

Table S1 Literature Search Strategies in English for the SLR

#	Search Terms
1.	"erosive esophagitis[Title/Abstract] OR "erosive oesophagitis"[Title/Abstract] OR "erosive gastroesophageal reflux disease "[Title/Abstract] OR "erosive reflux esophagitis"[Title/Abstract] OR " erosive gastro-oesophageal reflux disease"[Title/Abstract] OR "erosive gastroesophageal reflux disease"[Title/Abstract] OR "reflux oesophagitis"[Title/Abstract] OR "reflux esophagitis"[Title/Abstract] OR "EE"[Title/Abstract] OR "RE"[Title/Abstract]
2.	" proton pump inhibitors "[Title/Abstract] OR "PPI"[Title/Abstract]
3.	" potassium-competitive acid blockers"[Title/Abstract] OR " P-CAB "[Title/Abstract]
4.	" vonoprazan "[Title/Abstract]
5.	" pantoprazole"[Title/Abstract]
6.	" esomeprazole"[Title/Abstract]
7.	" lansoprazole "[Title/Abstract]
8.	" omeprazole "[Title/Abstract]
9.	" rabeprazole"[Title/Abstract]
10.	" llaprazole"[Title/Abstract]
11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
12.	randomized controlled trial [pt]
13.	controlled clinical trial [pt]
14.	randomized [TIAB]
15.	randomised [TIAB]
16.	"random allocation" [TIAB]
17.	clinical trials as topic [mesh: noexp]
18.	randomly [TIAB]
19.	trial [ti]
20.	"double blind" OR "double blinded" OR "double masked"
21.	"single blind" OR "single blinded" OR "single masked"
22.	#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
23.	#1 AND #11 AND #22
24.	#23 Limits: Humans
25.	#24 Limits: Adult: 19+ Years
26.	#25 Limits: English
27.	#27 Limits: Publication Date 1995-2019

Abbreviations: SLR, systematic literature review; EE, erosive esophagitis; RE, reflux esophagitis; PPI, proton pump inhibitor; P-CAB, potassium-competitive acid blocker

Table S2 PICOS criteria to assess studies for the SLR

PICOS elements	
Population	Adult patients with RE diagnosed by endoscopic examination
Interventions	<ul style="list-style-type: none"> • VPZ monotherapy (standard dose in acute treatment phase and low dose in maintenance phase) • Any PPI monotherapy (standard dose in acute treatment phase and low dose in maintenance phase) approved by National Medical Products Administration in China
Comparators	Any PPI monotherapy (standard dose in acute treatment phase and low dose in maintenance phase) approved by National Medical Products Administration in China
Outcomes	<ul style="list-style-type: none"> • Healing rate at week 4 in treatment phase • Healing rate at week 8 in treatment phase • Relapse rate at week 24 in maintenance phase
Study design	RCT

Abbreviations: SLR, systematic literature review; RE, Reflux esophagitis; PPI, proton pump inhibitors; VPZ, Vonoprazan; RCT, randomized controlled trial.

Table S3 Cost calculation for proton pump inhibitors (PPI) group drug cost

Original PPI Brand	The average tender price of each PPI in 2020 was collected from YAOZHI® database*		Market shares were collected from a panel of nationwide hospital survey (n=12); The market share of original PPIs in <u>2019Q2</u> was used to calculate the weighted average price [#]
	Price of Standard Dose (CNY)	Price of Half Dose (CNY)	Market share by Prescriptions
Omeprazole (Losec)	8.71	5.06	3.6%
Esomeprazole (Nexium)	15.00	9.01	13.9%
Pantoprazole (Protonix)	9.62	4.81	4.0%
Lansoprazole (Prevacid, Takepron)	8.67	4.34	2.2%
Rabeprazole (Pariet)	20.81	10.54	11.0%
Ilaprazole	27.06	13.53	0.70%

PPI group drug cost was calculated based on average tender prices of each PPI available in China weighted by corresponding market shares. Note: *, average price of standard dose of $PPI = \frac{Price\ of\ Standard\ Dose + 2 * Price\ of\ Half\ Dose}{2}$. Each PPI has both standard dose and half dose. In clinical practice, PPI could be taken as 1 tablet with standard dose per day or 2 tablets with half dose per day. #, Market-share weighted average price of standard/half dose of $PPI\ group = \frac{\sum Price\ of\ PPI_i * Market\ Share\ of\ PPI_i}{\sum Market\ Share\ of\ PPI_i}$.

Table S4 Cost of other healthcare resources in a treatment course (Interview results)

Questionnaire	Answer
1 The frequency of outpatient visit and cost	<ul style="list-style-type: none"> • The Initiation of acute treatment needs one outpatient visit and several follow-up visits every 2 weeks for drug prescription. During 6-month maintenance treatment, the outpatient visit should be made every 4 weeks. • The average cost of an outpatient visit is 7\$.
2 The frequency of lab test and cost	<ul style="list-style-type: none"> • Patients were required to take an endoscopy test in the first outpatient visit for diagnosis. For patients who were unhealed after 8-week treatment, esophageal manometry and 24-hour pH monitoring were needed. • The average cost of an endoscopy test is 84\$. • The average cost of 24-hour pH monitoring is 116\$.

Other medical expenses associate with RE treatment were collected via local clinical expert interviews (n=10). RE, reflux esophagitis.

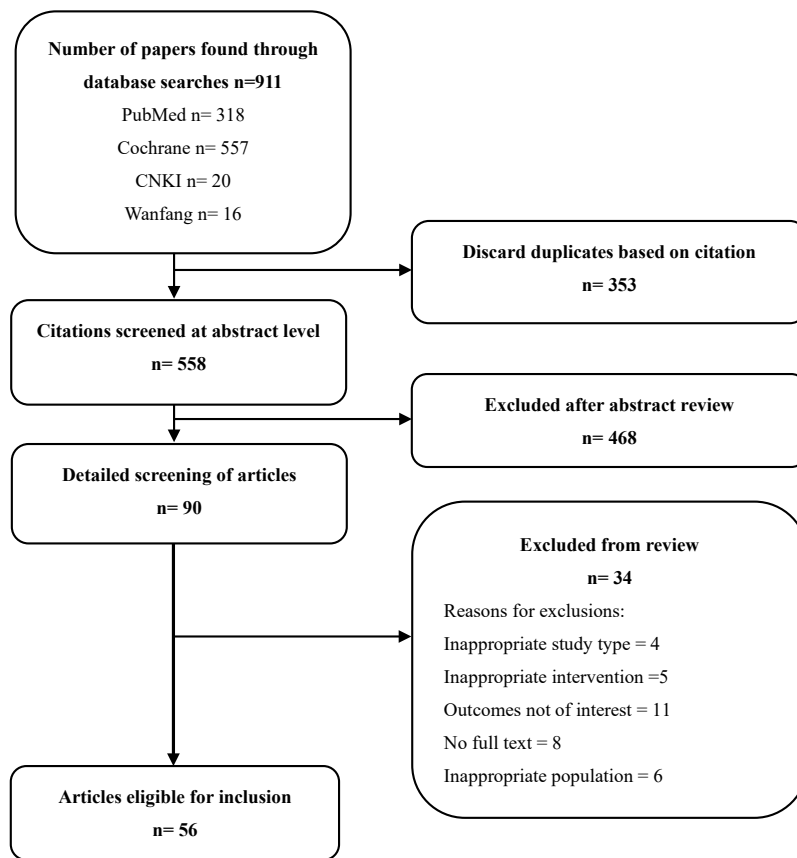


Figure S1 Flowchart of study selection.

