Search Strategy

Dyspepsia, heartburn, gastroesophageal reflux, esophagitis, dyspeps$, peptic ulcer, peptic adj5 ulcer

Helicobacter pylori, breath tests, gastroscopy, duodenoscopy, endoscopy, serology, *Helicobacter* adj5 *pylori*, near adj5 patient$ adj5 test$, anti-ulcer agents, histamine H2 antagonists, cimetidine, famotidine, ranitidine, nizatidine, omeprazole, lansoprazole, rabeprazole, pantoprazole, esomeprazole, amoxicillin, metronidazole, clarithromycin, bismuth, levofloxacin, anti?ulcer, histamine adj5 H2 adj5 antagonist$,

primary health care, family practice, physicians, family, primary adj5 health adj5 care, family adj5 practi$, physician$ adj5 family, family adj5 medic$, physician$ adj5 family, family adj5 medic$, general adj5 practi$.

Supplementary Table 1. Risk of Bias of Randomised Controlled Trials of Management Strategies for Uninvestigated Dyspepsia.

Study	Method of Generation of Randomisation Schedule	Method of Concealment of Treatment Allocation	Blinding	Evidence of Incomplete Outcomes Data	Evidence of Selective Reporting of Outcomes
Bytzer 1994 [13]	Unclear	Unclear	High	High	Low
Heaney 1999 [45]	Unclear	Unclear	High	High	Low
Delaney 2000 [15]	Low	Low	High	High	Low
Lassen 2000 [46]	Low	Low	High	High	Low
Delaney 2001 [16]	Low	Low	High	High	Low
Lewin van den Broek 2001 [51]	Low	Unclear	High	High	Low
McColl 2002 [17]	Low	Low	High	High	Low
Arents 2003 [47]	Unclear	Low	High	High	Low
Manes 2003 [49]	Low	Unclear	High	Low	Low
Jarbol 2006 [42]	Low	Low	High	High	Low
Kjeldsen 2007 [50]	Unclear	Unclear	High	High	Low
Delaney 2008 [14]	Low	Low	High	High	Low
Mahadeva 2008 [48]	Low	Unclear	High	Low	Low
Duggan 2009 [18]	Low	Low	High	Low	Low
Myres (unpublished, but data available in Ford 2005 [19]**)**	Unclear	Unclear	High	High	Low

Supplementary Table 2. *Netsplit* Analysis of Inconsistency for Likelihood of Remaining Symptomatic According to Intention-to-treat Analysis at the Last Point of Follow-up.

Comparison	k	Prop.	NMA	Direct	Indirect	RoR	z	*p*-value
"Test and scope" *vs.* "Test and treat"	1	0.47	1.0322	0.9789	1.0816	0.9050	-0.63	0.5282
"Test and scope" *vs.* Empirical acid suppression	1	0.46	0.9629	0.9921	0.9392	1.0563	0.34	0.7306
"Test and scope" *vs.* Prompt endoscopy	1	0.41	1.0205	1.0615	0.9923	1.0697	0.43	0.6653
"Test and scope" *vs.* Symptom-based management	1	0.61	0.9201	0.9169	0.9250	0.9913	-0.06	0.9544
"Test and treat" *vs.* Empirical acid suppression	4	0.68	0.9328	0.9134	0.9758	0.9361	-0.71	0.4748
"Test and treat" *vs.* Prompt endoscopy	7	0.79	0.9886	1.0107	0.9110	1.1095	1.11	0.2649
"Test and treat" *vs.* Symptom-based management	0	0	0.8914	0.8914	NA	NA	NA	NA
Empirical acid suppression *vs.* Prompt endoscopy	4	0.62	1.0598	1.0370	1.0976	0.9448	-0.63	0.5289
Empirical acid suppression *vs.* Symptom-based management	1	0.39	0.9556	0.9314	0.9712	0.9590	-0.30	0.7670
Prompt endoscopy *vs.* Symptom-based management	2	0.69	0.9016	0.9047	0.8950	1.0108	0.08	0.9379

Legend

Comparison: Treatment comparison
k: Number of studies providing direct evidence
Prop.: Direct evidence proportion
NMA: Estimated treatment effect (RR) in network meta-analysis
Direct: Estimated treatment effect (RR) derived from direct evidence
Indirect: Estimated treatment effect (RR) derived from indirect evidence
RoR: Ratio of Ratios (direct versus indirect)
z: z-value of test for disagreement (direct versus indirect)
p-value: *p*-value of test for disagreement (direct versus indirect)

Supplementary Table 3. *Netsplit* Analysis of Inconsistency for Likelihood of Remaining Symptomatic According to Per Protocol Analysis at the Last Point of Follow-up.

Comparison	k	Prop.	NMA	Direct	Indirect	RoR	z	*p*-value
"Test and scope" *vs.* "Test and treat"	1	0.43	1.0222	0.9638	1.0687	0.9018	-0.49	0.6223
"Test and scope" *vs.* Empirical acid suppression	1	0.44	0.9326	0.9164	0.9453	0.9694	-0.15	0.8818
"Test and scope" *vs.* Prompt endoscopy	1	0.40	1.0058	1.0312	0.9894	1.0423	0.20	0.8418
"Test and scope" *vs.* Symptom-based management	1	0.59	0.8921	0.9080	0.8694	1.0444	0.22	0.8290
"Test and treat" *vs.* Empirical acid suppression	4	0.68	0.9123	0.8890	0.9626	0.9236	-0.75	0.4512
"Test and treat" *vs.* Prompt endoscopy	7	0.79	0.9839	1.0042	0.9121	1.1010	0.90	0.3670
"Test and treat" *vs.* Symptom-based management	0	0	0.8727	NA	0.8727	NA	NA	NA
Empirical acid suppression *vs.* Prompt endoscopy	4	0.60	1.0785	1.0538	1.1160	0.9443	-0.55	0.5793
Empirical acid suppression *vs.* Symptom-based management	1	0.44	0.9566	0.9242	0.9831	0.9401	-0.37	0.7097
Prompt endoscopy *vs.* Symptom-based management	2	0.71	0.8870	0.8827	0.8973	0.9838	-0.10	0.9240

Legend

Comparison:	Treatment comparison
k:	Number of studies providing direct evidence
Prop.:	Direct evidence proportion
NMA:	Estimated treatment effect (RR) in network meta-analysis
Direct:	Estimated treatment effect (RR) derived from direct evidence
Indirect:	Estimated treatment effect (RR) derived from indirect evidence
RoR:	Ratio of Ratios (direct versus indirect)
z:	z-value of test for disagreement (direct versus indirect)
p-value:	*p*-value of test for disagreement (direct versus indirect)

Supplementary Table 4. Summary Treatment Effects from the Network Meta-analysis for Likelihood of Remaining Symptomatic According to Per Protocol Analysis at the Last Point of Follow-up.

