SUPPLEMENT

Search Strategy

MEDLINE, EMBASE and EMBASE Classic, and the Cochrane central register of controlled trials were searched. The search was limited to humans. No restrictions were applied with regard to language of publication. A recursive search of the bibliography of relevant articles was also conducted. Conference proceedings from Digestive Diseases Week, Asia Pacific Digestive Week, and United European Gastroenterology Week were searched. The literature search used is given below.

For randomised controlled trials of eradication therapy for *H. pylori*-positive functional dyspepsia:

1 exp Dyspepsia/

2 dyspep* or "NUD" or "FD"

3 indigestion or indigestive

4 1 or 2 or 3

5 exp helicobacter

6 exp helicobacter infections

7 exp helicobacter pylori

8 helicobacter or pylori or pyloridis or "HP" or Campylobacter

9 5 or 6 or 7 or 8

10 4 and 9

11 randomized controlled trial

12 controlled clinical trial.pt

13 random*

14 placebo

15 drug therapy

16 trial

17 groups

18 11 or 12 or 13 or 14 or 15 or 16 or 17

19 exp animals/ not

20 18 not 19

21 10 and 20

For randomised controlled trials of drugs for functional dyspepsia:

1 dyspepsia.mp. or Dyspepsia/

2 dyspep$.mp.

3 1 or 2

4 Antidepressive Agents, Second-Generation/ or Antidepressive Agents/ or venlafaxine.mp. or Serotonin Uptake Inhibitors/

5 psychotropic drugs.mp. or Psychotropic Drugs/

6 antidepressive agents.mp. or Antidepressive Agents/

7 Antidepressive Agents, Tricyclic/ or Desipramine/ or tricyclic.mp. or Nortriptyline/ or Serotonin Uptake Inhibitors/ or Imipramine/

8 desimipramine.mp.

9 doxepin.mp. or Doxepin/

10 dothiepin.mp. or Dothiepin/

11 Amitriptyline/ or amitryptiline.mp.

12 paroxetine.mp. or Paroxetine/

13 sertraline.mp. or Sertraline/

14 fluoxetine.mp. or Fluoxetine/

15 citalopram.mp. or Citalopram/

16 trimipramine.mp. or Trimipramine/

17 desipramine.mp. or Desipramine/

18 imipramine.mp. or Imipramine/

19 nortiptyline.mp. or Nortriptyline/

20 venlafaxine.mp.

21 duloxetine.mp.

22 escitalopram.mp.

23 Sulpiride/ or levosulpiride.mp.

24 mirtazapine.mp.

25 pregabalin

26 gabapentin

27 Histamine 2 receptor antagonists.mp.

28 Histamine-2 receptor antagonists.mp.

29 H2 receptor antagonists.mp.

30 H-2 receptor antagonists.mp.

31 famotidine.mp.

32 nizatidine.mp.

33 ranitidine.mp.

34 cimetidine.mp.

35 proton pump inhibitors.mp.

36 PPIs.mp. 35 omeprazole.mp.

37 esomeprazole.mp.

38 lansoprazole.mp.

39 dexlansoprazole.mp.

40 rabeprazole.mp.

41 pantoprazole.mp.

42 zantac.mp.

43 tagamet.mp.

44 losec.mp.

45 prilosec.mp.

46 zoton.mp.

47 nexium.mp.

48 pariet.mp.

49 protium.mp.

50 mosapride.mp.

51 itopride.mp.

52 Ganaton.mp.

53 acotiamide.mp.

54 Acofide.mp.

55 tegaserod.mp.

56 zelnorm.mp.

57 serotonin norepinephrine reuptake inhibitors.mp or Serotonin and Noradrenaline Reuptake Inhibitors/

58 Serotonin 5-HT1 Receptor agonists/ or tandospirone.mp or Receptor, Serotonin, 5-HT1A/

59. buspirone.mp or Buspirone/

60 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59

61 3 and 60

Supplementary Table 1. Summary of Evidence from Randomised Controlled Trials of Drugs in Functional Dyspepsia.

Intervention	Number of RCTs	Number of Patients	FD Subtype	Relative Risk of Symptoms not Improving (95% CI)	Recommendation	Quality of Evidence
***H. pylori* eradication therapy is effective in FD**	29	6781	Not stated	0.87 (0.83 to 0.92)	Strong	High
Histamine-$_2$-receptor antagonists may be effective in FD	12	2268	Not stated	0.79 (0.68 to 0.92)	Weak	Low
Proton pump inhibitors are effective in FD						
Any dose	16	6017	Not stated	0.88 (0.83 to 0.93)	Strong	High
High dose	5	1627	Not stated	0.86 (0.74 to 1.01)	Strong	High
Standard dose	9	2890	Not stated	0.86 (0.78 to 0.95)	Strong	High
Low dose	9	2755	Not stated	0.89 (0.81 to 0.97)	Strong	High