Table S5 Baseline characteristics of included trials

First author	Publication year	Study Sample (N)	Treatment	Initial duration	Diagnosis level	Evaluable population (N)	Age (year)		Male (%)
							Mean	SD	
Corinaldesi, R., et al. (1)	1995	241	pantoprazole40mg	8 weeks	SM 2-3	120	50	-	78 (65)
			omeprazole20mg	8 weeks	SM 2-3	121	52	-	75 (62)
Mössner, J., et al. (2)	1995	286	pantoprazole40mg	8 weeks	SM 2-3	191	53	-	133 (70)
			omeprazole20mg	8 weeks	SM 2-3	95	55	-	66 (69)
Castell, D. O., et al. (3)	1996	1284	lansoprazole30mg	8 weeks	other 2-4	422	-	-	-
			omeprazole20mg	8 weeks	other 2-4	431	-	-	-
Mee, A. S., et al. (4)	1996	604	lansoprazole30mg	8 weeks	SM 1-4	300	53.4	-	198 (66)
			omeprazole20mg	8 weeks	SM 1-4	304	52.4	-	204 (67)
Dekkers, C. P., et al. (5)	1999	202	rabeprazole20mg	8 weeks	HD 2-4	100	54	15.7	53 (53)
			omeprazole20mg	8 weeks	HD 2-4	102	52	15.56	73 (72)
Delchier, J. C., et al. (6)	2000	310	rabeprazole20mg	8 weeks	HD 2-4	104	55	15.7	47 (45)
			omeprazole20mg	8 weeks	HD 2-4	103	53	15.1	40 (39)
Kahrilas, P. J., et al. (7)	2000	1960	esomeprazole40mg	8 weeks	LA A-D	654	44.8	13	384 (58.7)
			omeprazole20mg	8 weeks	LA A-D	650	46.5	13.5	399 (61.4)
Richter, J. E., et al. (8)	2000	603	pantoprazole40mg	8 weeks	HD 2-4	173	49.3	13.6	121 (69.9)
Dupas, J. L., et al. (9)	2001	461	pantoprazole40mg	8 weeks	SM 2-3	225	53	14.5	165 (73)
			lansoprazole30mg	8 weeks	SM 2-3	236	55	14.7	178 (58)
Richter, J. E., et al. (10)	2001	2425	esomeprazole40mg	8 weeks	LA A-D	1216	-	-	772 (59.4)
			omeprazole20mg	8 weeks	LA A-D	1209	-	-	760 (62.9)
Castell, D. O., et al. (11)	2002	5241	esomeprazole40mg	8 weeks	LA A-D	2624	47	13	1504 (57.3)
			lansoprazole30mg	8 weeks	LA A-D	2617	47.4	13.1	1501 (57.4)
Howden, C. W., et al. (12)	2002	284	lansoprazole30mg	8 weeks	other 2-4	143	47	-	57 (82)
			esomeprazole40mg	8 weeks	other 2-4	141	46	-	54 (76)
Körner, T., et al. (13)	2003	669	pantoprazole40mg	8 weeks	SM 2-3	337	53.7	14.3	216 (64)
Gillissen, A., et al.(14)	2004	227	pantoprazole40mg	8 weeks	LA B-C	113	53	15	64 (57)
			esomeprazole40mg	8 weeks	LA B-C	114	54	14	57 (50)
Pace, F., et al.(15)	2005	560	rabeprazole20mg	8 weeks	SM 1-3	283	47.7	14.2	190 (67)
			omeprazole20mg	8 weeks	SM 1-3	277	47.1	14.9	184 (66)
Fennerty, M. B., et al. (16)	2005	999	esomeprazole40mg	8 weeks	LA C-D	498	47.3	13.2	327 (65.7)
			lansoprazole30mg	8 weeks	LA C-D	501	47.1	12.9	333 (66.5)
Labenz, J., et al.(17)	2005	3151	esomeprazole40mg	8 weeks	LA A-D	1562	50.6	14	969 (62)
			pantoprazole40mg	8 weeks	LA A-D	1589	50.5	13.8	1102 (63.7)
Lightdale, C. J., et al.(18)	2006	1175	omeprazole20mg	8 weeks	LA A-D	588	45.3	13	376 (63.9)
Schmitt, C., et al.(19)	2006	1148	esomeprazole40mg	8 weeks	LA A-D	576	47.1	13.3	346 (60.1)
			omeprazole20mg	8 weeks	LA A-D	572	46.2	13.6	335 (58.6)
Vcev, A., et al.(20)	2006	180	esomeprazole40mg	8 weeks	LA A-C	90	51.2	14.5	57 (63.3)
			pantoprazole40mg	8 weeks	LA A-C	90	49.4	13.9	59 (65.6)
Bardhan, K.D., et al.(21)	2007	581	pantoprazole40mg	8 weeks	LA A-D	288	53	13	141 (49)
			esomeprazole40mg	8 weeks	LA A-D	293	54	14	154 (53)
Sharma, P., et al.(22)	2009	2038	lansoprazole30mg	8 weeks	LA A-D	690	47.3	13.74	365 (52.9)
Sharma,P., et al.(22)	2009	2054	lansoprazole30mg	8 weeks	LA A-D	673	47.3	13.65	362 (53.8)
Zheng, R.N., et al.(23)	2009	274	omeprazole20mg	8 weeks	LA A-D	68	57.9	14.1	33 (48.5)
			lansoprazole30mg	8 weeks	LA A-D	69	58.1	13	35 (50.7)
			pantoprazole40mg	8 weeks	LA A-D	69	57.8	13.2	34 (49.3)
			esomeprazole40mg	8 weeks	LA A-D	68	57.4	12.8	33 (48.5)
Ashida, K., et al.(24)	2015	733	lansoprazole30mg	8 weeks	LA A-D	140	55.8	13.92	99 (70.7)
			vonoprazan20mg	8 weeks	LA A-D	154	58.3	13.86	115 (74.7)
Ashida, K., et al(25)	2016	409	vonoprazan20mg	8 weeks	LA A-D	207	58.3	13.8	137 (66.2)
			lansoprazole30mg	8 weeks	LA A-D	202	57.4	13.2	154 (76.2)
Chen, M.H., et al(26)	2018	274	vonoprazan20mg	8 weeks	LA A-D	143	51.8	13.7	105 (73.4)
			lansoprazole30mg	8 weeks	LA A-D	131	51.5	12.5	110 (82.7)
Bardhan, K. D. et al(27)	1995	239	lansoprazole30mg	8 weeks	Endoscopic appearance 0-3	77	48	-	50 (65)
Mulder, C. J. et al(28)	1996	211	lansoprazole30mg	8 weeks	SM 2-4	106	54.4	14.3	73 (70)
Rensburg, C.V., et al (29)	1996	192	pantoprazole40mg	8 weeks	SM 1-4	97	46	-	57 (59)
Jansen, J.B., et al(30)	1999	133	lansoprazole30mg	8 weeks	SM 2-3	68	53.7	14.8	42 (61)
Festen, H. P., et al(31)	1999	446	omeprazole20mg	8 weeks	SM 1-2	222	51.1	14.5	118 (53)
Farley, A., et al(32)	2000	338	rabeprazole20mg	8 weeks	HD 0-5	167	51.4	14.9	118 (70)
Kovacs, T. O. G., et al(33)	2002	221	pantoprazole40mg	8 weeks	HD 0-5	76	49.4	13.8	52 (68)
Kawano, S., et al(34)	2002	47	omeprazole20mg	8 weeks	LA A-D	-	56	18	14 (58)
Meneghelli, U. G., et al(35)	2002	256	pantoprazole40mg	8 weeks	SM 2-3	128	46.5	-	80 (63)
Cho, Y. K., et al(36)	2012	129	pantoprazole40mg	8 weeks	LA A-C	74	50	13	61 (82)
Song, F., et al.(37)	2012	180	llaprazole10mg	8 weeks	LA A-D	60	-	-	-
			esomeprazole40mg			60			
Xue, Y., et al.(38)	2016	318	llaprazole10mg	8 weeks	LA A-D	107	48.9	12.6	75 (70)
			esomeprazole40mg			105	47.9	11.7	72 (69)
Ashida, K., et al.(39)	2018	607	Lansoprazole15mg	24 W	LA A-D	196	57.8	12.9	69.70%
			Vonoprazan10mg			197	55.2	13.8	79.20%
Bate, C. M., et al.(40)	1995	193	Omeprazole10mg	52 W	LA A-D	60	53	-	44%
DeVault, K.R., et al.(41)	2006	1026	Esomeprazole20mg	24 W	LA A-D	501	47.5	-	59.30%
			Lansoprazole15mg			500	47.9	-	58.60%
Robinson,M., et al.(42)	1996	115	Lansoprazole15mg	52W	LA A-D	59	-	-	-
Labenz, J., et al.(43)	2005	3170	Esomeprazole20mg	24W	LA A-D	1377	50.2	14.1	64.50%
			Pantoprazole20mg			1389	50.7	13.8	61.60%
Lauritsen, K., et al.(44)	2003	1224	Esomeprazole20mg	24W	LA A-D	615	49.3	-	63.10%
			Lansoprazole15mg			609	49.2	-	58.50%
Richter, J. E., et al.(45)	2004	176	Pantopraole20mg	52W	LA A-D	88	48.99	13.35	69.30%
Vakil, N. B., et al.(46)	2001	281	Esomeprazole20mg	24W	LA A-D	98	45.2	12.8	59.00%
Metz, D.C., et al.(47)	2003	274	Pantoprazole20mg	52W	Grade 2-5	91	49.19	13.39	61.30%
Gough, A. L., et al.(48)	1996	185	Lansoprazole15mg	52W	-	96	57.8	-	68.80%
Kovacs,T.O., et al.(49)	2009	100	Lansoprazole15mg	52W	HD 0-4	100	49.6	13.4	72%
Escourrou, J., et al(50)	1999	396	Pantoprazole20mg	52W	Grade 2-3	203	50	-	72%
Plein, K., et al.(51)	2000	433	Pantoprazole20mg	52W	Grade 2-3	221	-	-	-
Johnson, D.A., et al.(52)	2001	82	Esomeprazole20mg	52W	-	82	-	-	-
Goh, K.L., et al.(53)	2007	1303	Pantoprazole20mg	24W	-	636	49	14.1	58.60%
			Esomeprazole20mg			667	48.8	14.5	85%
Caos, A., et al.(54)	2005	70	Rabeprazole10mg	24W	HD 0-2	70	-	-	-
Birbara, C., et al.(55)	2000	95	Rabeprazole10mg	24W	-	95	-	-	-
Bardhan, K.D., et al.(56)	1998	130	Omeprazole10mg	24W	-	130	-	-	-