"Test and treat"	1.00 (0.91; 1.11)	1.04 (0.76; 1.42)	0.89 (0.79; 1.00)	N/A
0.98 (0.90; 1.07)	**Prompt endoscopy**	0.97 (0.71; 1.33)	0.95 (0.83; 1.08)	0.88 (0.74; 1.06)
0.98 (0.80; 1.20)	0.99 (0.81; 1.21)	**"Test and scope"**	0.92 (0.67; 1.25)	0.91 (0.71; 1.17)
0.91 (0.83; 1.01)	0.93 (0.84; 1.02)	0.93 (0.76; 1.14)	**Empirical acid suppression**	0.92 (0.72; 1.18)
0.87 (0.74; 1.03)	0.89 (0.76; 1.03)	0.89 (0.73; 1.08)	0.96 (0.81; 1.12)	**Symptom-based management**

Relative risk with 95% confidence intervals in parentheses. Comparisons, column versus row, should be read from left to right, and are ordered relative to their overall effectiveness. The treatment in the top left position is ranked as best after the network meta-analysis of direct and indirect effects. Direct comparisons are provided above the strategy labels, and indirect comparisons are below.

N/A; not applicable, no RCTs making direct comparisons.

Supplementary Table 5. *Netsplit* Analysis of Inconsistency for Likelihood of Receiving Endoscopy.

Comparison	k	Prop.	NMA	Direct	Indirect	RoR	z	*p*-value
"Test and scope" *vs.* "Test and treat"	1	0.54	2.3660	1.8884	3.0802	0.6131	-0.79	0.4318
"Test and scope" *vs.* Empirical acid suppression	1	0.59	1.4035	1.1884	1.7825	0.6667	-0.63	0.5309
"Test and scope" *vs.* Prompt endoscopy	1	0.55	0.5482	0.5081	0.6015	0.8447	-0.28	0.7795
"Test and scope" *vs.* Symptom-based management	1	0.62	1.4130	1.7917	0.9610	1.8645	0.91	0.3612
"Test and treat" *vs.* Empirical acid suppression	4	0.71	0.5932	0.7199	0.3699	1.9463	1.69	0.0918
"Test and treat" *vs.* Prompt endoscopy	7	0.82	0.2317	0.2053	0.4056	0.5063	-1.71	0.0880
"Test and treat" *vs.* Symptom-based management	0	0	0.5972	NA	0.5972	NA	NA	NA
Empirical acid suppression *vs.* Prompt endoscopy	3	0.62	0.3906	0.4830	0.2758	1.7516	1.47	0.1405
Empirical acid suppression *vs.* Symptom-based management	0	0	1.0067	NA	1.0067	NA	NA	NA
Prompt endoscopy *vs.* Symptom-based management	1	0.64	2.5774	2.0634	3.8472	0.5363	-0.91	0.3612

Legend

Comparison: Treatment comparison
k: Number of studies providing direct evidence
Prop.: Direct evidence proportion
NMA: Estimated treatment effect (RR) in network meta-analysis
Direct: Estimated treatment effect (RR) derived from direct evidence
Indirect: Estimated treatment effect (RR) derived from indirect evidence
RoR: Ratio of Ratios (direct versus indirect)
z: z-value of test for disagreement (direct versus indirect)
p-value: *p*-value of test for disagreement (direct versus indirect)

Supplementary Table 6. Summary Treatment Effects from the Network Meta-analysis for Participant Dissatisfaction with Management.

Prompt endoscopy	0.86 (0.42; 1.79)	0.75 (0.50; 1.11)	0.54 (0.31; 0.92)
0.70 (0.37;1.32)	**"Test and scope"**	0.93 (0.45; 1.92)	1.06 (0.51; 2.20)
0.67 (0.46; 0.98)	0.97 (0.51; 1.83)	**"Test and treat"**	1.03 (0.61; 1.74)
0.58 (0.37; 0.91)	0.83 (0.43; 1.59)	0.85 (0.54; 1.34)	**Empirical acid suppression**

Relative risk with 95% confidence intervals in parentheses. Comparisons, column versus row, should be read from left to right, and are ordered relative to their overall effectiveness. The treatment in the top left position is ranked as best after the network meta-analysis of direct and indirect effects. Boxes highlighted in green indicate significant differences. Direct comparisons are provided above the strategy labels, and indirect comparisons are below.

Supplementary Table 7. *Netsplit* Analysis of Inconsistency for Participant Dissatisfaction with Management.

Comparison	k	Prop.	NMA	Direct	Indirect	RoR	z	*p*-value
"Test and scope" *vs.* "Test and treat"	1	0.77	0.9666	0.9308	1.0971	0.8484	-0.21	0.8315
"Test and scope" *vs.* Empirical acid suppression	1	0.81	0.8256	1.0588	0.2934	3.6089	1.52	0.1290
"Test and scope" *vs.* Prompt endoscopy	1	0.76	1.4338	1.1596	2.8467	0.4074	-1.17	0.2420
"Test and treat" *vs.* Empirical acid suppression	2	0.74	0.8542	1.0346	0.4923	2.1016	1.41	0.1572
"Test and treat" *vs.* Prompt endoscopy	4	0.88	1.4834	1.3415	3.1338	0.4281	-1.44	0.1511
Prompt endoscopy *vs.* Empirical acid suppression	2	0.72	0.5758	0.5385	0.6845	0.7867	-0.46	0.6431

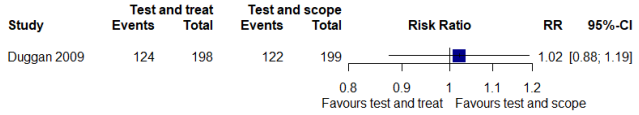
Legend

Comparison: Treatment comparison
k: Number of studies providing direct evidence
Prop.: Direct evidence proportion
NMA: Estimated treatment effect (RR) in network meta-analysis
Direct: Estimated treatment effect (RR) derived from direct evidence
Indirect: Estimated treatment effect (RR) derived from indirect evidence
RoR: Ratio of Ratios (direct versus indirect)
z: z-value of test for disagreement (direct versus indirect)
p-value: *p*-value of test for disagreement (direct versus indirect)

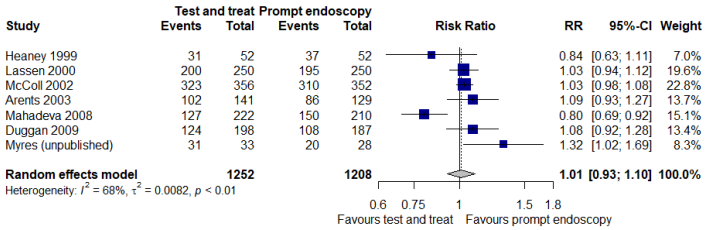
SUPPLEMENTARY FIGURES

Supplementary Figure 1. Pairwise Meta-analysis for Likelihood of Remaining Symptomatic According to Intention-to-treat Analysis at the Last Point of Follow-up.