Prokinetics may be effective in FD						
Acotiamide	6	2429	Mainly PDS	0.89 (0.78 to 1.00)	Weak	Low
Itopride	5	1854	Not stated	0.88 (0.77 to 1.01)	Weak	Low
Mosapride	1	589	Not stated	0.99 (0.80 to 1.23)	Weak	Low
Tegaserod	2	2667	Not stated	0.89 (0.82 to 0.96)	Strong	Moderate
Antipsychotic drugs (sulpiride and levosulpiride) may be effective in FD	3	172	Not stated	0.50 (0.37 to 0.67)	Weak	Low
Tricyclic antidepressants are effective in FD	4	400	Not stated	0.75 (0.62 to 0.90)	Strong	Moderate
Selective serotonin reuptake inhibitors are not effective in FD	2	388	Not stated	1.01 (0.89 to 1.15)	Weak	Moderate
Serotonin norepinephrine reuptake inhibitors are not effective in FD	1	160	Not stated	1.02 (0.80 to 1.30)	Weak	Low
Tandospirone may be effective in FD	1	150	Not stated	0.79 (0.66 to 0.94)	Weak	Low
Buspirone is not effective in FD	1	16	Not stated	0.48 (0.20 to 1.15)	Weak	Low

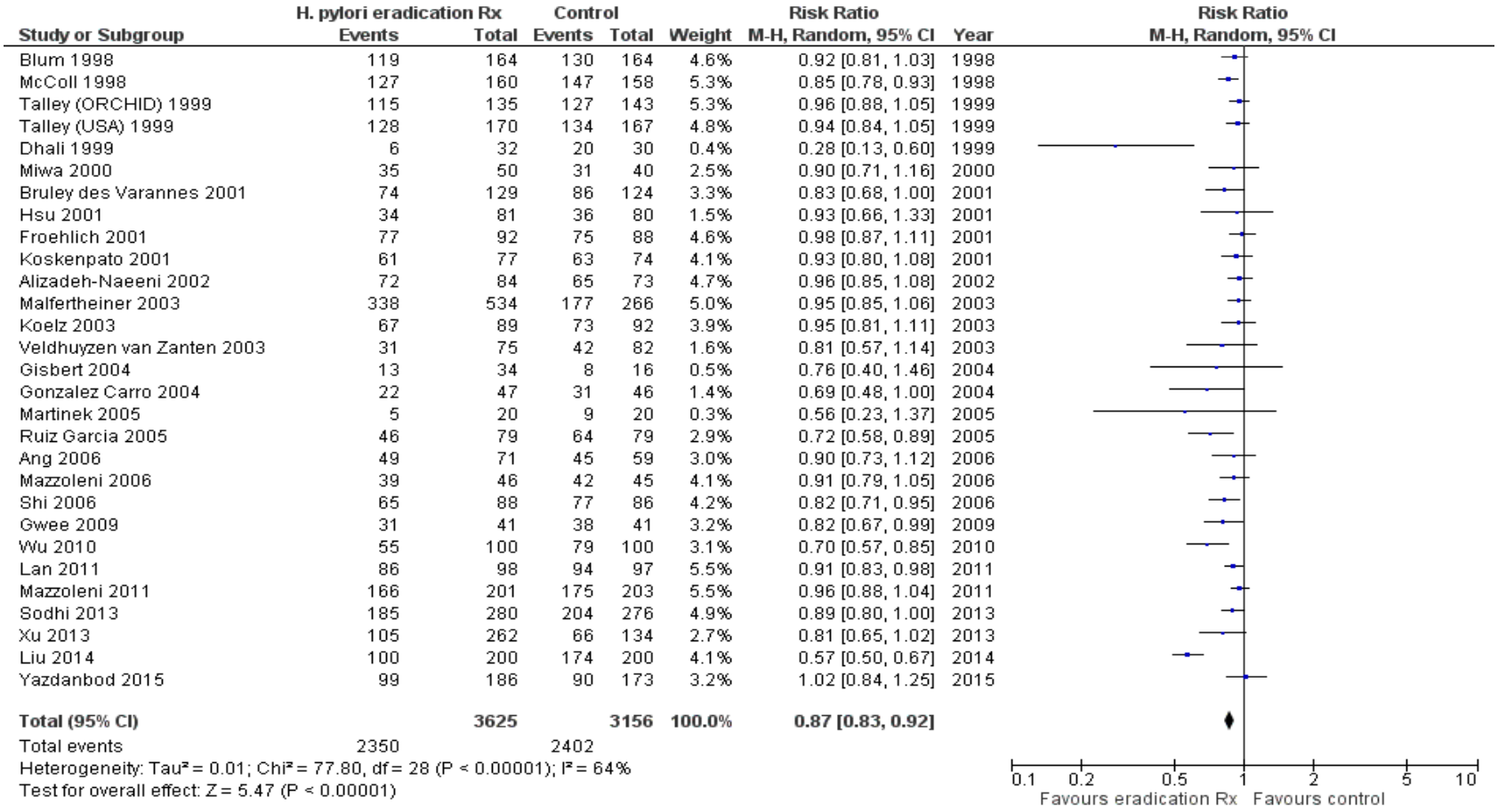
Pregabalin may be effective in FD	1	72	Not stated	0.53 (0.29 to 0.96)	Weak	Low

Supplementary Table 2. Total Number of Trials of Each Treatment, and Total Number of Included Patients Assigned to Each Drug and Placebo in the Network Meta-analysis of Drugs Used First or Second Line in FD.

