERY LOW**	14.10(9.44, 21.09)	MODERATE
Omeprazole 20mg VS. Placebo	14.3 (9.55, 21.4)	MODERATE†	2.04(0.86, 4.84)	VERY LOW**	10.18(6.93, 14.48)	MODERATE
Omeprazole 40mg VS. Placebo	—	—	14.93(9.56, 23.12)	MODERATE¶	14.93(9.56, 23.12)	MODERATE
Pantoprazole 10-20mg VS. Placebo	4.35 (2.60, 7.26)	HIGH	67.98(21.58, 214.20)	VERY LOW**	6.88(4.23, 10.82)	HIGH
Pantoprazole 40mg VS. Placebo	14.7 (7.71, 28.2)	HIGH	10.63(7.17, 15.76)	LOW**	11.64(8.16, 16.05)	HIGH
Pantoprazole 80mg VS. Placebo	—	—	14.74(9.42, 23.30)	LOW**	14.74(9.42, 23.30)	LOW
Rabeprazole 5-10mg VS. Placebo	—	—	9.56(5.63, 14.62)	LOW**	9.56(5.63, 14.62)	LOW
Rabeprazole 20mg VS. Placebo	—	—	12.04(7.78, 17.95)	MODERATE¶	12.04(7.78, 17.95)	MODERATE
Rabeprazole 40-50mg VS. Placebo	—	—	15.07(9.58, 23.51)	LOW**	15.07(9.58, 23.51)	LOW
Cimetidine 1600mg VS. Placebo	4.15 (2.13, 8.09)	MODERATE※	2.21(1.26, 3.88)	LOW¶,‡	2.87(1.81, 4.28)	MODERATE
Famotidine 40mg VS. Placebo	11.6 (5.90, 22.9)	LOW‡,※	1.76(0.94, 3.26)	VERY LOW**.,‡	4.15(2.57, 6.42)	VERY LOW‡‡
Famotidine 80mg VS. Placebo	—	—	4.71(2.87, 7.38)	VERY LOW**	4.71(2.87, 7.38)	VERY LOW
Nizatidine 300mg VS. Placebo	1.63 (1.01, 2.61)	LOW†,※	4.91(2.65, 9.08)	VERY LOW**	2.46(1.66, 3.52)	LOW
Nizatidine 600mg VS. Placebo	1.84 (1.28, 2.63)	MODERATE※	4.16(1.84, 9.40)	VERY LOW**	3.01(1.99, 4.44)	MODERATE
Ranitidine ≤300mg VS. Placebo	1.86 (0.96, 3.60)	VERY LOW†,§,※	3.29(2.31, 4.67)	LOW**	2.90(2.06, 3.83)	LOW
Ranitidine 600mg VS. Placebo	3.73 (2.05, 6.79)	MODERATE†	3.35(2.36, 4.74)	LOW**	3.44(2.54, 4.64)	MODERATE
Ranitidine 1200mg VS. Placebo	4.22 (2.84, 6.27)	HIGH	3.37(1.46, 7.78)	LOW**	4.05(2.86, 5.85)	HIGH

Esomeprazole 40mg VS. Esomeprazole 20mg	1.76 (1.17, 2.66)	LOW ^{‡,※}	0.84(0.48, 1.45)	VERY LOW ^{** ,‡}	1.35(1.02, 1.97)	LOW
Lansoprazole 15mg VS. Esomeprazole 20mg	—	—	0.73(0.40, 1.14)	VERY LOW ^{** ,‡}	0.73(0.40, 1.14)	VERY LOW
Lansoprazole 30mg VS. Esomeprazole 20mg	—	—	1.08(0.75, 1.58)	VERY LOW ^{** ,‡}	1.08(0.75, 1.58)	VERY LOW
Lansoprazole 60mg VS. Esomeprazole 20mg	—	—	1.24(0.82, 1.90)	VERY LOW ^{** ,‡}	1.24(0.82, 1.90)	VERY LOW
Omeprazole 20mg VS. Esomeprazole 20mg	0.74 (0.59, 0.93)	LOW ^{‡,※}	1.55(1.15, 2.08)	LOW ^{**}	0.89(0.62, 1.25)	VERY LOW [‡]
Omeprazole 40mg VS. Esomeprazole 20mg	—	—	1.32(0.81, 2.17)	VERY LOW ^{** ,‡}	1.32(0.81, 2.17)	VERY LOW
Pantoprazole 10-20mg VS. Esomeprazole 20mg	—	—	0.61(0.34, 0.998)	VERY LOW ^{** ,‡‡}	0.61(0.34, 0.998)	VERY LOW
Pantoprazole 40mg VS. Esomeprazole 20mg	—	—	1.03(0.70, 1.50)	VERY LOW ^{** ,‡}	1.03(0.70, 1.50)	VERY LOW
Pantoprazole 80mg VS. Esomeprazole 20mg	—	—	1.30(0.82, 2.18)	VERY LOW ^{** ,‡}	1.30(0.82, 2.18)	VERY LOW
Rabeprazole 5-10mg VS. Esomeprazole 20mg	—	—	0.84(0.47, 1.31)	VERY LOW ^{** ,‡}	0.84(0.47, 1.31)	VERY LOW
Rabeprazole 20mg VS. Esomeprazole 20mg	—	—	1.06(0.67, 1.59)	VERY LOW ^{** ,‡}	1.06(0.67, 1.59)	VERY LOW
Rabeprazole 40-50mg VS. Esomeprazole 20mg	—	—	1.32(0.86, 2.07)	VERY LOW ^{** ,‡}	1.32(0.86, 2.07)	VERY LOW
Cimetidine 1600mg VS. Esomeprazole 20mg	—	—	0.26(0.14, 0.42)	LOW ^{**}	0.26(0.14, 0.42)	LOW
Famotidine 40mg VS. Esomeprazole 20mg	—	—	0.37(0.21, 0.63)	LOW ^{**}	0.37(0.21, 0.63)	LOW
Famotidine 80mg VS. Esomeprazole 20mg	—	—	0.42(0.23, 0.74)	VERY LOW ^{**}	0.42(0.23, 0.74)	VERY LOW
Nizatidine 300mg VS. Esomeprazole 20mg	—	—	0.22(0.13, 0.35)	LOW ^{**}	0.22(0.13, 0.35)	LOW
Nizatidine 600mg VS. Esomeprazole 20mg	—	—	0.27(0.15, 0.44)	LOW ^{**}	0.27(0.15, 0.44)	LOW
Ranitidine ≤300mg VS. Esomeprazole 20mg	—	—	0.26(0.17, 0.39)	VERY LOW ^{**}	0.26(0.17, 0.39)	VERY LOW
Ranitidine 600mg VS. Esomeprazole 20mg	—	—	0.31(0.20, 0.46)	LOW ^{**}	0.31(0.20, 0.46)	LOW
Ranitidine 1200mg VS. Esomeprazole 20mg	—	—	0.36(0.22, 0.58)	LOW ^{**}	0.36(0.22, 0.58)	LOW
Lansoprazole 15mg VS. Esomeprazole 40mg	—	—	0.54(0.31, 0.85)	MODERATE [¶]	0.54(0.31, 0.85)	MODERATE
Lansoprazole 30mg VS. Esomeprazole 40mg	0.68 (0.58, 0.79)	MODERATE [‡]	1.58(1.32, 1.90)	VERY LOW ^{**}	0.81(0.60, 1.06)	LOW [‡]
Lansoprazole 60mg VS. Esomeprazole 40mg	—	—	0.93(0.66, 1.33)	VERY LOW ^{** ,‡}	0.93(0.66, 1.33)	VERY LOW
Omeprazole 20mg VS. Esomeprazole 40mg	0.49 (0.29, 0.84)	LOW ^{‡,※}	0.76(0.54, 1.06)	VERY LOW ^{** ,‡}	0.67(0.50, 0.88)	LOW
Omeprazole 40mg VS. Esomeprazole 40mg	—	—	0.98(0.65, 1.50)	VERY LOW ^{** ,‡}	0.98(0.65, 1.50)	VERY LOW
Pantoprazole 10-20mg VS. Esomeprazole 40mg	—	—	0.46(0.26, 0.75)	VERY LOW ^{**}	0.46(0.26, 0.75)	VERY LOW