Abbreviations: SD, standard deviation; LA, Los Angeles grade ; HD, Hetzel–Dent scale ; SM, Savary–Miller scale

Table S6 Main outcomes of included trials for treatment studies

First author	Publication Year	Study Sample (N)	Treatment (n)	Evaluable population (All), N	All patients Healing rates at week 4	All patients Healing rates at week 8	Evaluable population (Moderate-severe), N	Moderate-severe patients Healing rate at week 4	Moderate-severe patients Healing rate at week 8
Corinaldesi, R., <i>et al.</i> (1)	1995	241	pantoprazole 40 mg	120	81/120	97/120	/	/	/
			omeprazole 20 mg	121	83/121	96/121	/	/	/
MöSsner, J., <i>et al.</i> (2)	1995	286	pantoprazole 40 mg	191	126/191	153/191	/	/	/
			omeprazole 20 mg	95	67/95	81/95	/	/	/
Castell, D. O., <i>et al.</i> (3)	1996	1284	lansoprazole 30 mg	422	352/422	380/422	/	/	/
			omeprazole 20 mg	431	353/431	391/431	/	/	/
Mee, A. S., <i>et al.</i> (4)	1996	604	lansoprazole 30 mg	300	186/300	226/300	40	18/40	26/40
			omeprazole 20 mg	304	172/304	216/304	42	24/42	25/42
Dekkers, C. P., <i>et al.</i> (5)	1999	202	rabeprazole 20 mg	100	81/100	92/100	/	/	/
			omeprazole 20 mg	102	83/102	96/102	/	/	/
Delchier, J. C., <i>et al.</i> (6)	2000	310	rabeprazole 20 mg	104	92/104	95/104	/	/	/
			omeprazole 20 mg	103	94/103	97/103	/	/	/
Kahrilas, P. J., <i>et al.</i> (7)	2000	1960	esomeprazole 40 mg	654	496/654	615/654	/	/	/
			omeprazole 20 mg	650	411/650	565/650	/	/	/
Richter, J. E. <i>et al.</i> (8)	2000	603	pantoprazole 40 mg	173	125/173	152/173	/	/	/
Dupas, J. L., <i>et al.</i> (9)	2001	461	pantoprazole 40 mg	225	184/225	203/225	/	/	/
			lansoprazole 30 mg	236	189/236	201/236	/	/	/
Richter, J. E., <i>et al.</i> (10)	2001	2425	esomeprazole 40 mg	1216	993/1216	1139/1216	/	/	/
			omeprazole 20 mg	1209	831/1209	1018/1209	/	/	/
Castell, D. O., <i>et al.</i> (11)	2002	5241	esomeprazole 40 mg	2624	2083/2624	2430/2624	/	/	/
			lansoprazole 30 mg	2617	1965/2617	2324/2617	/	/	/
Howden, C. W., <i>et al.</i> (12)	2002	284	lansoprazole 30 mg	143	107/143	127/143	52	/	48/52
			esomeprazole 40 mg	141	108/141	123/141	57	/57	47/57
Körner, T., <i>et al.</i> (13)	2003	669	pantoprazole 40 mg	337	220/337	284/337	/	/	/
Gillessen, A., <i>et al.</i> (14)	2004	227	pantoprazole 40 mg	113	55/113	94/113	/	/	/
			esomeprazole 40 mg	114	68/114	92/114	/	/	/
Pace, F., <i>et al.</i> (15)	2005	560	rabeprazole 20 mg	283	212/283	228/283	/	/	/
			omeprazole 20 mg	277	213/277	231/277	/	/	/
Fennerty, M. B., <i>et al.</i> (16)	2005	999	esomeprazole 40 mg	498	278/498	386/498	498	278/498	386/498
			lansoprazole 30 mg	501	/	/	501	238/501	367/501
Labenz, J., <i>et al.</i> (17)	2005	3151	esomeprazole 40 mg	1562	1231/1562	1493/1562	374	259/374	340/374
			pantoprazole 40 mg	1589	1157/1589	1463/1589	395	219/395	333/395
Lightdale, C. J., <i>et al.</i> (18)	2006	1175	omeprazole 20 mg	588	/	484/588	154	/154	110/154
Schmitt, C., <i>et al.</i> (19)	2006	1148	esomeprazole 40 mg	576	393/576	501/576	189	115/189	167/189
			omeprazole 20 mg	572	379/572	491/572	169	81/169	131/169
Vcev, A., <i>et al.</i> (20)	2006	180	esomeprazole 40 mg	90	70/90	83/90	13	8/13	10/13
			pantoprazole 40 mg	90	65/90	82/90	16	8/16	12/16
Bardhan, K.D., <i>et al.</i> (21)	2007	581	pantoprazole 40 mg	288	199/288	248/288	/	/	/
			esomeprazole 40 mg	293	202/293	243/293	/	/	/
Sharma, P., <i>et al.</i> (22)	2009	2038	lansoprazole 30 mg	690	/	518/690	210	/210	130/210
Sharma, P., <i>et al.</i> (22)	2009	2054	lansoprazole 30 mg	673	/	548/673	194	/194	150/194
Zheng, R.N., <i>et al.</i> (23)	2009	274	omeprazole 20 mg	68	/	57/68	/	/	/
			lansoprazole 30 mg	69	/	60/69	/	/	/
			pantoprazole 40 mg	69	/	61/69	/	/	/
			esomeprazole 40 mg	68	/	62/68	/	/	/
Ashida, K., <i>et al.</i> (24)	2015	733	lansoprazole 30 mg	140	123/140	126/140	47	40/47	43/47
			vonoprazan20 mg	154	136/154	139/154	51	50/51	50/51
Ashida, K., <i>et al.</i> (25)	2016	409	vonoprazan20 mg	207	198/207	203/207	75	72/75	74/75
			lansoprazole 30 mg	202	184/202	190/202	73	58/73	63/73
Chen, M.H., <i>et al.</i> (26)	2018	274	vonoprazan20 mg	143	120/143	131/143	54	38/54	45/54
			lansoprazole 30 mg	131	109/131	116/131	46	32/46	36/46
Bardhan, K. D., <i>et al.</i> (27)	1995	239	lansoprazole 30 mg	77	63/77	70/77	58	45/58	51/58
Mulder, C. J., <i>et al.</i> (28)	1996	211	lansoprazole 30 mg	106	91/106	99/106	29	24/29	27/29
Rensburg, C.V., <i>et al.</i> (29)	1996	192	pantoprazole 40 mg	97	67/97	82/97	/	/	/
Jansen, J.B., <i>et al.</i> (30)	1999	133	lansoprazole 30 mg	68	54/68	62/68	/	/	/
Festen, H. P., <i>et al.</i> (31)	1999	446	omeprazole 20 mg	222	135/222	165/222	/	/	/
Farley, A., <i>et al.</i> (32)	2000	338	rabeprazole 20 mg	167	98/167	146/167	/	/	/
Kovacs, T. O. G., <i>et al.</i> (33)	2002	221	pantoprazole 40 mg	76	48/76	58/76	30	11/30	16/30
Kawano, S., <i>et al.</i> (34)	2002	47	omeprazole 20 mg	/	/	/	7	/	4/7
Meneghelli, U. G., <i>et al.</i> (35)	2002	256	pantoprazole 40 mg	128	69/128	96/128	24	12/24	17/24
Cho, Y. K., <i>et al.</i> (36)	2012	129	pantoprazole 40 mg	74	52/74	60/74	/	/	/
Song, F., <i>et al.</i> (37)	2012	180	lansoprazole 10 mg	60	51/60	54/60	/	/	/
			esomeprazole 40 mg	60	52/60	55/60	/	/	/
Xue, Y., <i>et al.</i> (38)	2016	318	lansoprazole 10 mg	107	87/107	95/107	/	/	/
			esomeprazole 40 mg	105	75/105	89/105	/	/	/