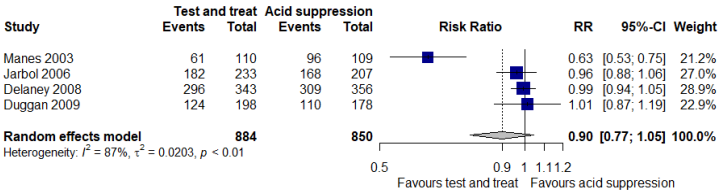
a. "Test and treat" *vs.* "Test and scope"



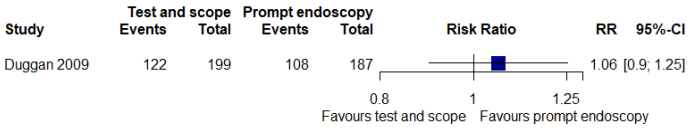
b. "Test and treat" *vs.* Prompt endoscopy



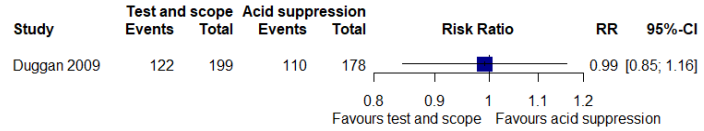
c. "Test and treat" *vs.* Empirical acid suppression



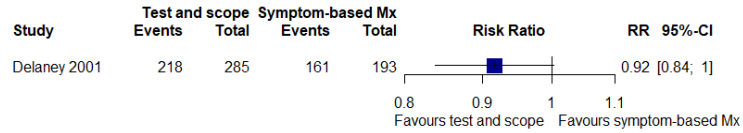
d. "Test and scope" *vs.* Prompt endoscopy



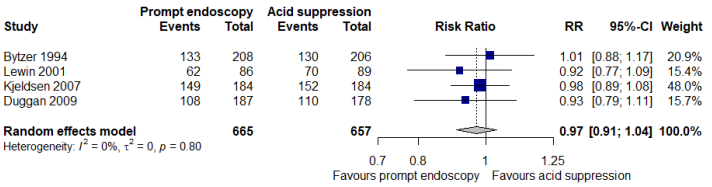
e. "Test and scope" *vs.* Empirical acid suppression



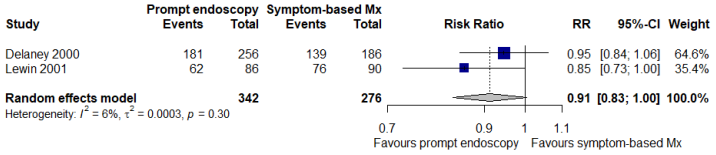
f. "Test and scope" *vs.* Symptom-based management



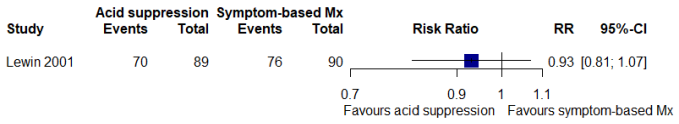
g. Prompt endoscopy *vs.* Empirical acid suppression



h. Prompt endoscopy *vs.* Symptom-based management



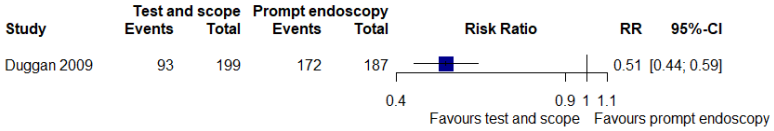
i. Empirical acid suppression *vs.* Symptom-based



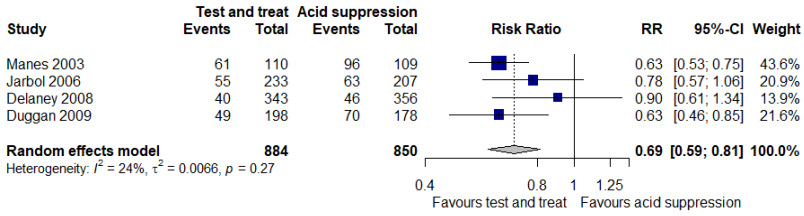
Note: there were no studies making direct comparisons between "test and treat" *vs.* symptom-based management.

Supplementary Figure 2. Pairwise Meta-analysis for Likelihood of Receiving Endoscopy.

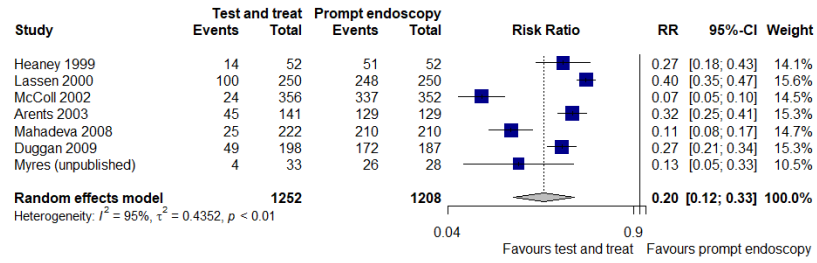
a. "Test and scope" *vs*. Prompt endoscopy



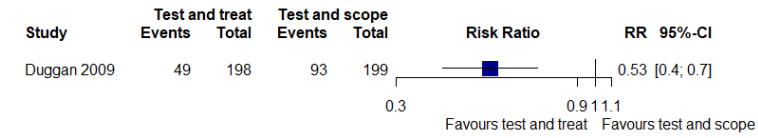
b. "Test and treat" *vs*. Empirical acid suppression



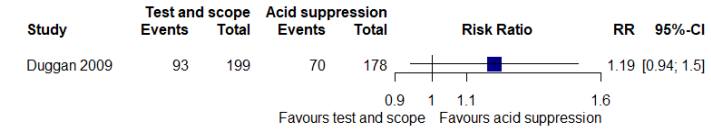
c. "Test and treat" *vs*. Prompt endoscopy



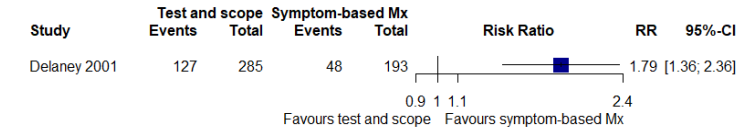
d. "Test and treat" *vs*. "Test and scope"



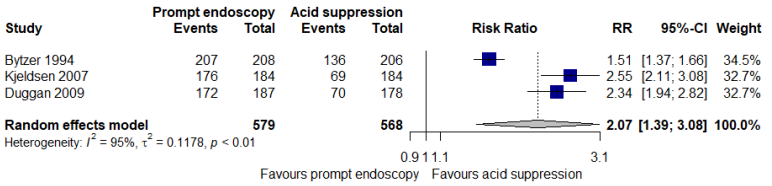
e. "Test and scope" *vs*. Empirical acid suppression