Pantoprazole 40mg VS. Esomeprazole 40mg	0.91 (0.62, 1.32)	VERY LOW §,※	0.60(0.39, 0.92)	VERY LOW**	0.76(0.57, 1.01)	VERY LOW
Pantoprazole 80mg VS. Esomeprazole 40mg	—	—	0.97(0.66, 1.46)	VERY LOW**,‡	0.97(0.66, 1.46)	VERY LOW
Rabeprazole 5-10mg VS. Esomeprazole 40mg	—	—	0.63(0.37, 0.92)	LOW**	0.63(0.37, 0.92)	LOW
Rabeprazole 20mg VS. Esomeprazole 40mg	—	—	0.79(0.53, 1.09)	VERY LOW**,‡	0.79(0.53, 1.09)	VERY LOW
Rabeprazole 40-50mg VS. Esomeprazole 40mg	1.12 (0.80, 1.57)	LOW §	0.34(0.13, 0.88)	LOW**	0.98(0.71, 1.34)	LOW
Cimetidine 1600mg VS. Esomeprazole 40mg	—	—	0.19(0.11, 0.30)	LOW**	0.19(0.11, 0.30)	LOW
Famotidine 40mg VS. Esomeprazole 40mg	—	—	0.27(0.17, 0.43)	LOW**	0.27(0.17, 0.43)	LOW
Famotidine 80mg VS. Esomeprazole 40mg	—	—	0.31(0.19, 0.51)	LOW**	0.31(0.19, 0.51)	LOW
Nizatidine 300mg VS. Esomeprazole 40mg	—	—	0.16(0.10, 0.26)	VERY LOW**	0.16(0.10, 0.26)	VERY LOW
Nizatidine 600mg VS. Esomeprazole 40mg	—	—	0.20(0.12, 0.32)	VERY LOW**	0.20(0.12, 0.32)	VERY LOW
Ranitidine ≤300mg VS. Esomeprazole 40mg	—	—	0.19(0.13, 0.27)	VERY LOW**	0.19(0.13, 0.27)	VERY LOW
Ranitidine 600mg VS. Esomeprazole 40mg	—	—	0.23(0.16, 0.33)	MODERATE ¶	0.23(0.16, 0.33)	MODERATE
Ranitidine 1200mg VS. Esomeprazole 40mg	—	—	0.27(0.18, 0.41)	VERY LOW**	0.27(0.18, 0.41)	VERY LOW
Lansoprazole 30mg VS. Lansoprazole 15mg	2.06 (1.41, 3.03)	MODERATE ※	0.19(0.09, 0.43)	VERY LOW**	1.56(1.04, 2.49)	MODERATE
Lansoprazole 60mg VS. Lansoprazole 15mg	1.56 (0.61, 3.94)	VERY LOW §,※	1.89(1.06, 3.35)	VERY LOW**,‡	1.79(1.13, 3.01)	LOW §§
Omeprazole 20mg VS. Lansoprazole 15mg	2.20 (1.45, 3.34)	HIGH	0.01(0.003, 0.03)	VERY LOW**	1.29(0.83, 2.02)	MODERATE ‡
Omeprazole 40mg VS. Lansoprazole 15mg	—	—	1.91(1.07, 3.39)	MODERATE ¶	1.91(1.07, 3.39)	MODERATE
Pantoprazole 10-20mg VS. Lansoprazole 15mg	—	—	0.86(0.51, 1.37)	LOW ¶,‡	0.86(0.51, 1.37)	LOW
Pantoprazole 40mg VS. Lansoprazole 15mg	—	—	1.48(0.93, 2.42)	VERY LOW**,‡	1.48(0.93, 2.42)	VERY LOW
Pantoprazole 80mg VS. Lansoprazole 15mg	—	—	1.89(1.07, 3.44)	LOW**	1.89(1.07, 3.44)	LOW
Rabeprazole 5-10mg VS. Lansoprazole 15mg	—	—	1.21(0.70, 2.01)	VERY LOW**,‡	1.21(0.70, 2.01)	VERY LOW
Rabeprazole 20mg VS. Lansoprazole 15mg	—	—	1.53(0.92, 2.55)	VERY LOW**,‡	1.53(0.92, 2.55)	VERY LOW
Rabeprazole 40-50mg VS. Lansoprazole 15mg	—	—	1.92(1.09, 3.43)	LOW**	1.92(1.09, 3.43)	LOW
Cimetidine 1600mg VS. Lansoprazole 15mg	—	—	0.37(0.20, 0.63)	MODERATE ¶	0.37(0.20, 0.63)	MODERATE
Famotidine 40mg VS. Lansoprazole 15mg	—	—	0.54(0.27, 1.01)	LOW**	0.54(0.27, 1.01)	LOW
Famotidine 80mg VS. Lansoprazole 15mg	—	—	0.61(0.30, 1.16)	LOW**	0.61(0.30, 1.16)	LOW