Table S7 Main outcomes of included trials for maintenance studies

First author	Publication year	Study Sample (N)	Treatment (n)	Evaluable population (All), N	All patients Remission rate* at week 24	Evaluable population (Moderate-severe), N	Moderate-severe patients Remission rate* at week 24
Ashida, K., <i>et al.</i> (39)	2018	607	Lansoprazole 15 mg	196	172/196	41	25/41
			Vonoprazan 10 mg	197	192/197	40	33/38
Bate, C. M., <i>et al.</i> (40)	1995	193	Omeprazole 10 mg	60	/	/	/
DeVault, K.R., <i>et al.</i> (41)	2006	1026	Esomeprazole 20 mg	501	432/501	121	96/121
			Lansoprazole 15 mg	500	388/500	131	91/131
Robinson, M., <i>et al.</i> (42)	1996	115	Lansoprazole 15 mg	59	48/59		
Labenz, J., <i>et al.</i> (43)	2005	3170	Esomeprazole 20 mg	1377	1198/1377	323	263/323
			Pantoprazole 20 mg	1389	1040/1389	317	208/317
Lauritsen, K., <i>et al.</i> (44)	2003	1224	Esomeprazole 20 mg	615	510/615	114	86/114
			Lansoprazole 15 mg	609	451/609	102	60/102
Richter, J. E., <i>et al.</i> (45)	2004	176	Pantoprazole 20 mg	88	/	/	/
Vakil, N. B., <i>et al.</i> (46)	2001	281	Esomeprazole 20 mg	98	77/98	/	/
Metz, D.C., <i>et al.</i> (47)	2003	274	Pantoprazole 20 mg	91	/	23	16/23
Gough, A. L., <i>et al.</i> (48)	1996	185	Lansoprazole 15 mg	96	78/96	/	/
Kovacs, T.O., <i>et al.</i> (49)	2009	100	Lansoprazole 15 mg	100	/	/	/
Escourrou, J., <i>et al.</i> (50)	1999	396	Pantoprazole 20 mg	203	171/203	/	/
Plein, K., <i>et al.</i> (51)	2000	433	Pantoprazole 20 mg	221	177/221	/	/
Johnson, D.A., <i>et al.</i> (52)	2001	82	Esomeprazole 20 mg	82	76/82	/	/
Goh, K.L., <i>et al.</i> (53)	2007	1303	Pantoprazole 20 mg	636	534/636	/	/
			Esomeprazole 20 mg	667	567/667	/	/
Caos, A., <i>et al.</i> (54)	2005	70	Rabeprazole 10 mg	70	54/70	/	/
Birbara, C., <i>et al.</i> (55)	2000	95	Rabeprazole 10 mg	95	81/95	/	/
Bardhan, K.D., <i>et al.</i> (56)	1998	130	Omeprazole 10 mg	130	107/130	/	/

*Remission rate is the proportion of patients who remained healed during the 6 months. This is the widely reported endpoint in majority clinical trials' *Relapse rate = 1 - remission rate

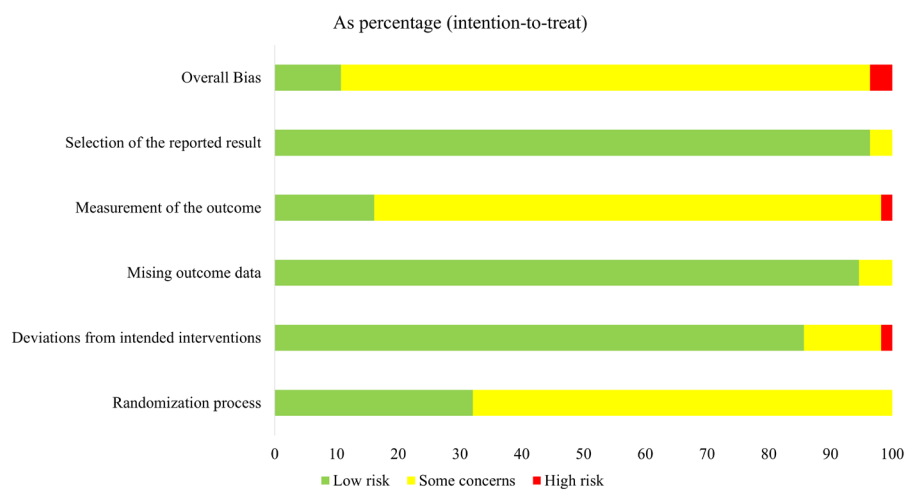


Figure S2 Risk of bias assessment for included clinical trials: overall judgements at each level per domain.

	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Corinaldesi_1995	?	?	+	?	?	!
Mössner_1995	?	+	?	?	+	!
Castell_1996	?	+	+	?	+	!
Mee_1996	+	?	+	?	+	!
Dekkers_1999	?	+	+	+	+	!
Delchier_2000	?	+	+	?	+	!
Kahrilas_2000	+	+	+	?	+	!
Richter_2000	?	+	+	?	+	+
Dupas_2001	?	+	+	?	+	!
Richter_2001	+	+	+	?	+	!
Castell_2002	+	+	+	?	+	!
Howden_2002	?	+	+	+	+	!
Körner_2003	?	+	+	?	+	!
Gillessen_2004	?	+	+	?	+	!
Pace_2005	+	+	+	?	+	!
Fennerty_2005	+	+	+	?	+	!
Labenz_2005	?	+	+	?	+	!
Lightdale_2006	+	+	+	?	+	!
Schmitt_2006	+	+	+	?	+	!
Vcev_2006	?	?	+	?	+	?
Bardhan_2007	+	+	+	?	+	!
Sharma_2009	?	+	+	?	+	+
Zheng_2009	+	+	+	?	+	!
Ashida_2015	?	+	+	?	+	!
Ashida_2016	+	+	+	?	+	!
Chen_2018	?	+	+	?	+	!
Bardhan_1995	?	+	+	?	+	!
Mulder_1996	?	+	+	?	+	!
Rensburg_1996	?	+	+	?	+	!
Jansen_1999	?	+	+	?	+	!
Festen_1999	?	?	+	?	+	!
Farley_2000	?	+	+	+	+	+
Kovacs_2002	?	+	+	+	+	!
Kawano_2002	?	?	+	?	+	!
Meneghelli_2002	?	+	+	?	+	!
Cho_2012	?	?	?	?	?	!
Song_2012	?	+	+	?	+	!
Xue_2016	?	+	+	?	+	!
Ashida_2018	+	+	+	+	+	+
Bate_1995	?	+	+	?	+	!
DeVault_2006	+	?	+	+	+	?
Robinson_1996	?	?	+	+	+	!
Labenz_2005	?	+	+	?	+	!
Lauritsen_2003	?	+	+	?	+	!
Richter_2004	+	+	+	?	+	!
Vakil_2001	+	+	+	+	+	+
Metz_2003	?	+	+	?	+	!
Gough_1996	+	+	+	?	+	!
Kovacs_2009	?	+	+	?	+	!
Escourrou_1999	?	+	?	?	+	!
Plein_2000	?	+	+	?	+	!
Johnson_2001	+	+	+	+	+	+
Goh_2007	?	+	+	?	+	!
Caos_2000	?	+	+	?	+	!
Birbara_2000	?	+	+	?	+	!
Bardhan_1998	+	+	+	?	+	!

Figure S3 Risk of bias assessment for included clinical trials: judgements at each level per domain, study-by-study.