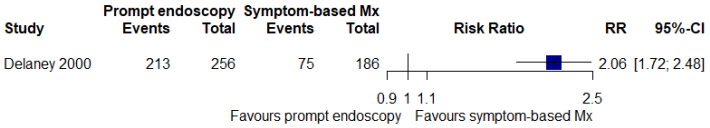
f. "Test and scope" *vs*. Symptom-based management



g. Prompt endoscopy *vs*. Empirical acid suppression



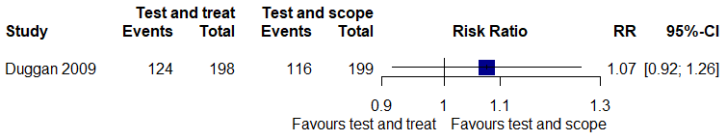
h. Prompt endoscopy *vs*. Symptom-based management



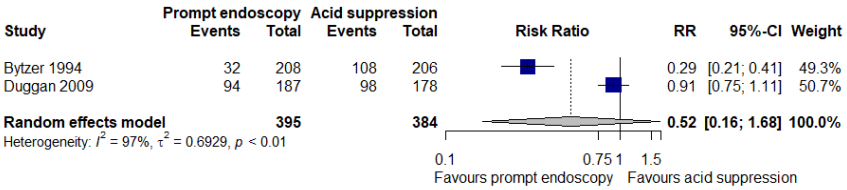
Note: there were no studies making direct comparisons between: "test and treat" *vs*. symptom-based management, or empirical acid suppression *vs*. symptom-based management.

Supplementary Figure 3. Pairwise Meta-analysis for Participant Dissatisfaction with Management.

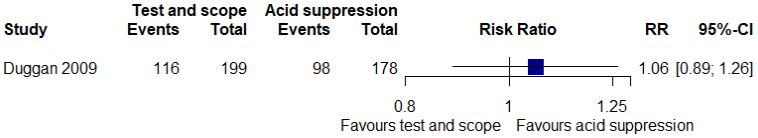
a. "Test and treat" *vs*. "Test and scope"



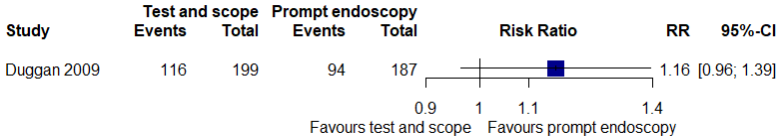
b. Prompt endoscopy *vs*. Empirical acid suppression



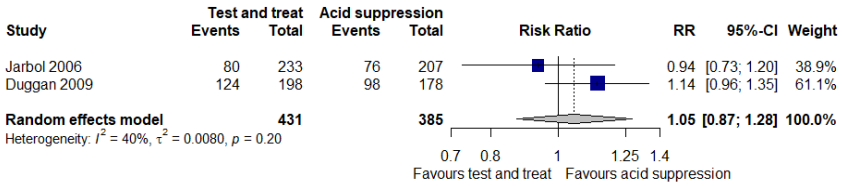
c. "Test and scope" *vs*. Empirical acid suppression



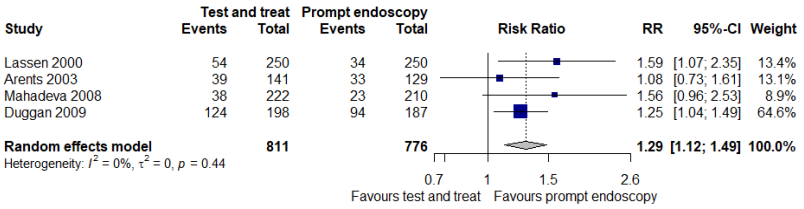
d. "Test and scope" *vs*. Prompt endoscopy