Nizatidine 300mg VS. Lansoprazole 15mg	—	—	0.31(0.18, 0.53)	LOW**	0.31(0.18, 0.53)	LOW
Nizatidine 600mg VS. Lansoprazole 15mg	—	—	0.39(0.22, 0.66)	MODERATE¶	0.39(0.22, 0.66)	MODERATE
Ranitidine ≤300mg VS. Lansoprazole 15mg	—	—	0.37(0.22, 0.59)	LOW**	0.37(0.22, 0.59)	LOW
Ranitidine 600mg VS. Lansoprazole 15mg	—	—	0.44(0.26, 0.73)	MODERATE¶	0.44(0.26, 0.73)	MODERATE
Ranitidine 1200mg VS. Lansoprazole 15mg	—	—	0.52(0.29, 0.93)	MODERATE¶	0.52(0.29, 0.93)	MODERATE
Lansoprazole 60mg VS. Lansoprazole 30mg	0.64 (0.21, 1.92)	VERY LOW†,§,※	1.17(0.96, 1.44)	VERY LOW**,‡	1.15(1.003, 1.53)	LOW§§
Omeprazole 20mg VS. Lansoprazole 30mg	0.76 (0.53, 1.09)	VERY LOW*, §	0.96(0.63, 1.47)	VERY LOW**,‡	0.84(0.63, 1.09)	LOW
Omeprazole 40mg VS. Lansoprazole 30mg	—	—	1.23(0.83, 1.84)	VERY LOW**,‡	1.23(0.83, 1.84)	VERY LOW
Pantoprazole 10-20mg VS. Lansoprazole 30mg	—	—	0.57(0.34, 0.88)	VERY LOW**	0.57(0.34, 0.88)	VERY LOW
Pantoprazole 40mg VS. Lansoprazole 30mg	0.71 (0.34, 1.48)	VERY LOW*, §	1.02(0.73, 1.42)	VERY LOW**,‡	0.96(0.70, 1.28)	VERY LOW
Pantoprazole 80mg VS. Lansoprazole 30mg	—	—	1.21(0.82, 1.89)	VERY LOW**,‡	1.21(0.82, 1.89)	VERY LOW
Rabeprazole 5-10mg VS. Lansoprazole 30mg	—	—	0.78(0.47, 1.14)	VERY LOW**,‡	0.78(0.47, 1.14)	VERY LOW
Rabeprazole 20mg VS. Lansoprazole 30mg	0.88 (0.32, 2.40)	VERY LOW*, §	1.01(0.68, 1.51)	VERY LOW**,‡	0.99(0.66, 1.39)	VERY LOW
Rabeprazole 40-50mg VS. Lansoprazole 30mg	—	—	1.24(0.84, 1.82)	VERY LOW**,‡,‡‡	1.24(0.84, 1.82)	VERY LOW
Cimetidine 1600mg VS. Lansoprazole 30mg	—	—	0.24(0.14, 0.37)	LOW**	0.24(0.14, 0.37)	LOW
Famotidine 40mg VS. Lansoprazole 30mg	—	—	0.34(0.21, 0.54)	LOW**	0.34(0.21, 0.54)	LOW
Famotidine 80mg VS. Lansoprazole 30mg	—	—	0.39(0.23, 0.64)	LOW**	0.39(0.23, 0.64)	LOW
Nizatidine 300mg VS. Lansoprazole 30mg	—	—	0.20(0.12, 0.31)	LOW**	0.20(0.12, 0.31)	LOW
Nizatidine 600mg VS. Lansoprazole 30mg	—	—	0.25(0.15, 0.39)	LOW**	0.25(0.15, 0.39)	LOW
Ranitidine ≤300mg VS. Lansoprazole 30mg	0.16 (0.06, 0.40)	LOW†,※	0.25(0.18, 0.35)	VERY LOW**	0.24(0.17, 0.32)	LOW
Ranitidine 600mg VS. Lansoprazole 30mg	0.19 (0.07, 0.51)	MODERATE※	0.31(0.21, 0.45)	LOW**	0.29(0.20, 0.40)	MODERATE
Ranitidine 1200mg VS. Lansoprazole 30mg	—	—	0.34(0.23, 0.51)	LOW**	0.34(0.23, 0.51)	LOW
Omeprazole 20mg VS. Lansoprazole 60mg	—	—	0.74(0.49, 1.001)	VERY LOW**	0.74(0.49, 1.001)	VERY LOW
Omeprazole 40mg VS. Lansoprazole 60mg	—	—	1.08(0.68, 1.65)	LOW¶,‡	1.08(0.68, 1.65)	LOW
Pantoprazole 10-20mg VS. Lansoprazole 60mg	—	—	0.50(0.28, 0.80)	LOW¶,‡‡	0.50(0.28, 0.80)	LOW
Pantoprazole 40mg VS. Lansoprazole 60mg	—	—	0.84(0.57, 1.17)	VERY LOW**,‡	0.84(0.57, 1.17)	VERY LOW