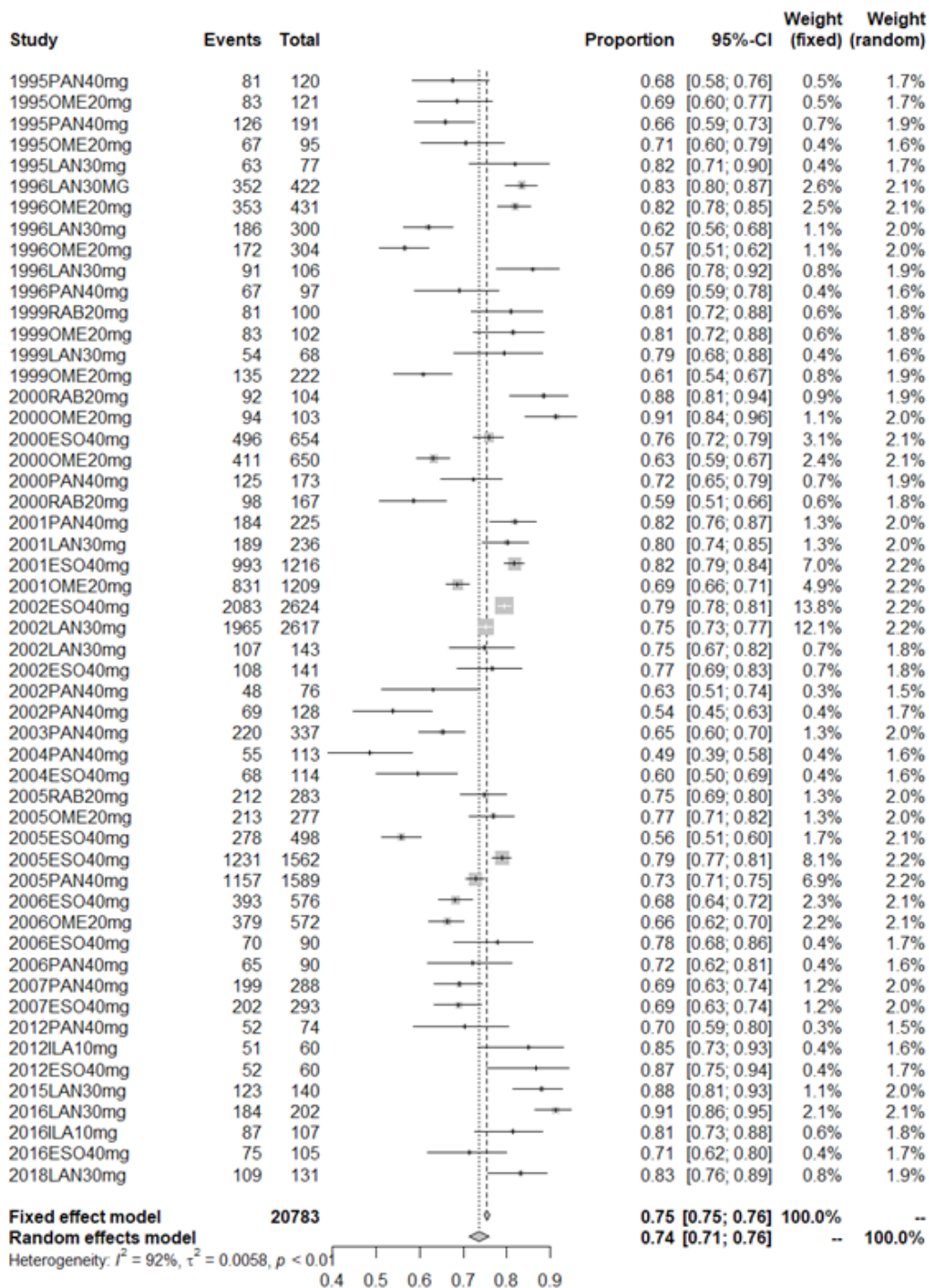


Figure S4 Meta-analysis results – Healing rate of PPI group at week 4 for all patients.

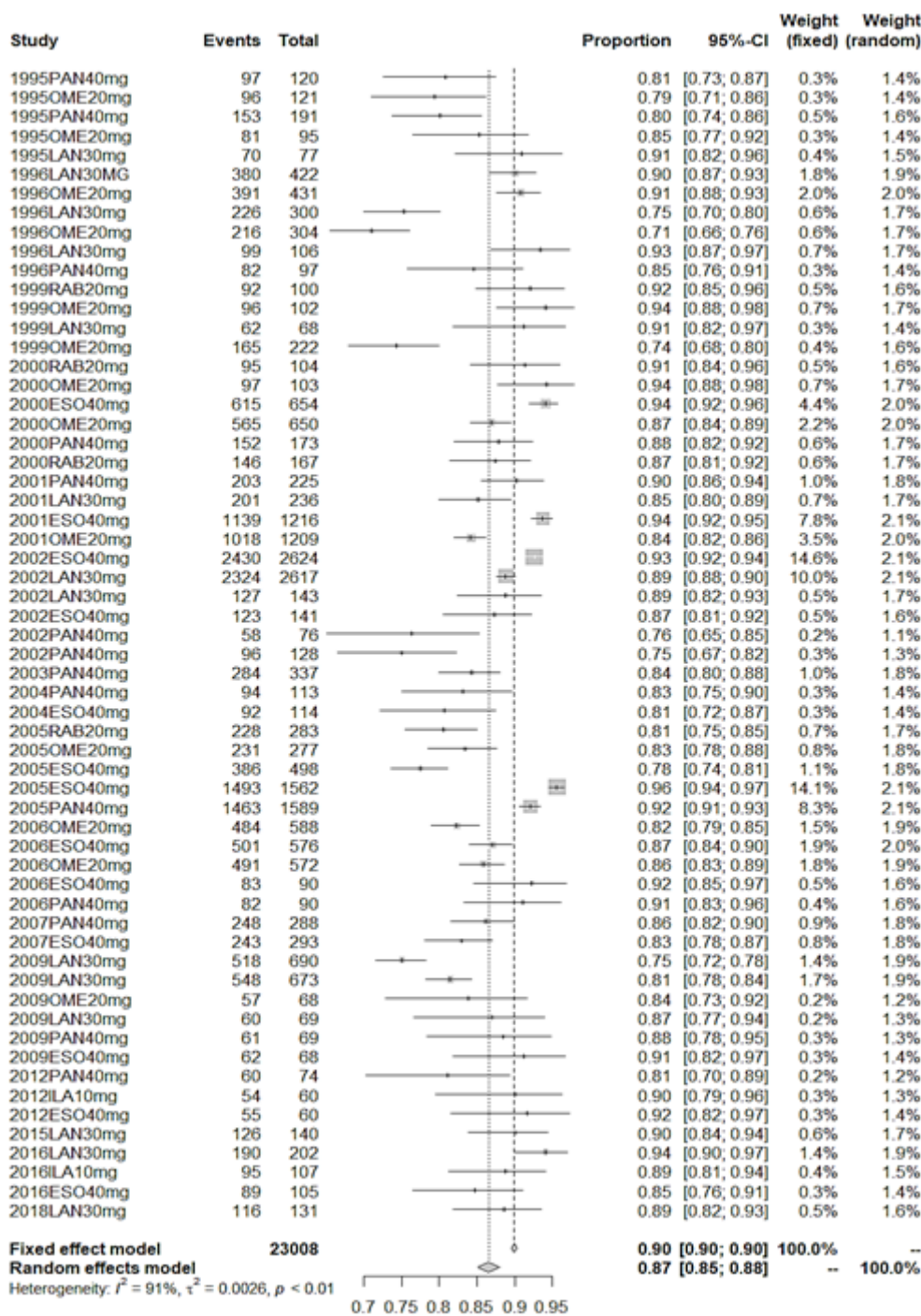


Figure S5 Meta-analysis results – Healing rate of PPI group at week 8 for all patients.

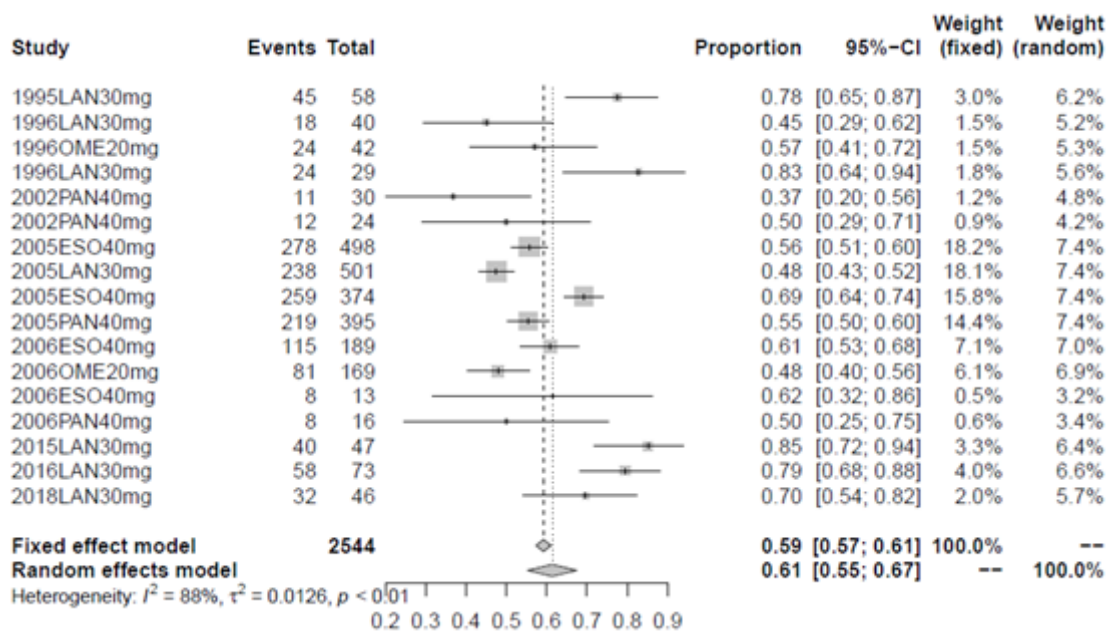


Figure S6 Meta-analysis results – Healing rate of PPI group at week 4 for moderate-to-severe patients.