e. "Test and treat" *vs*. Empirical acid suppression

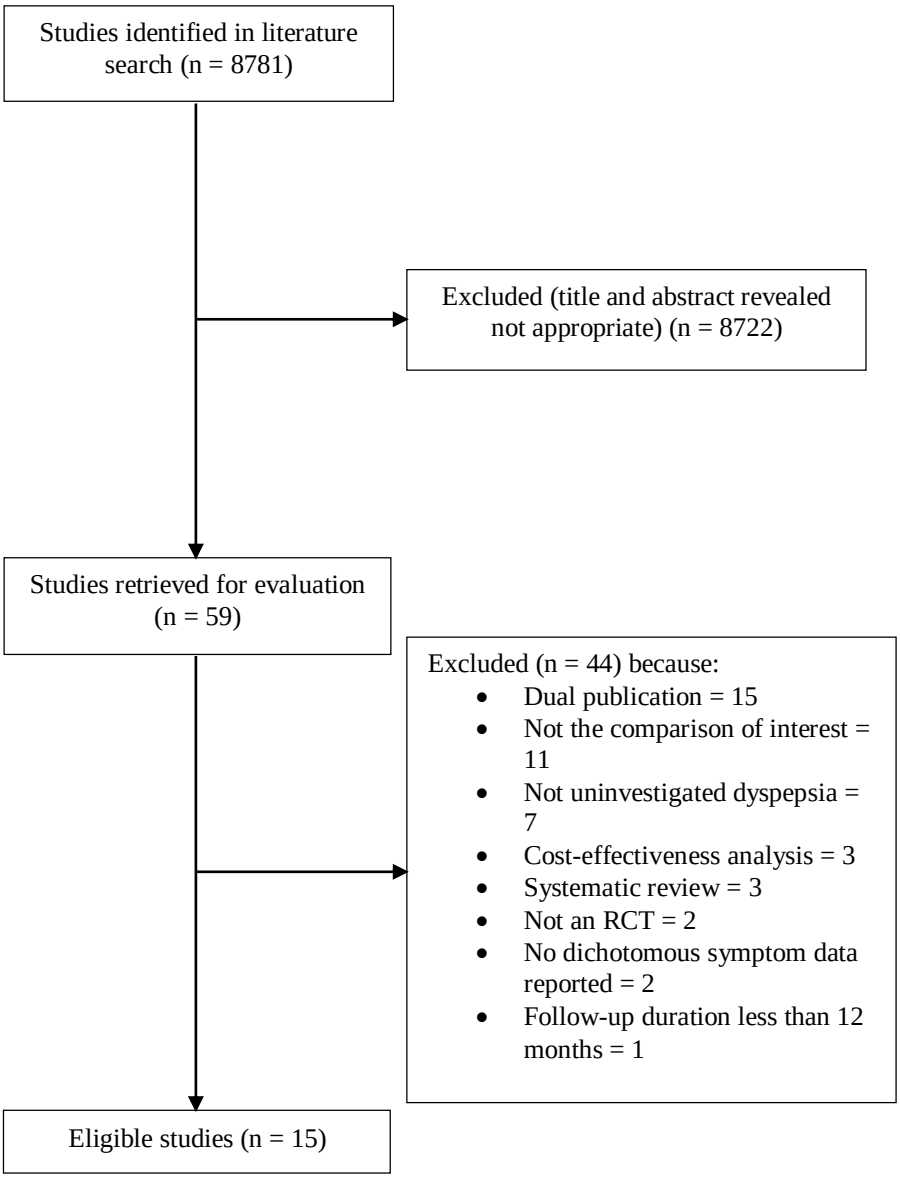


f. "Test and treat" *vs*. Prompt endoscopy

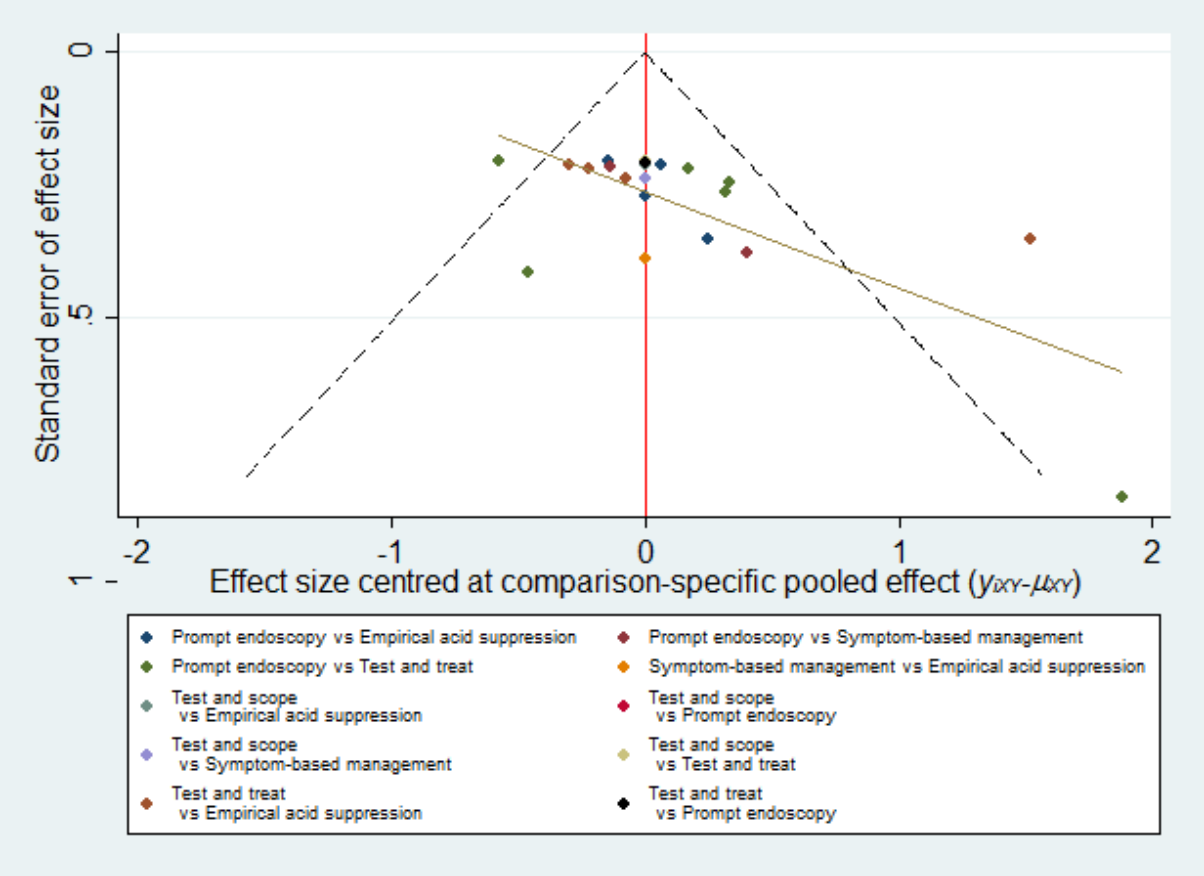


Note: there were no studies making direct comparisons between: "test and treat" *vs.* symptom-based management; "test and scope *vs.* symptom-based management; prompt endoscopy *vs.* symptom-based management; or empirical acid suppression *vs.* symptom-based management.

Supplementary Figure 4. Flow Diagram of Assessment of Studies Identified in the Systematic Review.

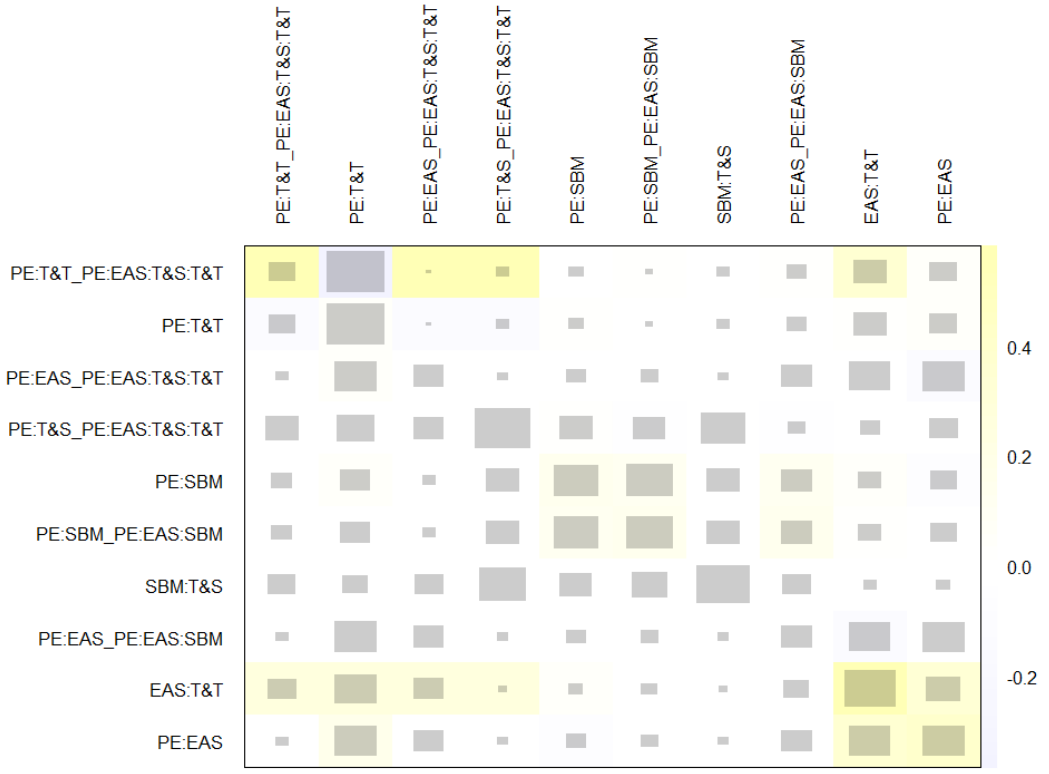


Supplementary Figure 5. Funnel Plot for Likelihood of Remaining Symptomatic According to Intention-to-treat Analysis at the Last Point of Follow-up.