Pantoprazole 80mg VS. Lansoprazole 60mg	—	—	1.07(0.68, 1.69)	VERY LOW**, [‡]	1.07(0.68, 1.69)	VERY LOW
Rabeprazole 5-10mg VS. Lansoprazole 60mg	—	—	0.69(0.39, 1.02)	VERY LOW**, [‡]	0.69(0.39, 1.02)	VERY LOW
Rabeprazole 20mg VS. Lansoprazole 60mg	—	—	0.87(0.55, 1.25)	VERY LOW**, [‡]	0.87(0.55, 1.25)	VERY LOW
Rabeprazole 40-50mg VS. Lansoprazole 60mg	—	—	1.09(0.69, 1.62)	VERY LOW**, [‡]	1.09(0.69, 1.62)	VERY LOW
Cimetidine 1600mg VS. Lansoprazole 60mg	—	—	0.21(0.12, 0.34)	VERY LOW**	0.21(0.12, 0.34)	VERY LOW
Famotidine 40mg VS. Lansoprazole 60mg	—	—	0.30(0.18, 0.49)	LOW**	0.30(0.18, 0.49)	LOW
Famotidine 80mg VS. Lansoprazole 60mg	—	—	0.34(0.20, 0.56)	LOW**	0.34(0.20, 0.56)	LOW
Nizatidine 300mg VS. Lansoprazole 60mg	—	—	0.18(0.10, 0.28)	LOW**	0.18(0.10, 0.28)	LOW
Nizatidine 600mg VS. Lansoprazole 60mg	—	—	0.22(0.13, 0.35)	MODERATE¶	0.22(0.13, 0.35)	MODERATE
Ranitidine ≤300mg VS. Lansoprazole 60mg	0.25 (0.12, 0.51)	MODERATE※	0.20(0.13, 0.31)	VERY LOW**	0.21(0.14, 0.30)	MODERATE
Ranitidine 600mg VS. Lansoprazole 60mg	—	—	0.25(0.17, 0.36)	MODERATE¶	0.25(0.17, 0.36)	MODERATE
Ranitidine 1200mg VS. Lansoprazole 60mg	—	—	0.30(0.19, 0.46)	MODERATE¶	0.30(0.19, 0.46)	MODERATE
Omeprazole 40mg VS. Omeprazole 20mg	—	—	1.49(1.03, 2.31)	VERY LOW**	1.49(1.03, 2.31)	VERY LOW
Pantoprazole 10-20mg VS. Omeprazole 20mg	0.56 (0.30, 1.04)	VERY LOW*, §	0.83(0.44, 1.57)	VERY LOW**, [‡]	0.68(0.42, 1.02)	LOW§§
Pantoprazole 40mg VS. Omeprazole 20mg	1.14 (0.56, 2.35)	VERY LOW*, [‡] ,§	1.16(0.84, 1.62)	VERY LOW**, [‡]	1.16(0.85, 1.55)	VERY LOW
Pantoprazole 80mg VS. Omeprazole 20mg	—	—	1.47(0.99, 2.29)	VERY LOW**, [‡]	1.47(0.99, 2.29)	VERY LOW
Rabeprazole 5-10mg VS. Omeprazole 20mg	0.65 (0.22, 1.89)	LOW §	1.02(0.64, 1.64)	VERY LOW**, [‡]	0.95(0.58, 1.38)	LOW
Rabeprazole 20mg VS. Omeprazole 20mg	1.36 (0.35, 5.28)	VERY LOW*, [‡] ,§,※	1.19(0.81, 1.74)	VERY LOW**, [‡]	1.20(0.82, 1.70)	VERY LOW
Rabeprazole 40-50mg VS. Omeprazole 20mg	0.65 (0.22, 1.91)	LOW §	1.69(1.12, 2.53)	VERY LOW**, [‡] , [‡]	1.50(1.02, 2.18)	MODERATE §§
Cimetidine 1600mg VS. Omeprazole 20mg	—	—	0.29(0.17, 0.45)	MODERATE¶	0.29(0.17, 0.45)	MODERATE
Famotidine 40mg VS. Omeprazole 20mg	0.29(0.16, 0.51)	MODERATE※	1.11(0.43, 2.82)	LOW**	0.42(0.25, 0.67)	MODERATE
Famotidine 80mg VS. Omeprazole 20mg	—	—	0.47(0.27, 0.80)	VERY LOW**	0.47(0.27, 0.80)	VERY LOW
Nizatidine 300mg VS. Omeprazole 20mg	—	—	0.25(0.15, 0.37)	VERY LOW**	0.25(0.15, 0.37)	VERY LOW
Nizatidine 600mg VS. Omeprazole 20mg	—	—	0.30(0.19, 0.47)	MODERATE¶	0.30(0.19, 0.47)	MODERATE
Ranitidine ≤300mg VS. Omeprazole 20mg	—	—	0.29(0.20, 0.40)	VERY LOW**	0.29(0.20, 0.40)	VERY LOW
Ranitidine 600mg VS. Omeprazole 20mg	—	—	0.35(0.24, 0.49)	VERY LOW**	0.35(0.24, 0.49)	VERY LOW