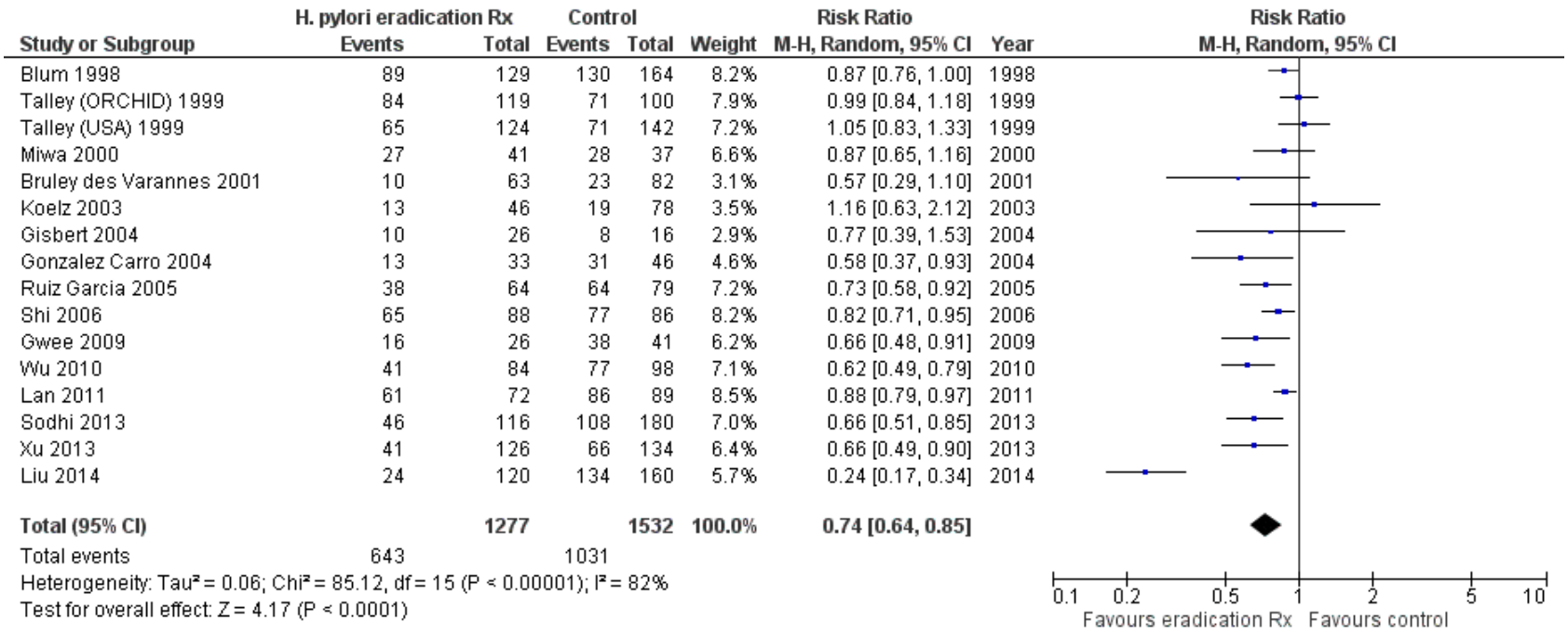
Treatment	Number of RCTs	Total Number of Patients
H_2-receptor antagonists	16	1293
Itopride	13	1653
Standard dose proton pump inhibitors	11	1693
Low dose proton pump inhibitors	10	1431
Mosapride	8	908
High dose proton pump inhibitors	7	1288
Domperidone	7	587
Acotiamide	6	1540
Tricyclic antidepressants	5	228
5-HT_{1A} agonists	5	158
Selective serotonin reuptake inhibitors	3	216
Antipsychotics	3	86
Tegaserod	2	1337
Mirtazapine	2	37
Serotonin norepinephrine reuptake inhibitors	1	80
Pregabalin	1	38

Placebo	55	6742

Supplementary Figure 1. Forest Plot of Randomised Controlled Trials of Eradication Therapy in *H. pylori*-positive FD in Terms of Effect on Cure or Improvement of Symptoms: Pairwise Meta-analysis.