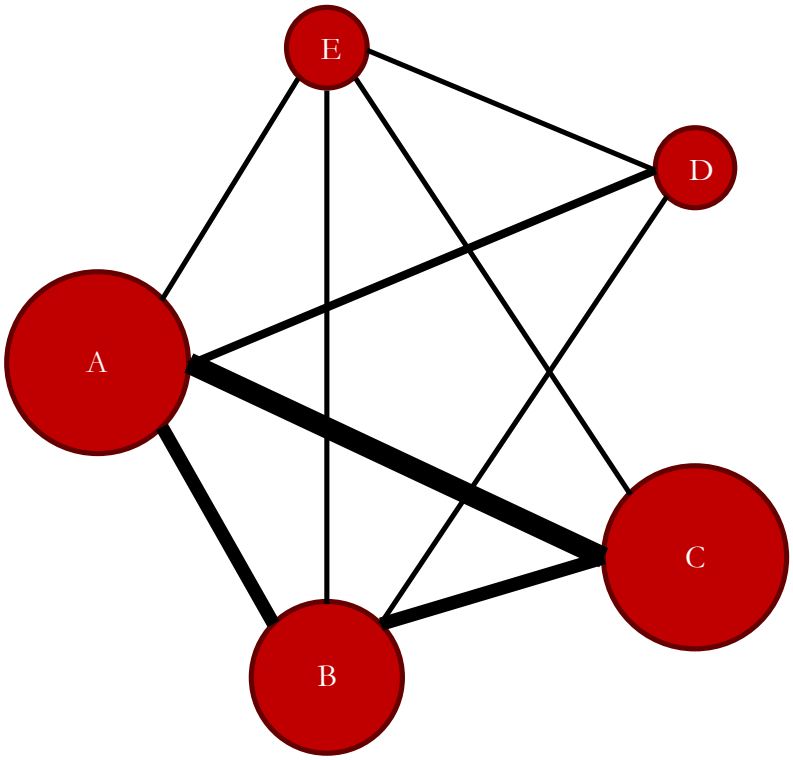
Note: The horizontal axis represents the difference between the comparison-specific and study-specific effect sizes.

Supplementary Figure 6. Network Heat Plot for Likelihood of Remaining Symptomatic According to Intention-to-treat Analysis at the Last Point of Follow-up.



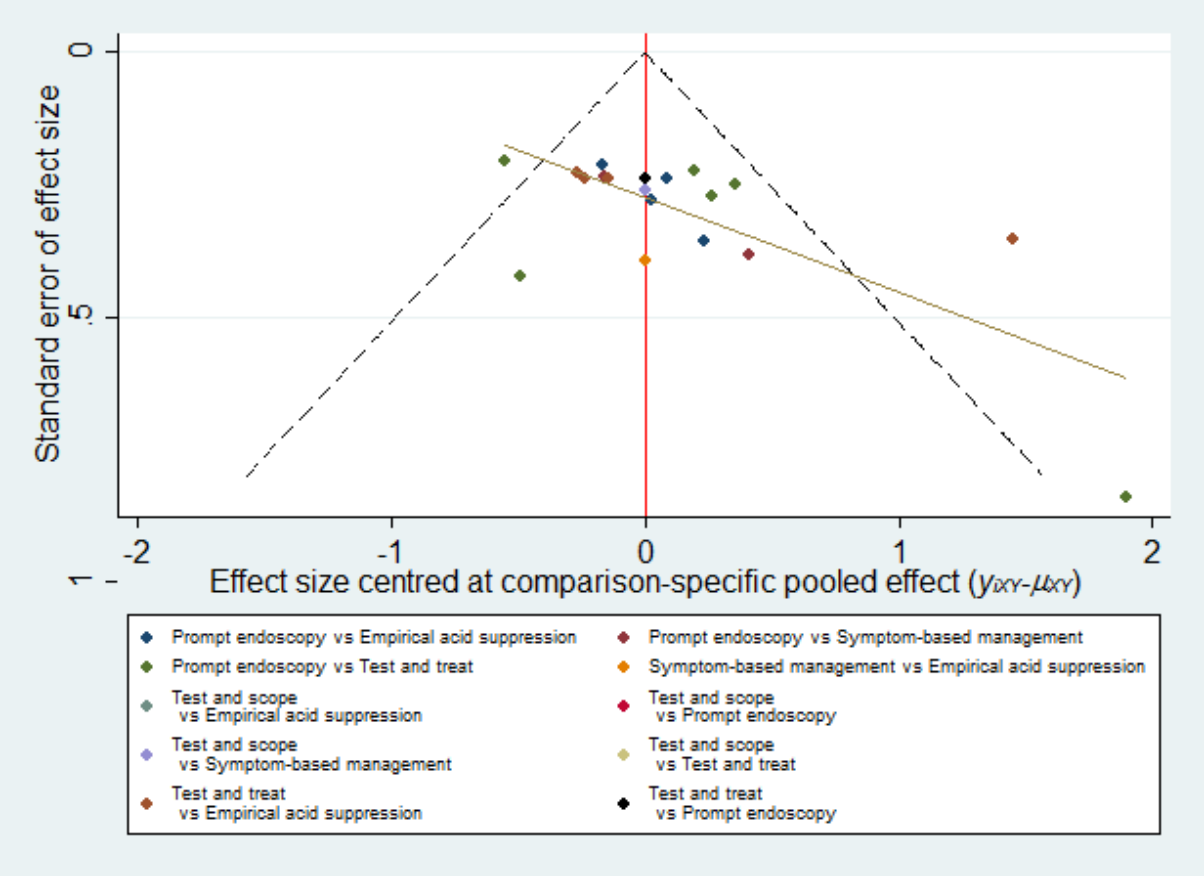
Legend	
Intervention	**Abbreviation**
Prompt endoscopy	PE
Empirical acid suppression	EAS
“Test and treat”	T&T
Symptom-based management	SBM
“Test and scope”	T&S

Supplementary Figure 7. Network Plot for Likelihood of Remaining Symptomatic According to Per Protocol Analysis at the Last Point of Follow-up.