Ranitidine 1200mg VS. Omeprazole 20mg	—	—	0.41(0.27, 0.63)	MODERATE ¶	0.41(0.27, 0.63)	MODERATE
Pantoprazole 10-20mg VS. Omeprazole 40mg	—	—	0.48(0.25, 0.81)	MODERATE ¶	0.48(0.25, 0.81)	MODERATE
Pantoprazole 40mg VS. Omeprazole 40mg	0.96 (0.70, 1.32)	LOW §	0.72(0.42, 1.25)	LOW ¶, †	0.80(0.52, 1.13)	LOW
Pantoprazole 80mg VS. Omeprazole 40mg	—	—	1.02(0.62, 1.59)	VERY LOW**, †	1.02(0.62, 1.59)	VERY LOW
Rabeprazole 5-10mg VS. Omeprazole 40mg	—	—	0.66(0.35, 1.03)	VERY LOW**, †	0.66(0.35, 1.03)	VERY LOW
Rabeprazole 20mg VS. Omeprazole 40mg	—	—	0.83(0.49, 1.24)	VERY LOW**, †	0.83(0.49, 1.24)	VERY LOW
Rabeprazole 40-50mg VS. Omeprazole 40mg	—	—	1.04(0.64, 1.57)	VERY LOW**, †	1.04(0.64, 1.57)	VERY LOW
Cimetidine 1600mg VS. Omeprazole 40mg	0.12 (0.04, 0.38)	HIGH	0.23(0.13, 0.43)	MODERATE ¶	0.20(0.11, 0.32)	HIGH
Famotidine 40mg VS. Omeprazole 40mg	—	—	0.29(0.16, 0.47)	LOW**	0.29(0.16, 0.47)	LOW
Famotidine 80mg VS. Omeprazole 40mg	—	—	0.33(0.19, 0.55)	LOW**	0.33(0.19, 0.55)	LOW
Nizatidine 300mg VS. Omeprazole 40mg	—	—	0.17(0.09, 0.28)	LOW**	0.17(0.09, 0.28)	LOW
Nizatidine 600mg VS. Omeprazole 40mg	—	—	0.21(0.12, 0.35)	MODERATE ¶	0.21(0.12, 0.35)	MODERATE
Ranitidine ≤300mg VS. Omeprazole 40mg	0.20 (0.11, 0.38)	HIGH	0.20(0.12, 0.34)	LOW**	0.20(0.13, 0.29)	HIGH
Ranitidine 600mg VS. Omeprazole 40mg	0.10 (0.04, 0.27)	HIGH	0.30(0.19, 0.48)	LOW**	0.24(0.15, 0.35)	HIGH
Ranitidine 1200mg VS. Omeprazole 40mg	—	—	0.28(0.17, 0.43)	LOW**	0.28(0.17, 0.43)	LOW
Pantoprazole 40mg VS. Pantoprazole 10-20mg	3.24 (1.99, 5.28)	HIGH	0.03(0.01, 0.11)	LOW †	1.77(1.09, 2.71)	HIGH
Pantoprazole 80mg VS. Pantoprazole 10-20mg	—	—	2.25(1.25, 3.96)	LOW**	2.25(1.25, 3.96)	LOW
Rabeprazole 5-10mg VS. Pantoprazole 10-20mg	—	—	1.44(0.83, 2.34)	VERY LOW**, †, ††	1.44(0.83, 2.34)	VERY LOW
Rabeprazole 20mg VS. Pantoprazole 10-20mg	—	—	1.83(1.07, 3.02)	VERY LOW**, †, ††	1.83(1.07, 3.02)	VERY LOW
Rabeprazole 40-50mg VS. Pantoprazole 10-20mg	—	—	2.30(1.23, 3.99)	VERY LOW**, †, ††	2.30(1.23, 3.99)	VERY LOW
Cimetidine 1600mg VS. Pantoprazole 10-20mg	—	—	0.44(0.24, 0.72)	VERY LOW**, †, ††	0.44(0.24, 0.72)	VERY LOW
Famotidine 40mg VS. Pantoprazole 10-20mg	—	—	0.64(0.31, 1.17)	VERY LOW**	0.64(0.31, 1.17)	VERY LOW
Famotidine 80mg VS. Pantoprazole 10-20mg	—	—	0.73(0.34, 1.35)	VERY LOW**, †, ††	0.73(0.34, 1.35)	VERY LOW
Nizatidine 300mg VS. Pantoprazole 10-20mg	—	—	0.37(0.22, 0.60)	MODERATE ¶	0.37(0.22, 0.60)	MODERATE
Nizatidine 600mg VS. Pantoprazole 10-20mg	—	—	0.46(0.26, 0.76)	MODERATE ¶	0.46(0.26, 0.76)	MODERATE
Ranitidine ≤300mg VS. Pantoprazole 10-20mg	0.49 (0.32, 0.77)	MODERATE※	0.42(0.08, 2.47)	MODERATE ¶	0.44(0.27, 0.67)	MODERATE

Ranitidine 600mg VS. Pantoprazole 10-20mg	—	—	0.53(0.31, 0.84)	VERY LOW**, [‡] _‡	0.53(0.31, 0.84)	VERY LOW
Ranitidine 1200mg VS. Pantoprazole 10-20mg	—	—	0.62(0.34, 1.07)	HIGH[]	0.62(0.34, 1.07)	HIGH
Pantoprazole 80mg VS. Pantoprazole 40mg	1.21 (0.68, 2.16)	LOW §	1.30(0.89, 1.88)	LOW¶, [‡]	1.27(1.01, 1.89)	MODERATE §§
Rabeprazole 5-10mg VS. Pantoprazole 40mg	—	—	0.83(0.50, 1.21)	VERY LOW**, [‡]	0.83(0.50, 1.21)	VERY LOW
Rabeprazole 20mg VS. Pantoprazole 40mg	1.39 (0.55, 3.51)	VERY LOW*, §	0.99(0.66, 1.47)	VERY LOW**, [‡]	1.04(0.71, 1.48)	VERY LOW
Rabeprazole 40-50mg VS. Pantoprazole 40mg	—	—	1.30(0.89, 1.90)	VERY LOW**, [‡] _‡	1.30(0.89, 1.90)	VERY LOW
Cimetidine 1600mg VS. Pantoprazole 40mg	—	—	0.25(0.15, 0.39)	VERY LOW**	0.25(0.15, 0.39)	VERY LOW
Famotidine 40mg VS. Pantoprazole 40mg	—	—	0.36(0.22, 0.57)	LOW**	0.36(0.22, 0.57)	LOW
Famotidine 80mg VS. Pantoprazole 40mg	—	—	0.41(0.25, 0.66)	LOW**	0.41(0.25, 0.66)	LOW
Nizatidine 300mg VS. Pantoprazole 40mg	0.26 (0.14, 0.47)	MODERATE†	0.19(0.11, 0.33)	LOW**	0.22(0.14, 0.32)	MODERATE
Nizatidine 600mg VS. Pantoprazole 40mg	—	—	0.26(0.16, 0.41)	VERY LOW**	0.26(0.16, 0.41)	VERY LOW
Ranitidine ≤300mg VS. Pantoprazole 40mg	0.32 (0.16, 0.62)	MODERATE†	0.24(0.17, 0.33)	LOW¶, [‡] _‡	0.25(0.19, 0.34)	MODERATE
Ranitidine 600mg VS. Pantoprazole 40mg	—	—	0.30(0.21, 0.42)	MODERATE¶	0.30(0.21, 0.42)	MODERATE
Ranitidine 1200mg VS. Pantoprazole 40mg	—	—	0.35(0.24, 0.53)	HIGH[]	0.35(0.24, 0.53)	HIGH
Rabeprazole 5-10mg VS. Pantoprazole 80mg	—	—	0.67(0.35, 1.05)	VERY LOW**, [‡]	0.67(0.35, 1.05)	VERY LOW
Rabeprazole 20mg VS. Pantoprazole 80mg	—	—	0.84(0.50, 1.26)	VERY LOW**, [‡]	0.84(0.50, 1.26)	VERY LOW
Rabeprazole 40-50mg VS. Pantoprazole 80mg	—	—	1.05(0.63, 1.61)	VERY LOW**, [‡]	1.05(0.63, 1.61)	VERY LOW
Cimetidine 1600mg VS. Pantoprazole 80mg	—	—	0.20(0.11, 0.33)	LOW**	0.20(0.11, 0.33)	LOW
Famotidine 40mg VS. Pantoprazole 80mg	—	—	0.29(0.17, 0.47)	LOW**	0.29(0.17, 0.47)	LOW
Famotidine 80mg VS. Pantoprazole 80mg	—	—	0.33(0.18, 0.56)	LOW**	0.33(0.18, 0.56)	LOW
Nizatidine 300mg VS. Pantoprazole 80mg	0.15 (0.07, 0.32)	HIGH	0.19(0.09, 0.38)	LOW**	0.17(0.10, 0.28)	HIGH
Nizatidine 600mg VS. Pantoprazole 80mg	—	—	0.21(0.12, 0.35)	VERY LOW**	0.21(0.12, 0.35)	VERY LOW
Ranitidine ≤300mg VS. Pantoprazole 80mg	—	—	0.20(0.12, 0.29)	LOW**	0.20(0.12, 0.29)	LOW
Ranitidine 600mg VS. Pantoprazole 80mg	—	—	0.24(0.15, 0.36)	LOW**	0.24(0.15, 0.36)	LOW
Ranitidine 1200mg VS. Pantoprazole 80mg	—	—	0.29(0.17, 0.45)	LOW**	0.29(0.17, 0.45)	LOW
Rabeprazole 20mg VS. Rabeprazole 5-10mg	—	—	1.29(1.01, 2.01)	VERY LOW**	1.29(1.01, 2.01)	VERY LOW