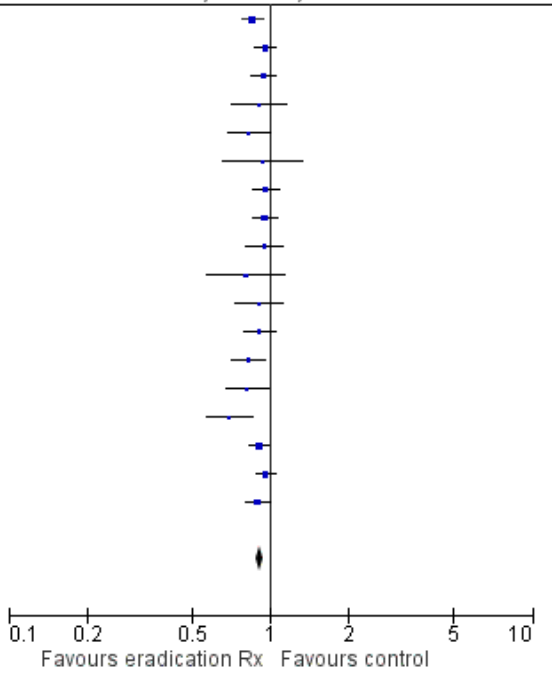
Supplementary Figure 2. Forest Plot of Randomised Controlled Trials of Eradication Therapy in *H. pylori*-positive FD in Terms of Effect on Cure or Improvement of Symptoms in Patients with Successful Eradication of *H. pylori*: Pairwise Meta-analysis.



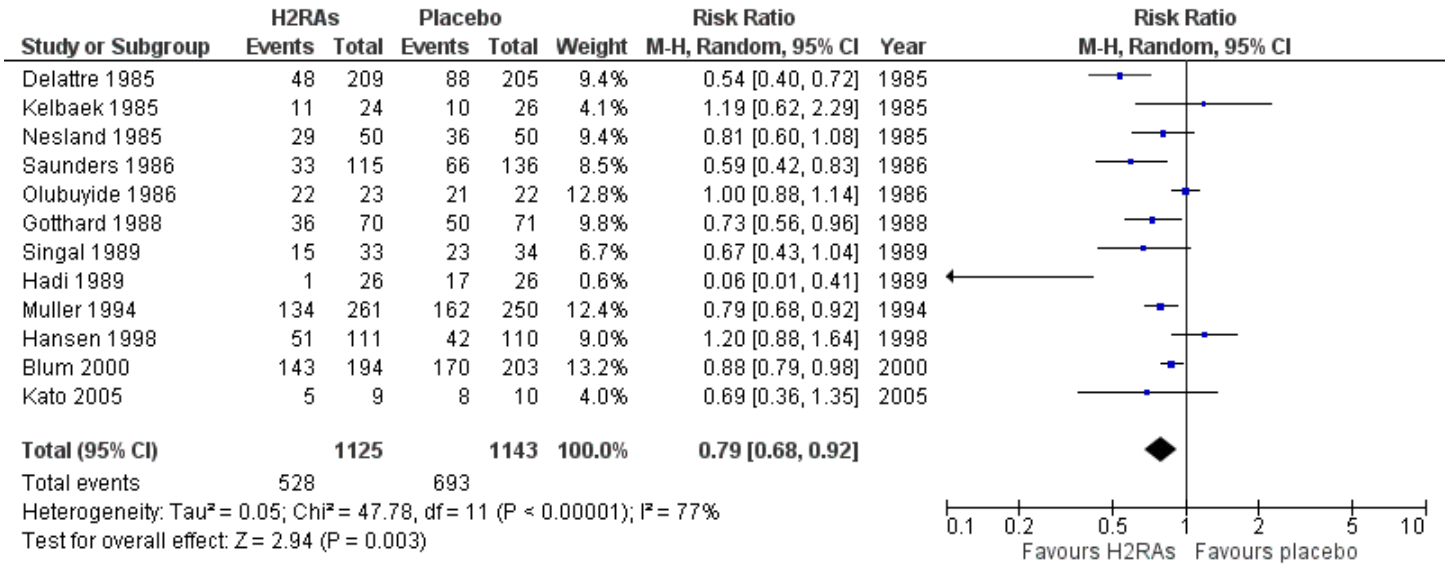
Supplementary Figure 3. Forest Plot of Randomised Controlled Trials of Eradication Therapy in *H. pylori*-positive FD in Terms of Effect on Cure of Symptoms: Pairwise Meta-analysis.

Study or Subgroup	H. pylori eradication Rx Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
McColl 1998	127	160	147	158	10.7%	0.85 [0.78, 0.93]	1998
Talley (ORCHID) 1999	115	135	127	143	10.4%	0.96 [0.88, 1.05]	1999
Talley (USA) 1999	128	170	134	167	6.9%	0.94 [0.84, 1.05]	1999
Miwa 2000	35	50	31	40	1.6%	0.90 [0.71, 1.16]	2000
Bruley des Varannes 2001	74	129	86	124	2.7%	0.83 [0.68, 1.00]	2001
Hsu 2001	34	81	36	80	0.8%	0.93 [0.66, 1.33]	2001
Alizadeh-Naeeni 2002	72	84	65	73	6.5%	0.96 [0.85, 1.08]	2002
Malfertheiner 2003	338	534	177	266	7.8%	0.95 [0.85, 1.06]	2003
Koelz 2003	67	89	73	92	3.8%	0.95 [0.81, 1.11]	2003
Veldhuyzen van Zanten 2003	31	75	42	82	0.8%	0.81 [0.57, 1.14]	2003
Ang 2006	49	71	45	59	2.2%	0.90 [0.73, 1.12]	2006
Mazzoleni 2006	39	46	42	45	4.4%	0.91 [0.79, 1.05]	2006
Shi 2006	65	88	77	86	4.5%	0.82 [0.71, 0.95]	2006
Gwee 2009	31	41	38	41	2.5%	0.82 [0.67, 0.99]	2009
Wu 2010	55	100	79	100	2.3%	0.70 [0.57, 0.85]	2010
Lan 2011	86	98	94	97	12.5%	0.91 [0.83, 0.98]	2011
Mazzoleni 2011	166	201	175	203	12.0%	0.96 [0.88, 1.04]	2011
Sodhi 2013	185	280	204	276	7.5%	0.89 [0.80, 1.00]	2013
Total (95% CI)		**2432**		**2132**	**100.0%**	**0.91 [0.88, 0.94]**	
Total events	1697		1672				