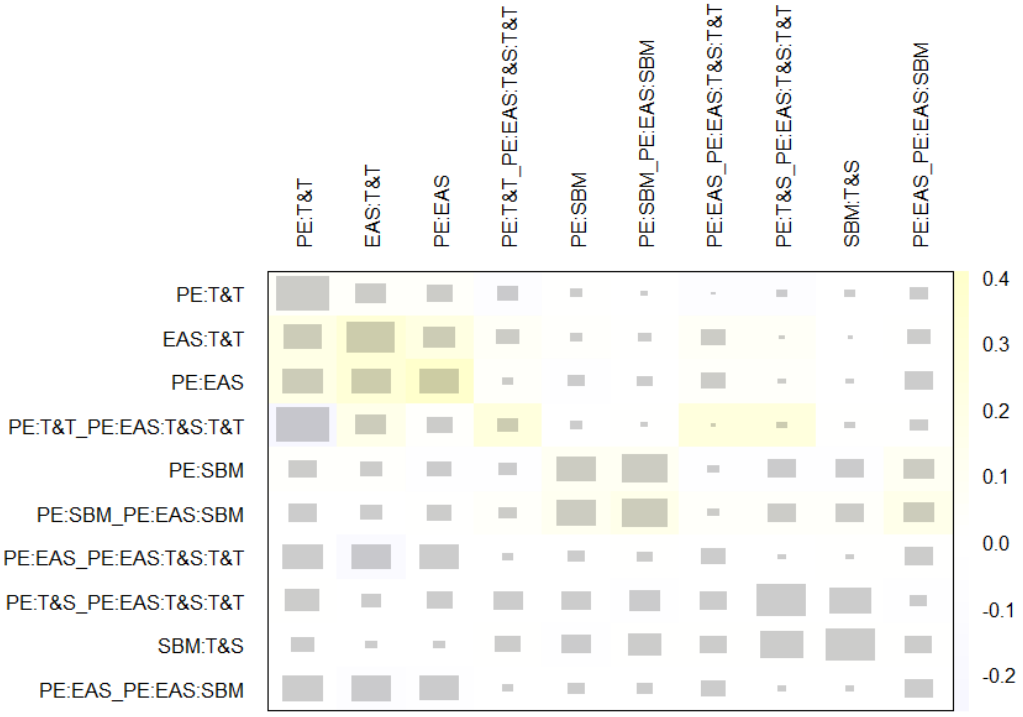
Legend			
Intervention	**Abbreviation**	**Number of trial arms**	**Number of participants**
Prompt endoscopy	A	11	1667
Empirical acid suppression	B	7	1150
“Test and treat”	C	10	1689
Symptom-based management	D	3	322
“Test and scope”	E	2	326

Supplementary Figure 8. Funnel Plot for Likelihood of Remaining Symptomatic According to Per Protocol Analysis at the Last Point of Follow-up.



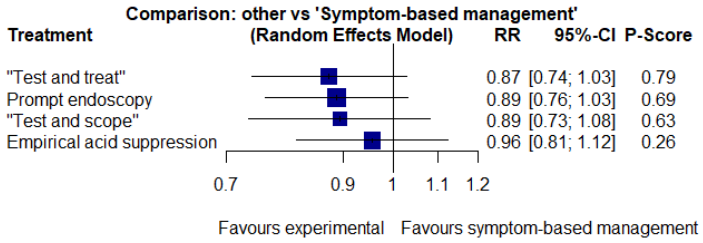
Note: The horizontal axis represents the difference between the comparison-specific and study-specific effect sizes.

Supplementary Figure 9. Network Heat Plot for Likelihood of Remaining Symptomatic According to Per Protocol Analysis at the Last Point of Follow-up.



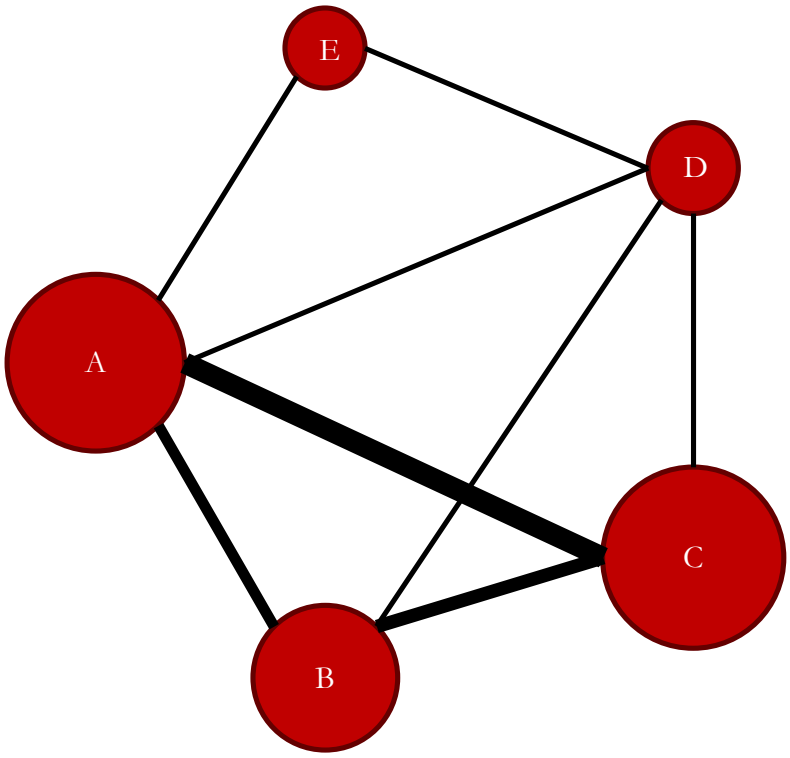
Legend	
Intervention	**Abbreviation**
Prompt endoscopy	PE
Empirical acid suppression	EAS
“Test and treat”	T&T
Symptom-based management	SBM
“Test and scope”	T&S

Supplementary Figure 10. Forest Plot for Likelihood of Remaining Symptomatic According to Per Protocol Analysis at the Last Point of Follow-up.



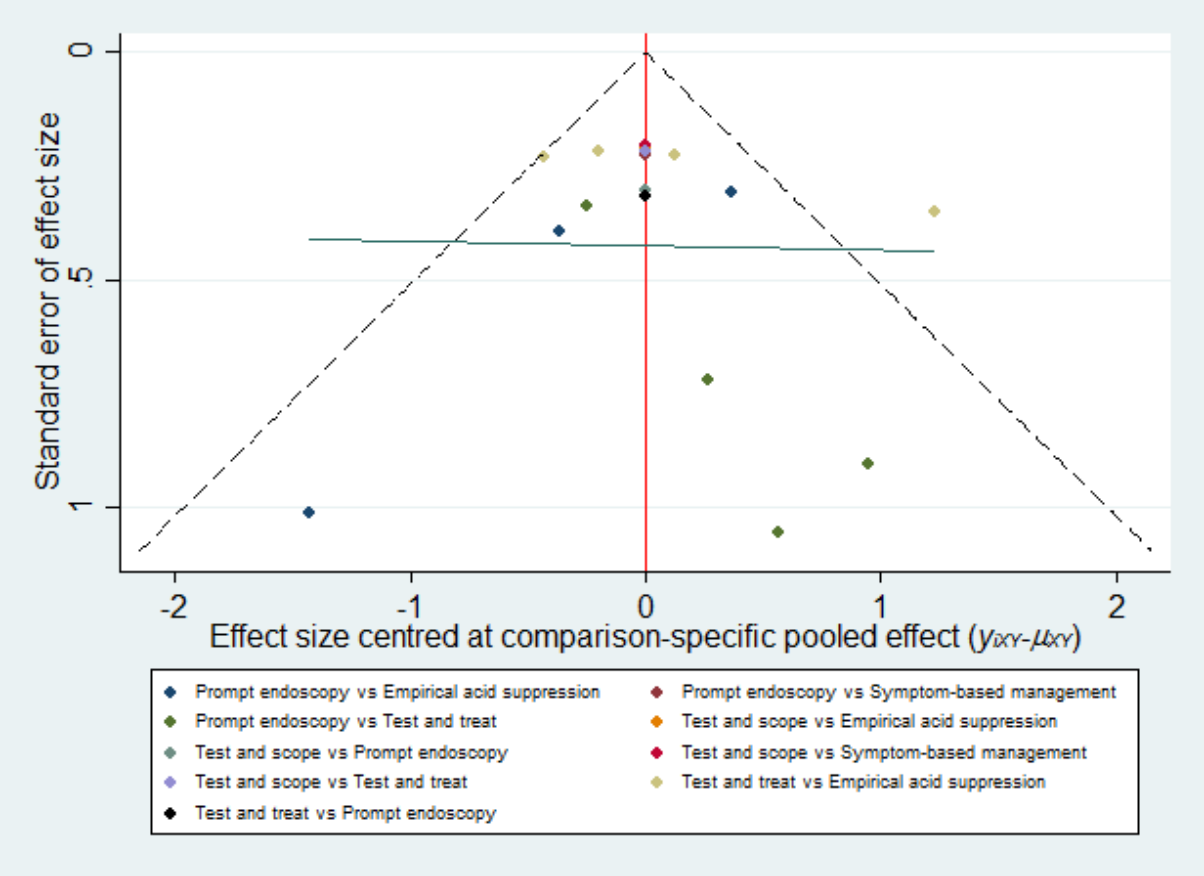
Note: The P-score is the probability of each treatment being ranked as best in the network analysis. A higher score equates to a greater probability of being ranked first.