Rabeprazole 40-50mg VS. Rabeprazole 5-10mg	1.01 (0.38, 2.66)	LOW §	1.87(1.11, 3.15)	LOW**	1.63(1.09, 2.73)	LOW
Cimetidine 1600mg VS. Rabeprazole 5-10mg	—	—	0.32(0.17, 0.54)	LOW**	0.32(0.17, 0.54)	LOW
Famotidine 40mg VS. Rabeprazole 5-10mg	—	—	0.46(0.24, 0.86)	LOW**	0.46(0.24, 0.86)	LOW
Famotidine 80mg VS. Rabeprazole 5-10mg	—	—	0.52(0.27, 0.98)	VERY LOW**	0.52(0.27, 0.98)	VERY LOW
Nizatidine 300mg VS. Rabeprazole 5-10mg	—	—	0.27(0.16, 0.45)	LOW**	0.27(0.16, 0.45)	LOW
Nizatidine 600mg VS. Rabeprazole 5-10mg	—	—	0.33(0.19, 0.58)	LOW**	0.33(0.19, 0.58)	LOW
Ranitidine ≤300mg VS. Rabeprazole 5-10mg	—	—	0.32(0.20, 0.50)	VERY LOW**	0.32(0.20, 0.50)	VERY LOW
Ranitidine 600mg VS. Rabeprazole 5-10mg	—	—	0.38(0.24, 0.63)	VERY LOW**	0.38(0.24, 0.63)	VERY LOW
Ranitidine 1200mg VS. Rabeprazole 5-10mg	—	—	0.45(0.26, 0.78)	LOW**	0.45(0.26, 0.78)	LOW
Rabeprazole 40-50mg VS. Rabeprazole 20mg	—	—	1.27(1.01, 1.89)	VERY LOW**	1.27(1.01, 1.89)	VERY LOW
Cimetidine 1600mg VS. Rabeprazole 20mg	—	—	0.25(0.14, 0.40)	MODERATE ¶	0.25(0.14, 0.40)	MODERATE
Famotidine 40mg VS. Rabeprazole 20mg	—	—	0.36(0.21, 0.61)	LOW**	0.36(0.21, 0.61)	LOW
Famotidine 80mg VS. Rabeprazole 20mg	—	—	0.40(0.23, 0.69)	LOW**	0.40(0.23, 0.69)	LOW
Nizatidine 300mg VS. Rabeprazole 20mg	—	—	0.21(0.12, 0.34)	VERY LOW**	0.21(0.12, 0.34)	VERY LOW
Nizatidine 600mg VS. Rabeprazole 20mg	—	—	0.26(0.15, 0.43)	VERY LOW**	0.26(0.15, 0.43)	VERY LOW
Ranitidine ≤300mg VS. Rabeprazole 20mg	—	—	0.25(0.16, 0.36)	LOW**	0.25(0.16, 0.36)	LOW
Ranitidine 600mg VS. Rabeprazole 20mg	0.28 (0.16, 0.49)	MODERATE*	0.33(0.17, 0.62)	VERY LOW**	0.3(0.19, 0.44)	MODERATE
Ranitidine 1200mg VS. Rabeprazole 20mg	—	—	0.35(0.22, 0.56)	LOW**	0.35(0.22, 0.56)	LOW
Cimetidine 1600mg VS. Rabeprazole 40-50mg	—	—	0.20(0.10, 0.33)	LOW**	0.20(0.10, 0.33)	LOW
Famotidine 40mg VS. Rabeprazole 40-50mg	—	—	0.29(0.17, 0.47)	LOW**	0.29(0.17, 0.47)	LOW
Famotidine 80mg VS. Rabeprazole 40-50mg	—	—	0.32(0.19, 0.54)	LOW**	0.32(0.19, 0.54)	LOW
Nizatidine 300mg VS. Rabeprazole 40-50mg	—	—	0.17(0.09, 0.28)	LOW**	0.17(0.09, 0.28)	LOW
Nizatidine 600mg VS. Rabeprazole 40-50mg	—	—	0.21(0.11, 0.34)	LOW**	0.21(0.11, 0.34)	LOW
Ranitidine ≤300mg VS. Rabeprazole 40-50mg	—	—	0.20(0.12, 0.30)	LOW**	0.20(0.12, 0.30)	LOW
Ranitidine 600mg VS. Rabeprazole 40-50mg	—	—	0.24(0.15, 0.36)	LOW**	0.24(0.15, 0.36)	LOW
Ranitidine 1200mg VS. Rabeprazole 40-50mg	—	—	0.28(0.17, 0.45)	LOW**	0.28(0.17, 0.45)	LOW