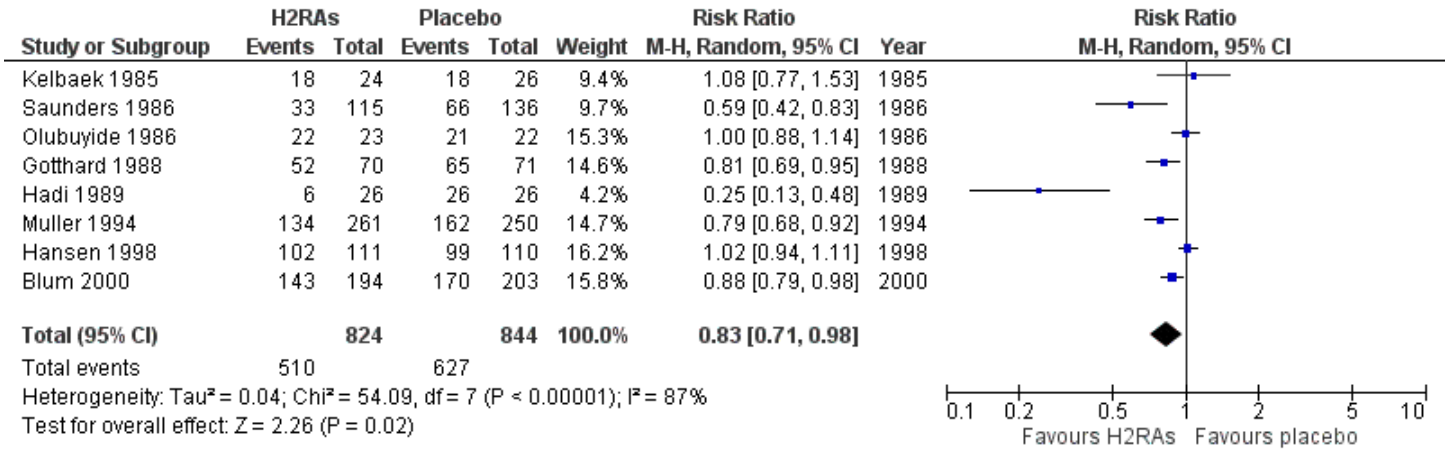
Heterogeneity: Tau² = 0.00; Chi² = 18.21, df = 17 (P = 0.38); I² = 7%
Test for overall effect: Z = 6.10 (P < 0.00001)