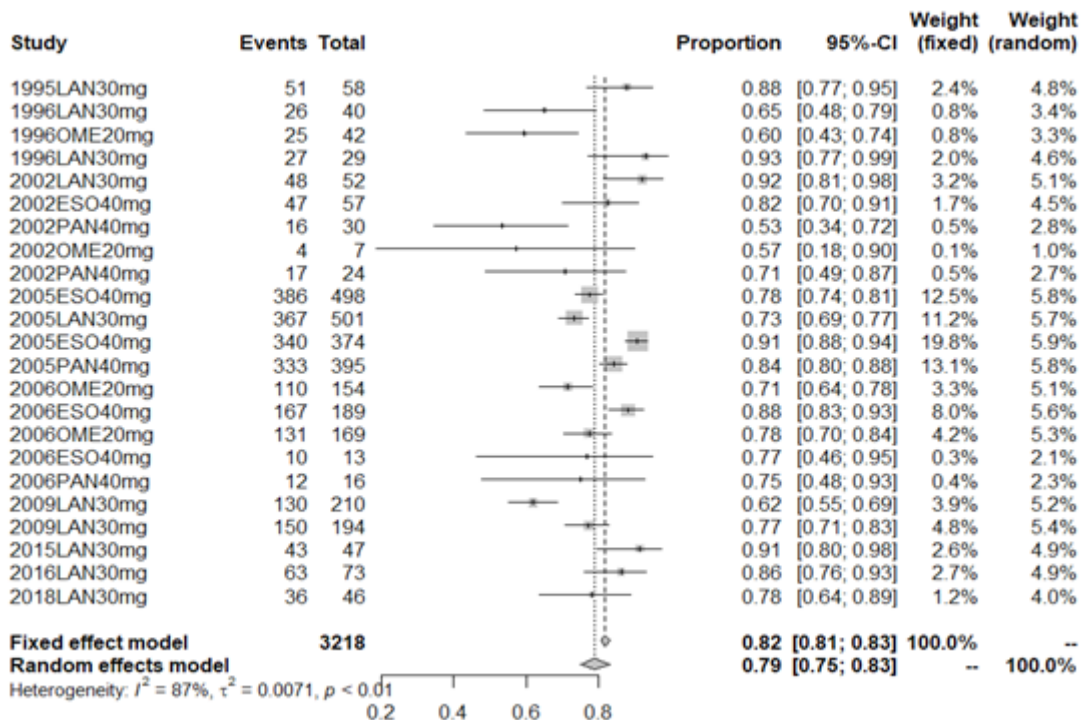


Figure S7 Meta-analysis results – Healing rate of PPI group at week 8 for moderate-to-severe patients.

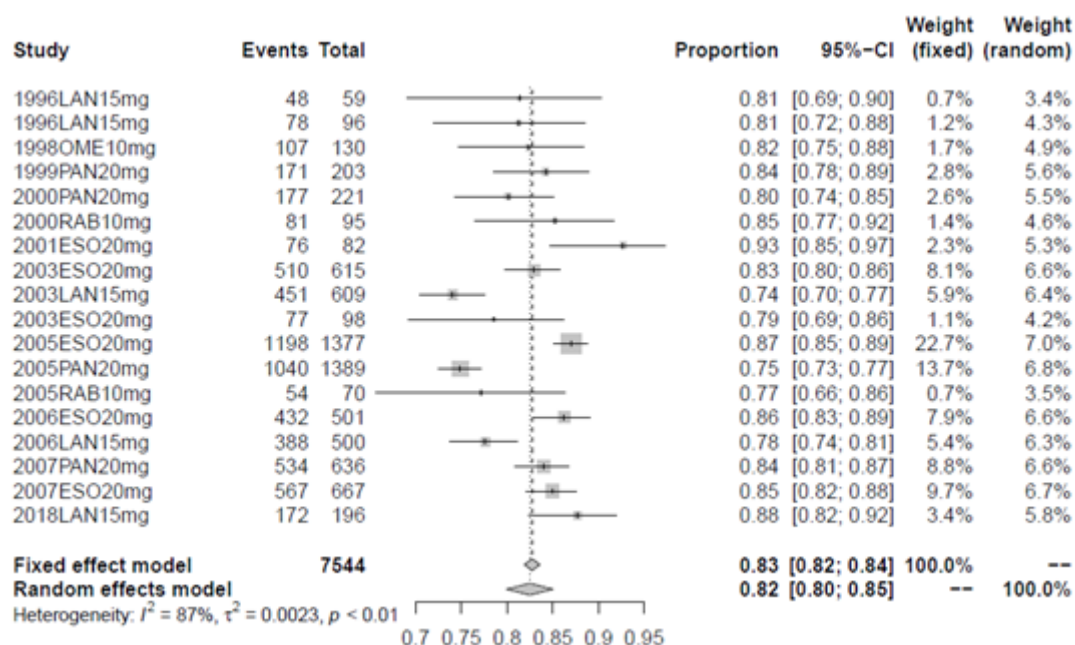


Figure S8 Meta-analysis results – Remission rate of PPI group at week 24 for all patients.

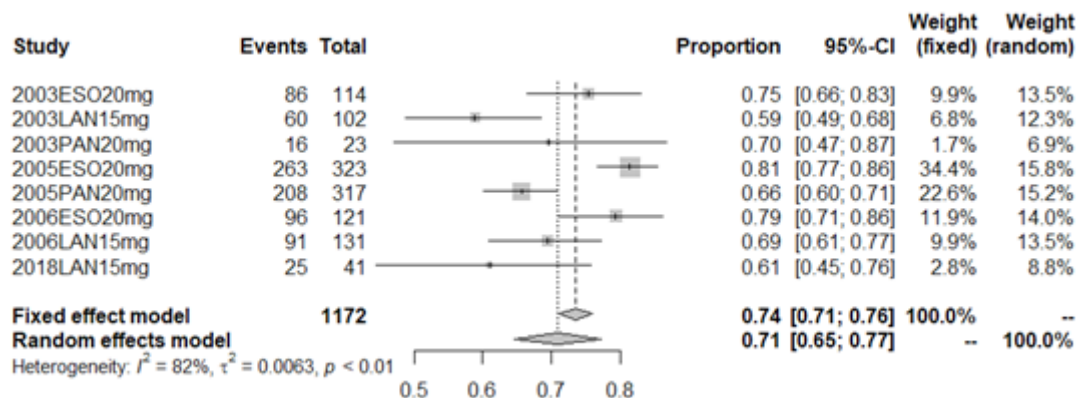


Figure S9 Meta-analysis results – Remission rate of PPI group at week 24 for moderate-to-severe patients.

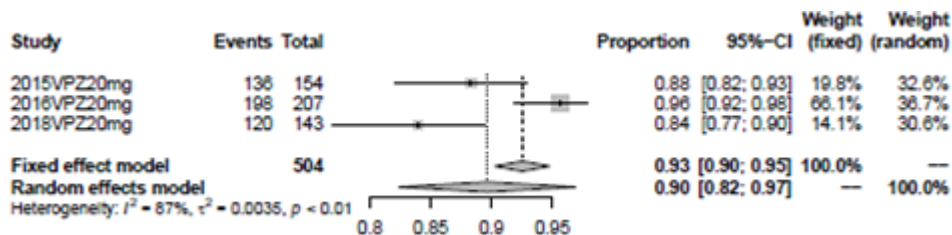


Figure S10 Meta-analysis results - Healing rate of VPZ at week 4 for all RE patients.

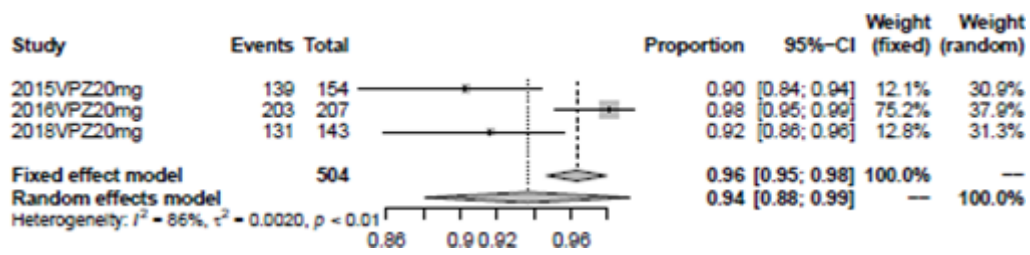


Figure S11 Meta-analysis results - Healing rate of VPZ at week 8 for all RE patients.