Famotidine 40mg VS. Cimetidine 1600mg	—	—	1.50(0.86, 2.62)	VERY LOW**, [‡]	1.50(0.86, 2.62)	VERY LOW
Famotidine 80mg VS. Cimetidine 1600mg	—	—	1.70(0.96, 2.99)	VERY LOW**, [‡]	1.70(0.96, 2.99)	VERY LOW
Nizatidine 300mg VS. Cimetidine 1600mg	—	—	0.89(0.52, 1.40)	VERY LOW**, [‡]	0.89(0.52, 1.40)	VERY LOW
Nizatidine 600mg VS. Cimetidine 1600mg	—	—	1.09(0.63, 1.79)	LOW [¶] , [‡]	1.09(0.63, 1.79)	LOW
Ranitidine ≤300mg VS. Cimetidine 1600mg	1.17 (0.82, 1.69)	VERY LOW*, §	0.62(0.31, 1.28)	MODERATE [¶] , [‡]	1.05(0.67, 1.55)	MODERATE
Ranitidine 600mg VS. Cimetidine 1600mg	1.86 (1.28, 2.72)	MODERATE*	0.08(0.03, 0.20)	MODERATE [¶]	1.24(0.81, 1.86)	LOW [‡]
Ranitidine 1200mg VS. Cimetidine 1600mg	—	—	1.46(0.92, 2.34)	LOW [¶] , [‡]	1.46(0.92, 2.34)	LOW
Famotidine 80mg VS. Famotidine 40mg	0.81 (0.49, 1.34)	LOW §	1.22(0.98, 1.51)	VERY LOW**, [‡]	1.14(1.004, 1.51)	MODERATE §§
Nizatidine 300mg VS. Famotidine 40mg	—	—	0.62(0.33, 1.01)	VERY LOW**, [‡]	0.62(0.33, 1.01)	VERY LOW
Nizatidine 600mg VS. Famotidine 40mg	—	—	0.76(0.40, 1.23)	VERY LOW**, [‡]	0.76(0.40, 1.23)	VERY LOW
Ranitidine ≤300mg VS. Famotidine 40mg	0.74 (0.45, 1.23)	LOW §	0.70(0.31, 1.60)	VERY LOW**, [‡]	0.73(0.45, 1.06)	LOW
Ranitidine 600mg VS. Famotidine 40mg	—	—	0.86(0.54, 1.26)	VERY LOW**, [‡]	0.86(0.54, 1.26)	VERY LOW
Ranitidine 1200mg VS. Famotidine 40mg	—	—	1.01(0.62, 1.55)	VERY LOW**, [‡]	1.01(0.62, 1.55)	VERY LOW
Nizatidine 300mg VS. Famotidine 80mg	—	—	0.55(0.28, 0.89)	LOW**	0.55(0.28, 0.89)	LOW
Nizatidine 600mg VS. Famotidine 80mg	—	—	0.67(0.35, 1.11)	VERY LOW**, [‡]	0.67(0.35, 1.11)	VERY LOW
Ranitidine ≤300mg VS. Famotidine 80mg	0.92 (0.60, 1.40)	LOW §	0.03(0.01, 0.13)	LOW**	0.64(0.39, 0.95)	LOW
Ranitidine 600mg VS. Famotidine 80mg	—	—	0.76(0.46, 1.11)	VERY LOW**, [‡]	0.76(0.46, 1.11)	VERY LOW
Ranitidine 1200mg VS. Famotidine 80mg	—	—	0.90(0.54, 1.36)	VERY LOW**, [‡]	0.90(0.54, 1.36)	VERY LOW
Nizatidine 600mg VS. Nizatidine 300mg	1.15 (0.67, 1.97)	VERY LOW [†] , §, ※	1.28(0.92, 1.77)	VERY LOW**, [‡]	1.24(1.01, 1.77)	LOW §§
Ranitidine ≤300mg VS. Nizatidine 300mg	—	—	1.21(0.81, 1.81)	LOW [¶] , [‡]	1.21(0.81, 1.81)	LOW
Ranitidine 600mg VS. Nizatidine 300mg	—	—	1.44(0.96, 2.16)	VERY LOW**, [‡]	1.44(0.96, 2.16)	VERY LOW
Ranitidine 1200mg VS. Nizatidine 300mg	—	—	1.70(1.08, 2.67)	VERY LOW**, [‡]	1.70(1.08, 2.67)	VERY LOW
Ranitidine ≤300mg VS. Nizatidine 600mg	—	—	0.99(0.64, 1.47)	VERY LOW**, [‡]	0.99(0.64, 1.47)	VERY LOW
Ranitidine 600mg VS. Nizatidine 600mg	—	—	1.18(0.75, 1.77)	LOW [¶] , [‡]	1.18(0.75, 1.77)	LOW
Ranitidine 1200mg VS. Nizatidine 600mg	—	—	1.39(0.86, 2.21)	LOW [¶] , [‡]	1.39(0.86, 2.21)	LOW
Ranitidine 600mg VS. Ranitidine ≤300mg	1.59 (1.09, 2.31)	LOW*, [‡]	1.01(0.76, 1.36)	VERY LOW**	1.20(1.01, 1.60)	LOW

Ranitidine 1200mg VS. Ranitidine ≤300mg	—	—	1.41(1.06, 2.07)	VERY LOW**	1.41(1.06, 2.07)	VERY LOW
Ranitidine 1200mg VS. Ranitidine 600mg	0.84 (0.57, 1.24)	LOW §	1.44(1.07, 1.94)	LOW¶,‡	1.18(1.01, 1.62)	MODERATE §§

—Not applicable. *Limitations (risk of bias). †Inconsistency. ‡Imprecision. §Severe imprecision. ※Publication bias. **Contributing direct evidence of low or very low quality. ¶Contributing direct evidence of moderate quality. ¶¶Contributing direct evidence of high quality. ‡‡Indirectness because of questionable comparability of trial populations to target population of NMA (level of disease from endoscopy) or because of intransitivity. §§Greater precision.