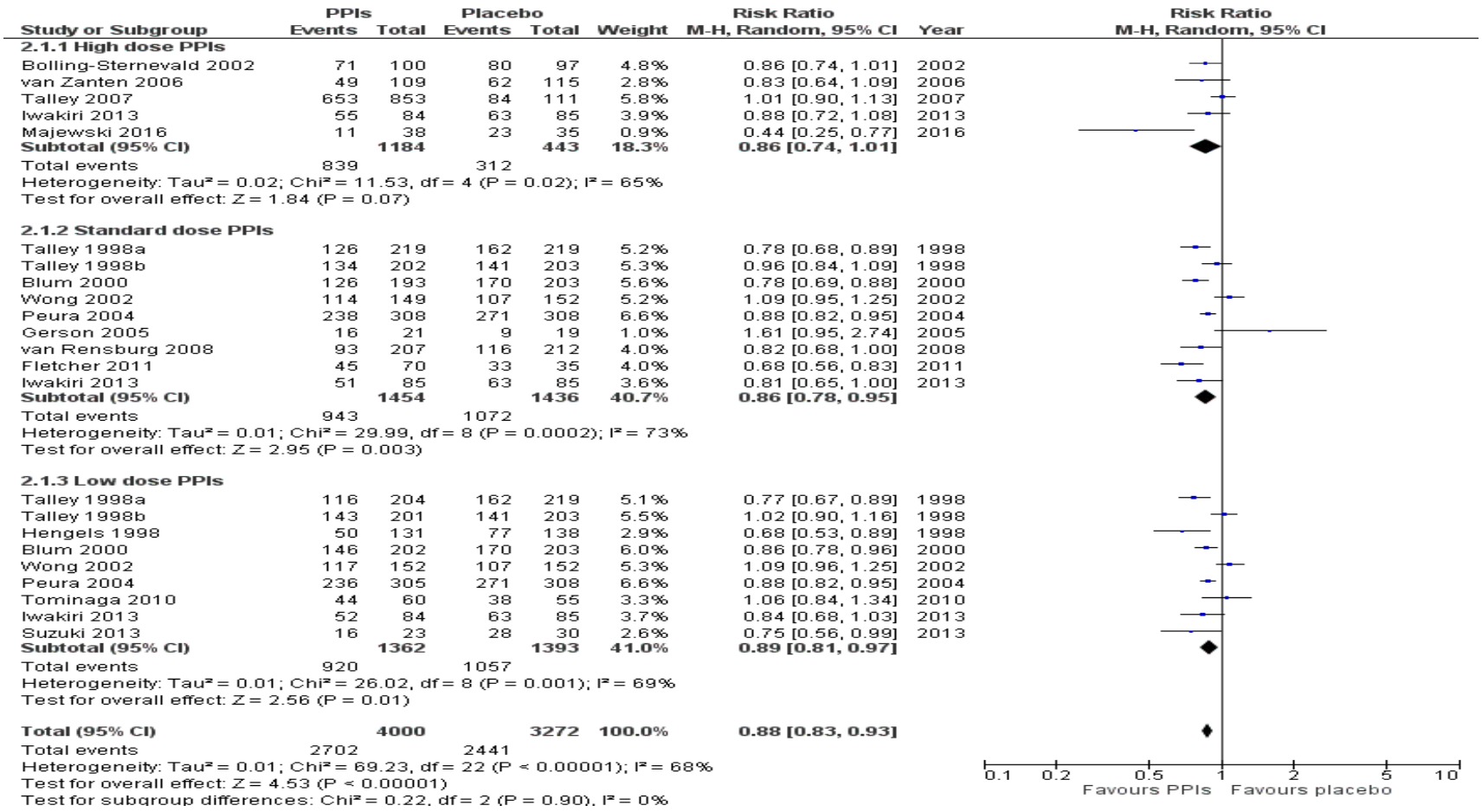
Supplementary Figure 4. Forest Plot of Randomised Controlled Trials of Histamine-$_2$-Receptor Antagonists in FD in Terms of Effect on Improvement of Symptoms: Pairwise Meta-analysis.



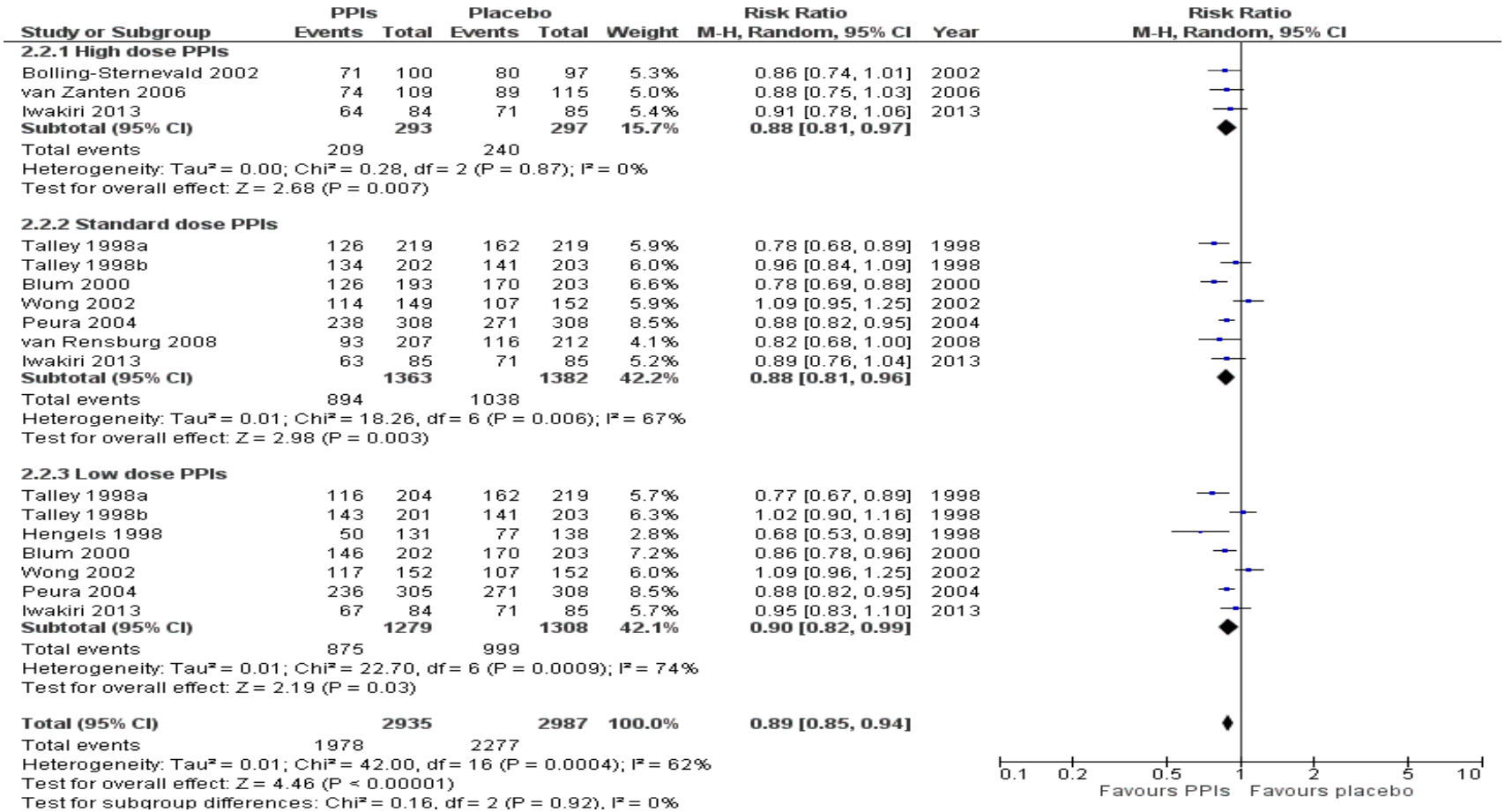
Supplementary Figure 5. Forest Plot of Randomised Controlled Trials of Histamine-$_2$-Receptor Antagonists in FD in Terms of Effect on Cure of Symptoms: Pairwise Meta-analysis.