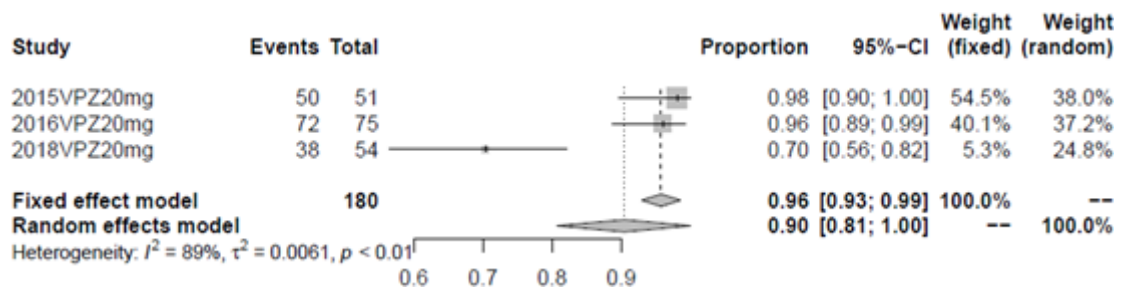


Figure S12 Meta-analysis results - Healing rate of VPZ at week 4 for moderate-to-severe patients.

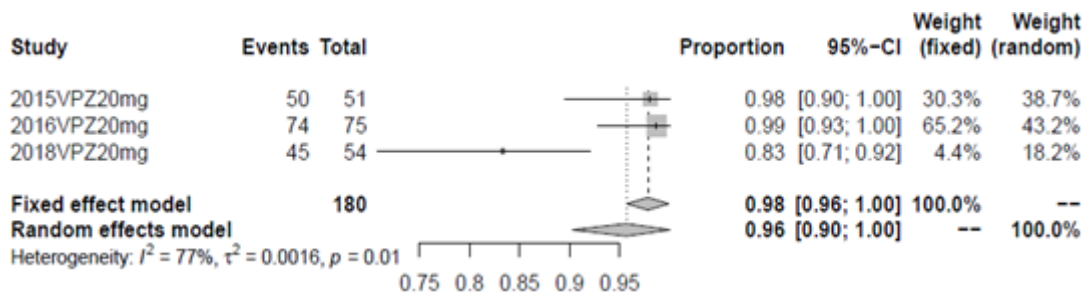


Figure S13 Meta-analysis results - Healing rate of VPZ at week 8 for moderate-to-severe patients.

References

1. Corinaldesi R, Valentini M, Belâiche J, et al. Pantoprazole and omeprazole in the treatment of reflux oesophagitis: a European multicentre study. *Aliment Pharmacol Ther.* 1995 Dec;9(6):667-671.
2. Mössner J, Hölscher AH, Herz R, et al. A double-blind study of pantoprazole and omeprazole in the treatment of reflux oesophagitis: a multicentre trial. *Aliment Pharmacol Ther.* 1995 Jun;9(3):321-6.
3. Castell DO, Richter JE, Robinson M, et al. Efficacy and safety of lansoprazole in the treatment of erosive reflux esophagitis. The Lansoprazole Group. *Am J Gastroenterol.* 1996 Sep;91(9):1749-57.
4. Mee AS, Rowley JL, THE LANSOPRAZOLE CLINICAL RESEARCH GROUP. Rapid symptom relief in reflux oesophagitis: a comparison of lansoprazole and omeprazole. *Aliment Pharmacol Ther.* 1996 Oct;10(5):757-63.
5. Dekkers CP, Beker JA, Thjodleifsson B, et al. Double-blind, placebo-controlled comparison of rabeprazole 20 mg vs. omeprazole 20 mg in the treatment of erosive or ulcerative gastro-oesophageal reflux disease. *Aliment Pharmacol Ther.* 1999 Jan;13(1):49-57.
6. Delchier JC, Cohen G, Humphries TJ. Rabeprazole, 20 mg once daily or 10 mg twice daily, is equivalent to omeprazole, 20 mg once daily, in the healing of erosive gastroesophageal reflux disease. *Scand J Gastroenterol.* 2000 Dec;35(12):1245-50.
7. Kahrilas PJ, Falk GW, Johnson DA, et al. Esomeprazole improves healing and symptom resolution as compared with omeprazole in reflux oesophagitis patients: a randomized controlled trial. *Aliment Pharmacol Ther.* 2000 Oct;14(10):1249-58.
8. Richter JE. Oral Pantoprazole for Erosive Esophagitis: A Placebo-Controlled, Randomized Clinical Trial. 2000;95(11):10.
9. Dupas JL, Houcke P, Samoyeau R. Pantoprazole versus lansoprazole in French patients with reflux esophagitis. *Gastroenterol Clin Biol.* 2001 Mar;25(3):245-50.
10. Richter JE, Breiter JR, Levine JG. Efficacy and Safety of Esomeprazole Compared With Omeprazole in GERD Patients With Erosive Esophagitis: A Randomized Controlled Trial. 2001;96(3):10.
11. Castell DO, Johnson DA. Esomeprazole (40 mg) Compared With Lansoprazole (30 mg) in the Treatment of Erosive Esophagitis. 2002;97(3):9.
12. Howden CW, Ballard ED, Robieson W. Evidence for Therapeutic Equivalence of Lansoprazole 30mg and Esomeprazole 40mg in the Treatment of Erosive Oesophagitis: *Clin Drug Investig.* 2002;22(2):99-109.
13. Körner T, Schütze K, van Leendert RJM, et al. Comparable Efficacy of Pantoprazole and Omeprazole in Patients with Moderate to Severe Reflux Esophagitis. *Digestion.* 2003;67(1-2):6-13.
14. Gillissen A, Beil W, Modlin IM, et al. 40 mg Pantoprazole and 40 mg Esomeprazole Are Equivalent in the Healing of Esophageal Lesions and Relief from Gastroesophageal Reflux Disease-related Symptoms. *J Clin Gastroenterol.* 2004 Apr;38(4):332-40.
15. Pace F, Annese V, Prada A, et al. Rabeprazole is equivalent to omeprazole in the treatment of erosive gastro-oesophageal reflux disease. *Dig Liver Dis.* 2005 Oct;37(10):741-50.
16. Fennerty MB, Johanson JF, Hwang C, et al. Efficacy of esomeprazole 40 mg vs. lansoprazole 30 mg for healing moderate to severe erosive oesophagitis. *Aliment Pharmacol Ther.* 2005 Feb;21(4):455-63.
17. Labenz J, Armstrong D, Lauritsen K, et al. A randomized comparative study of esomeprazole 40 mg versus pantoprazole 40 mg for healing erosive oesophagitis: the EXPO study. *Aliment Pharmacol Ther.* 2005 Mar 15;21(6):739-46.
18. Lightdale CJ, Schmitt C, Hwang C, et al. A Multicenter, Randomized, Double-Blind, 8-Week Comparative Trial of Low-Dose Esomeprazole (20 mg) and Standard-Dose Omeprazole (20 mg) in Patients with Erosive Esophagitis. *Dig Dis Sci.* 2006 May;51(5):852-7.
19. Schmitt C, Lightdale CJ, Hwang C, et al. A Multicenter, Randomized, Double-Blind, 8-Week Comparative Trial of Standard Doses of Esomeprazole (40 mg) and Omeprazole (20 mg) for the Treatment of Erosive Esophagitis. *Dig Dis Sci.* 2006 May;51(5):844-50.
20. Vcev A, Begić I, Ostojić R, et al. Esomeprazole versus pantoprazole for healing erosive oesophagitis. *Coll Antropol.* 2006 Sep;30(3):519-22.
21. Bardhan KD, Achim A, Riddermann T, et al. A clinical trial comparing pantoprazole and esomeprazole to explore the concept of achieving 'complete remission' in gastro-oesophageal reflux disease: ACHIEVING 'COMPLETE REMISSION' IN GASTRO-OESOPHAGEAL REFLUX DISEASE. *Aliment Pharmacol Ther.* 2007 Apr 9;25(12):1461-9.
22. Sharma P, Shaheen NJ, Perez MC, et al. Clinical trials: healing of erosive oesophagitis with dexlansoprazole MR, a proton pump inhibitor with a novel dual delayed-release