Supplementary Figure Legends

Supplementary Figure S1a. Risk of bias summary (continued)

Supplementary Figure S1b. Risk of bias summary (continued)

Supplementary Figure S1c. Risk of bias summary (continued)

Supplementary Figure S1d. Risk of bias summary

Supplementary Figure S1a. Risk of bias summary (continued)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Adachi 2003	?	+	?	?	?	+	?
Armstrong 2001	+	?	+	?	+	+	+
Armstrong a 2004	?	?	?	?	+	+	+
Armstrong b 2004	?	?	?	?	+	+	+
Armstrong c 2004	?	?	?	?	+	+	+
Bardhan 1995	+	+	+	+	+	+	+
Bardhan 2001	+	?	●	●	+	+	+
Bardhan 2007	+	+	+	?	+	+	+
Bate 1996	?	?	+	?	+	+	?
Bate 1997	?	?	?	?	+	+	?
Bytzer 2006	+	+	+	?	+	+	?
Castell 1996	?	?	+	?	+	+	?
Castell 2002	+	+	+	?	+	+	+
Cho 2012	+	?	+	?	+	+	?
Cloud 1992	+	?	+	?	+	+	+
Dehn 1990	?	?	+	?	?	+	?
Delchier 2000	?	?	+	?	+	+	?
Dettmer 1998	?	?	+	?	+	+	+
Earnest 1998	?	?	+	?	+	+	?
Eggleston 2009	?	?	+	+	+	+	+
Euler 1993	?	?	+	?	?	+	?
Farley 2000	?	?	+	+	+	+	+
Fass 2000	+	?	●	●	+	+	?
Fennerty 2005	+	+	+	+	+	+	?
Festen 1999	+	?	+	?	+	+	+

Supplementary Figure S1b. Risk of bias summary (continued)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Fock 2005	+	?	+	+	+	+	?
Galmiche 1997	?	?	+	?	+	+	?
Galmiche 1998	?	?	+	?	+	+	+
Gillessen 2004	+	?	+	?	+	+	+
Glatzel 2007	?	?	+	+	+	+	+
Havelund 1988	+	+	+	?	+	+	+
Holtmann 2002	+	?	+	+	+	+	+
Hongo 2008	+	+	+	?	+	+	+
Jansen 1999	?	+	+	?	+	+	+
Johnson 2005	+	+	+	+	+	+	+
Johnson 2010	+	+	+	+	+	+	+
Jones 1999	+	?	+	?	+	+	?
Kahrilas 2000	?	+	+	+	+	+	+
Kahrilas 2005	?	?	+	?	+	+	+
Kao 2003	?	?	+	+	+	+	?
Kaspari 2001	?	?	+	+	+	+	?
Katz a 2003	+	+	+	+	+	+	+
Katz b 2003	+	+	+	+	+	+	+
Kim 2015	+	?	+	●	+	+	?
Kinoshita 2011	+	+	+	+	+	+	?
Kobeissy 2012	+	?	●	●	+	+	+
Koop 1995	?	?	+	+	+	+	?
Korner 2003	+	?	+	+	+	+	+
Kovacs 2002	?	?	+	?	+	+	?
Kushner a 2009	?	?	+	+	+	+	+
Kushner b 2009	?	?	+	+	+	+	+

Supplementary Figure S1c. Risk of bias summary (continued)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Laine a 2011	+	+	+	+	+	+	+
Laine b 2011	+	+	+	+	+	+	+
Lightdale 2006	+	+	+	+	+	+	?
Lundell 1990	?	?	+	?	+	+	+
Maton 1999	?	?	+	?	+	+	+
Mccarty Dawson 1996	?	?	+	?	+	+	?
Mee 1996	+	+	+	+	+	+	+
Meneghelli 2002	+	?	+	+	+	+	+
Miner 2002	?	?	+	?	+	+	?
Monnikes 2007	+	+	+	?	+	+	+
Moraes Filho 2014	+	+	+	+	+	+	?
Mossner 1995	+	?	+	?	+	+	+
Mulder 2002	?	?	+	?	+	+	+
Ohara 2010	+	+	+	?	+	+	+
Pace 2005	+	?	+	+	+	+	?
Palmer 1990	?	?	+	?	+	+	+
Pappa a 1999	?	?	+	?	+	+	+
Pappa b 1999	?	?	+	?	+	+	?
Paul 2001	+	?	+	?	+	+	?
Peura 2009	?	?	+	?	+	+	?
Peura a 2014	+	+	+	?	+	+	?
Peura b 2014	+	+	+	?	+	+	?
Pilotto 2007	+	?	+	+	+	+	?
Quik 1990	?	?	+	?	+	+	?
Richer 1 2000	?	?	+	?	+	+	?

Supplementary Figure S1d. Risk of bias summary

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Richer 2 2000	?	?	+	?	+	+	?
Richter 1 2001	?	?	+	+	+	+	?
Richter 1999	?	?	+	?	+	+	?
Richter 2 2001	+	+	+	+	+	+	+
Riemann 1991	?	?	+	?	?	?	?
Robinson 1991	?	?	?	?	+	+	?
Robinson 1995	?	?	+	?	+	+	?
Robinson 1996	+	?	+	+	+	+	+
Roufail 1992	?	?	+	?	+	+	?
Sabesan 1991	?	?	+	?	+	+	?
Schmitt 2006	+	+	+	+	+	+	?
Scholten 2003	+	?	+	?	+	+	?
Silver 1996	?	?	+	?	+	+	?
Simon 1993	?	?	+	?	+	+	?
Sontag 1987	?	?	+	?	+	+	+
Tan 2011	+	+	+	+	+	+	+
Uemura 2008	?	?	+	?	+	+	?
Vantrappen 1988	?	?	+	?	+	+	+
Van Zyl 2000	+	?	+	+	+	+	+
Van Zyl 2004	+	?	+	?	+	+	+
Venables 1997	?	?	+	?	+	+	+
Zheng 2009	?	+	?	?	+	+	?