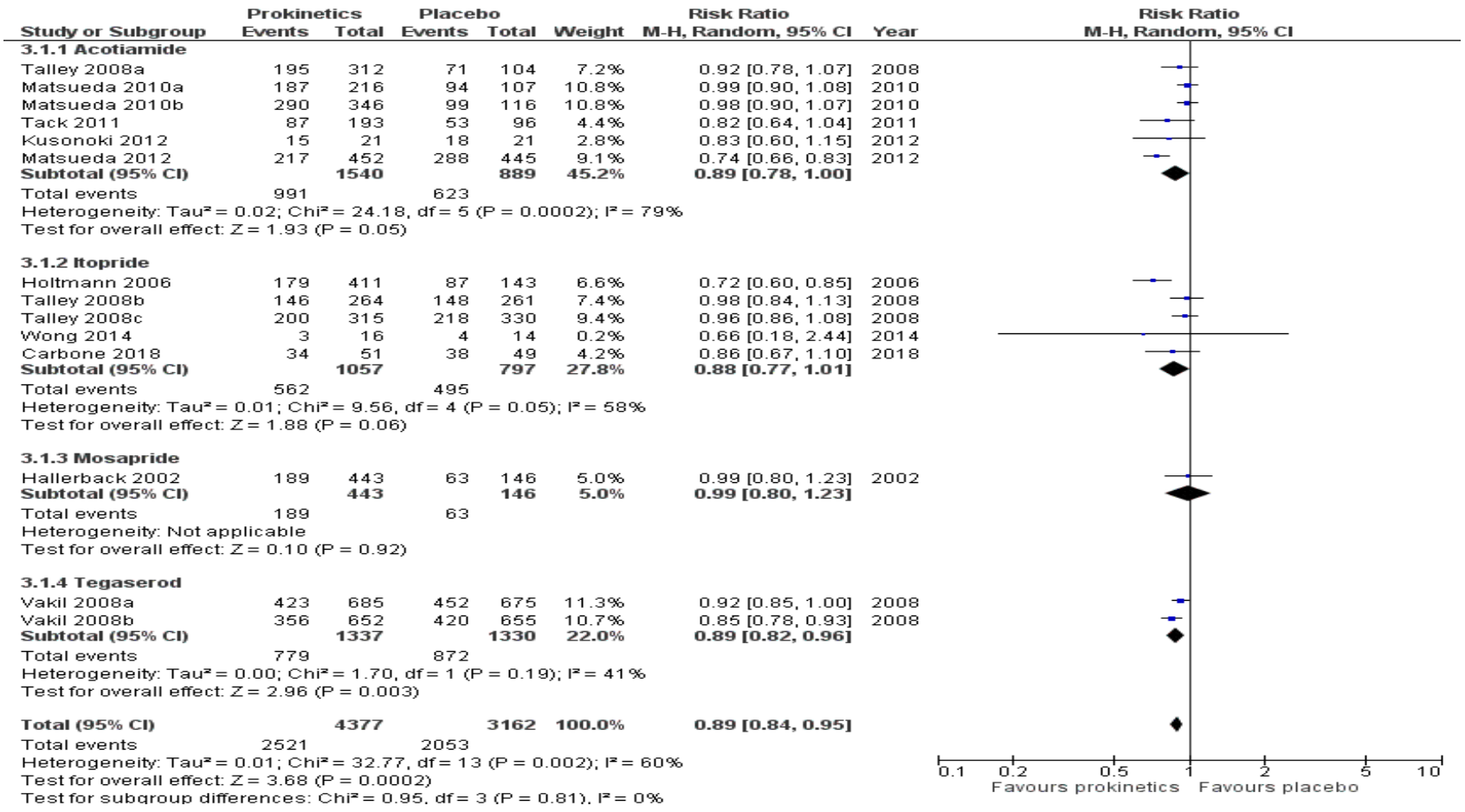
Supplementary Figure 6. Forest Plot of Randomised Controlled Trials of Proton Pump Inhibitors in FD in Terms of Effect on Improvement of Symptoms: Pairwise Meta-analysis.