- formulation - results from two randomized controlled studies. *Aliment Pharmacol Ther.* 2009 Apr;29(7):731–41.
23. Zheng RN. Comparative study of omeprazole, lansoprazole, pantoprazole and esomeprazole for symptom relief in patients with reflux esophagitis. *World J Gastroenterol WJG.* 2009 Feb 28;15(8):990–5.
 24. Ashida K, Sakurai Y, Nishimura A, et al. Randomised clinical trial: a dose-ranging study of vonoprazan, a novel potassium-competitive acid blocker, vs. lansoprazole for the treatment of erosive oesophagitis. *Aliment Pharmacol Ther.* 2015 Sep;42(6):685–95.
 25. Ashida K, Sakurai Y, Hori T, et al. Randomised clinical trial: vonoprazan, a novel potassium-competitive acid blocker, vs. lansoprazole for the healing of erosive oesophagitis. *Aliment Pharmacol Ther.* 2016 Jan;43(2):240–51.
 26. Chen MH, Dai N, Fei GJ, et al. A Phase 3, Randomized, Double-Blind, Multicenter Study to Evaluate the Efficacy and Safety of Vonoprazan 20 mg Once Daily Compared to Lansoprazole 30 mg Once Daily in Patients with Erosive Esophagitis: Results from a Chinese Cohort. 2018 United European Gastroenterology Week, October 20–24, Vienna, Austria. P1154.
 27. Bardhan KD, Hawkey CJ, Long RG, et al. Lansoprazole versus ranitidine for the treatment of reflux oesophagitis. UK Lansoprazole Clinical Research Group. *Aliment Pharmacol Ther.* 1995 Apr;9(2):145–51.
 28. Mulder CJ, Dekker W, Gerretsen M. Lansoprazole 30 mg versus omeprazole 40 mg in the treatment of reflux oesophagitis grade II, III and IVa (a Dutch multicentre trial). Dutch Study Group. *Eur J Gastroenterol Hepatol.* 1996 Nov 1;8(11):1101–6.
 29. Rensburg CV, Honiball PJ, Grundling HD, et al. Efficacy and tolerability of pantoprazole 40 mg versus 80 mg in patients with reflux oesophagitis. *Aliment Pharmacol Ther.* 1996;10(3):397–401.
 30. Jansen JB, Van Oene JC. Standard-dose lansoprazole is more effective than high-dose ranitidine in achieving endoscopic healing and symptom relief in patients with moderately severe reflux oesophagitis. The Dutch Lansoprazole Study Group. *Aliment Pharmacol Ther.* 1999 Dec;13(12):1611–20.
 31. Festen HP, Schenk E, Tan G, et al. Omeprazole versus high-dose ranitidine in mild gastroesophageal reflux disease: short- and long-term treatment. The Dutch Reflux Study Group. *Am J Gastroenterol.* 1999 Apr;94(4):931–6.
 32. Farley A, Wruble LD, Humphries TJ. Rabeprazole versus ranitidine for the treatment of erosive gastroesophageal reflux disease: a double-blind, randomized clinical trial. Rabeprazole Study Group. *Am J Gastroenterol.* 2000 Aug;95(8):1894–9.
 33. Kovacs TOG, Wilcox CM, Devault K, et al. Comparison of the efficacy of pantoprazole vs. nizatidine in the treatment of erosive oesophagitis: a randomized, active-controlled, double-blind study. *Aliment Pharmacol Ther.* 2002;16(12):2043–52.
 34. Kawano S, Murata H, Tsuji S, et al. Randomized comparative study of omeprazole and famotidine in reflux esophagitis. *J Gastroenterol Hepatol.* 2002;17(9):955–9.
 35. Meneghelli UG, Boaventura S, Moraes-Filho JPP, et al. Efficacy and tolerability of pantoprazole versus ranitidine in the treatment of reflux esophagitis and the influence of *Helicobacter pylori* infection on healing rate. *Dis Esophagus Off J Int Soc Dis Esophagus.* 2002;
 36. Cho YK, Choi M-G, Bak Y-T, et al. Efficacy of S-Pantoprazole 20 mg Compared with Pantoprazole 40 mg in the Treatment of Reflux Esophagitis: A Randomized, Double-Blind Comparative Trial. *Dig Dis Sci.* 2012 Dec 1;57(12):3189–94.
 37. Song F, He H, Shen L, et al. Efficacy and Safety of ilaprazole in the treatment of 180 patients with reflux esophagitis. *Chin J New Drugs.* 2012(21(8):905–7.
 38. Xue Y, Qin X, Zhou L, et al. A Randomized, Double-blind, Active-Controlled, Multi-center Study of Ilaprazole in the Treatment of Reflux Esophagitis. *Clin Drug Investig.* 2016 Dec;36(12):985–92.
 39. Ashida K, Iwakiri K, Hiramatsu N, et al. Maintenance for healed erosive esophagitis: Phase III comparison of vonoprazan with lansoprazole. *World J Gastroenterol.* 2018 Apr 14;24(14):1550–61.
 40. Bate CM, Booth SN, Crowe JP, et al. Omeprazole 10 mg or 20 mg once daily in the prevention of recurrence of reflux oesophagitis. Solo Investigator Group. *Gut.* 1995 Apr;36(4):492–8.
 41. DeVault KR, Johanson JF, Johnson DA, et al. Maintenance of Healed Erosive Esophagitis: A Randomized Six-Month Comparison of Esomeprazole Twenty Milligrams With Lansoprazole Fifteen Milligrams. *Clin Gastroenterol Hepatol.* 2006 Jul;4(7):852–9.
 42. Robinson M, Lanza F, Avner D, et al. Effective maintenance treatment of reflux esophagitis with low-dose lansoprazole. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med.* 1996 May 15;124(10):859–67.
 43. Labenz J, Armstrong D, Lauritsen K, et al. Esomeprazole 20 mg vs. pantoprazole 20 mg for maintenance therapy

- of healed erosive oesophagitis: results from the EXPO study1. *Aliment Pharmacol Ther.* 2005 Nov;22(9):803–11.
44. Lauritsen K, Deviere J, Bigard M-A, et al. Esomeprazole 20 mg and lansoprazole 15 mg in maintaining healed reflux oesophagitis: Metropole study results. *Aliment Pharmacol Ther.* 2003 Feb;17(3):333–41.
 45. Richter JE, Fraga P, Mack M, et al. Prevention of erosive oesophagitis relapse with pantoprazole. *Aliment Pharmacol Ther.* 2004 Sep 1;20(5):567–75.
 46. Vakil NB, Shaker R, Johnson DA, et al. The new proton pump inhibitor esomeprazole is effective as a maintenance therapy in GERD patients with healed erosive oesophagitis: a 6-month, randomized, double-blind, placebo-controlled study of efficacy and safety. *Aliment Pharmacol Ther.* 2001 Jul;15(7):927–35.
 47. Metz DC, Bochenek WJ. Pantoprazole maintenance therapy prevents relapse of erosive oesophagitis. *Aliment Pharmacol Ther.* 2003;17(1):155–64.
 48. Gough AL, Long RG, Cooper BT, et al. Lansoprazole versus ranitidine in the maintenance treatment of reflux oesophagitis. *Aliment Pharmacol Ther.* 1996;10(4):529–39.
 49. Kovacs TO, Freston JW, Haber MM, et al. Long-Term Efficacy of Lansoprazole in Preventing Relapse of Erosive Reflux Esophagitis. *Dig Dis Sci.* 2009 Mar 7;54(8):1693.
 50. Escourrou J, Deprez P, Saggiaro A, et al. Maintenance therapy with pantoprazole 20 mg prevents relapse of reflux oesophagitis. *Aliment Pharmacol Ther.* 1999 Nov;13(11):1481–91.
 51. Plein K, Hotz J, Wurzer H, et al. Pantoprazole 20 mg is an effective maintenance therapy for patients with gastro-oesophageal reflux disease. *Eur J Gastroenterol Hepatol.* 2000 Apr;12(4):425–32.
 52. Johnson DA, Benjamin SB, Vakil NB, et al. Esomeprazole once daily for 6 months is effective therapy for maintaining healed erosive esophagitis and for controlling gastroesophageal reflux disease symptoms: a randomized, double-blind, placebo-controlled study of efficacy and safety. *Am J Gastroenterol.* 2001 Jan;96(1):27–34.
 53. Goh K-L, Benamouzig R, Sander P, et al. Efficacy of pantoprazole 20mg daily compared with esomeprazole 20mg daily in the maintenance of healed gastroesophageal reflux disease: a randomized, double-blind comparative trial –the EMANCIPATE study: *Eur J Gastroenterol Hepatol.* 2007 Mar;19(3):205–11.
 54. Caos A, Moskovitz M, Dayal Y, et al. Rabeprazole for the prevention of pathologic and symptomatic relapse of erosive or ulcerative gastroesophageal reflux disease. Rabeprazole Study Group. *Am J Gastroenterol.* 2000 Nov 1;95(11):3081–8.
 55. Birbara C, Breiter J, Perdomo C, et al. Rabeprazole for the prevention of recurrent erosive or ulcerative gastro-oesophageal reflux disease. Rabeprazole Study Group. *Eur J Gastroenterol Hepatol.* 2000 Aug;12(8):889–97.
 56. Bardhan KD, Cherian P, Vaishnavi A, et al. Erosive oesophagitis: outcome of repeated long term maintenance treatment with low dose omeprazole 10 mg or placebo. *Gut.* 1998 Oct;43(4):458–64.