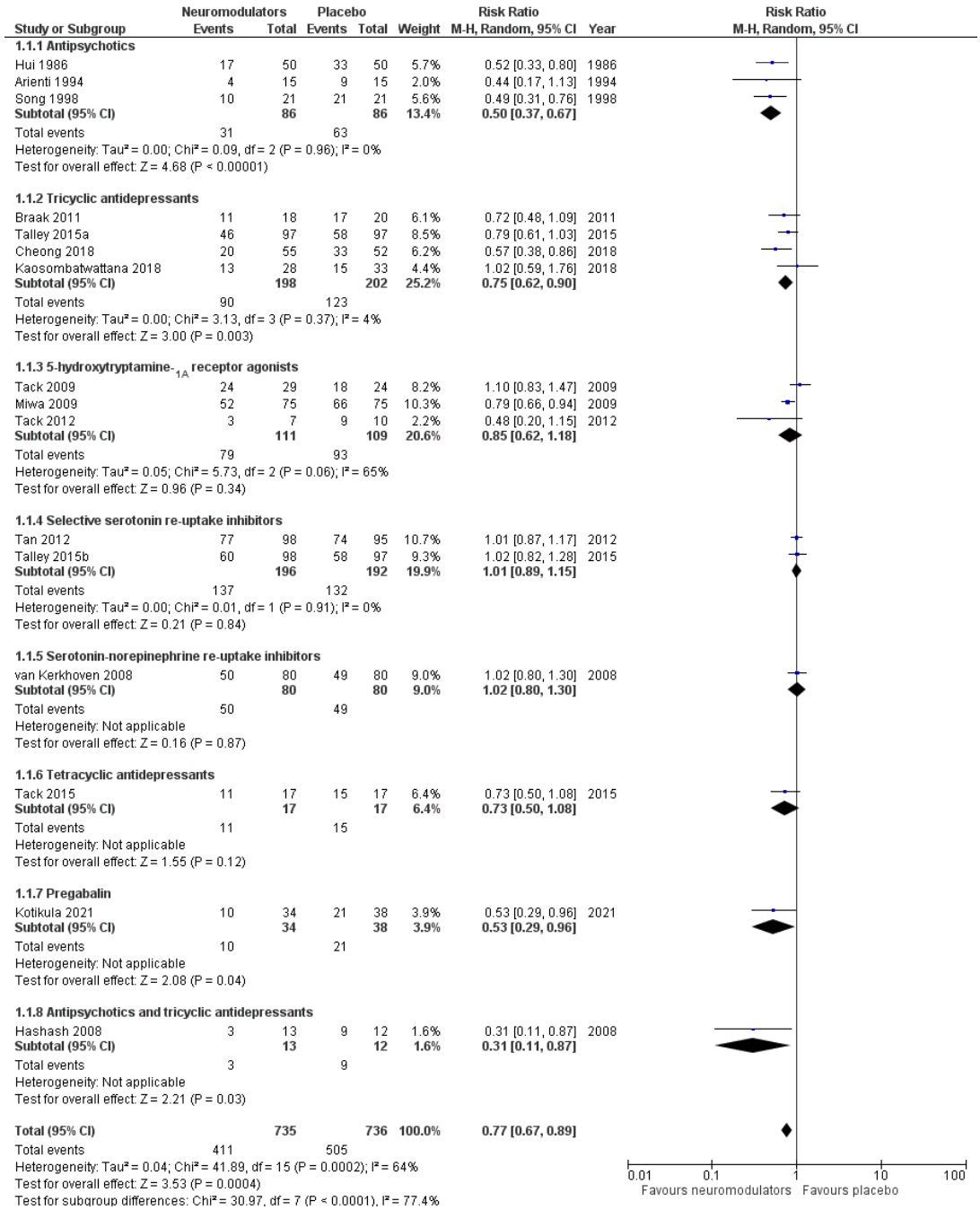
Supplementary Figure 7. Forest Plot of Randomised Controlled Trials of Proton Pump Inhibitors in FD in Terms of Effect on Cure of Symptoms: Pairwise Meta-analysis.



Supplementary Figure 8. Forest Plot of Randomised Controlled Trials of Prokinetics in FD in Terms of Effect on Improvement of Symptoms: Pairwise Meta-analysis.



Supplementary Figure 9. Forest Plot of Randomised Controlled Trials of Gut-brain Neuromodulators in FD in Terms of Effect on Improvement of Symptoms: Pairwise Meta-analysis.



Supplementary Figure 10. Forest Plot of Randomised Controlled Trials of Drugs Used First or Second Line in Terms of Effect on Improvement of Symptoms: Network Meta-analysis.