Supplementary Figure 11. Network Plot for Likelihood of Receiving Endoscopy.



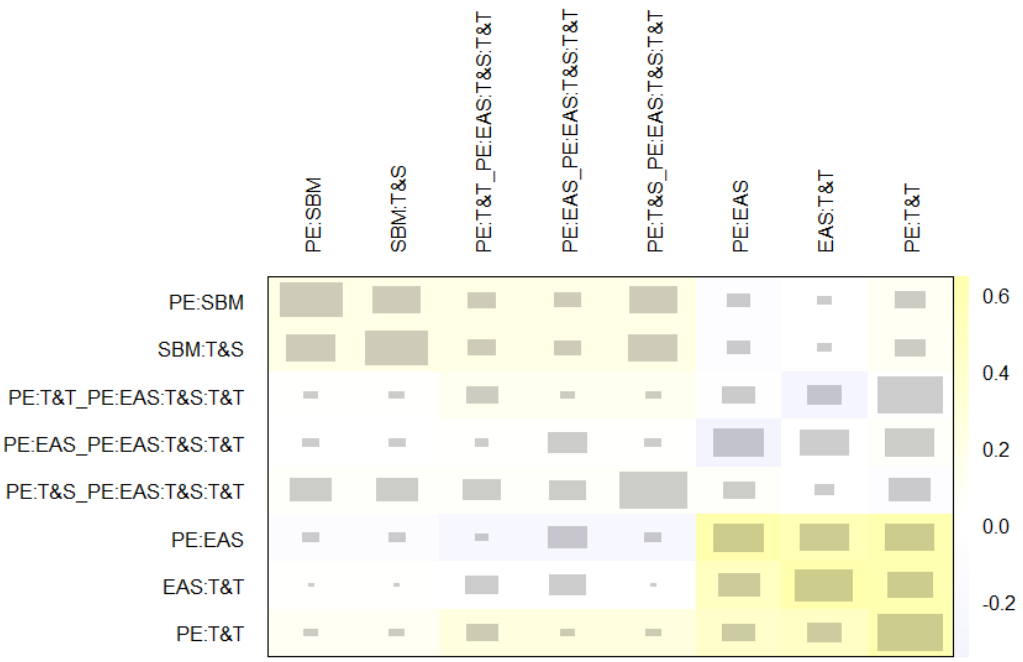
Legend			
Intervention	**Abbreviation**	**Number of trial arms**	**Number of participants**
Prompt endoscopy	A	10	1856
Empirical acid suppression	B	6	379
“Test and treat”	C	10	1938
“Test and scope”	D	2	484
Symptom-based management	E	2	1240

Supplementary Figure 12. Funnel Plot for Likelihood of Receiving Endoscopy.



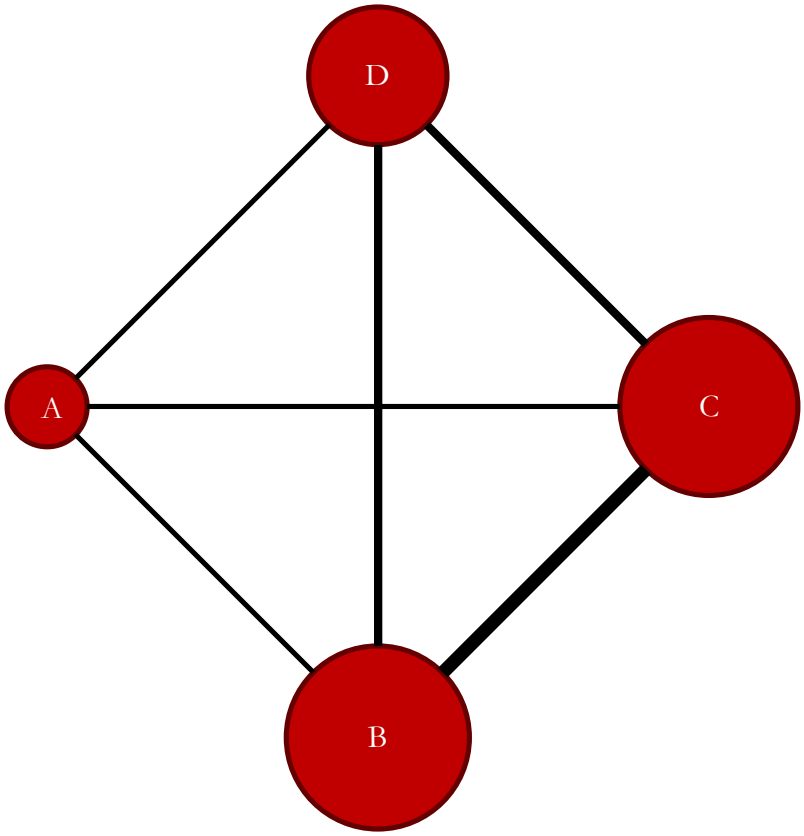
Note: The horizontal axis represents the difference between the comparison-specific and study-specific effect sizes.

Supplementary Figure 13. Network Heat Plot for Likelihood of Receiving Endoscopy.



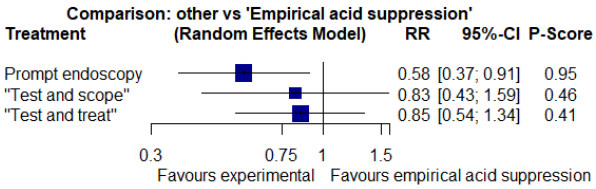
Legend	
Drug	**Abbreviation**
Prompt endoscopy	PE
Empirical acid suppression	EAS
“Test and treat”	T&T
Symptom-based management	SBM
“Test and scope”	T&S

Supplementary Figure 14. Network Plot for Participant Dissatisfaction with Management.



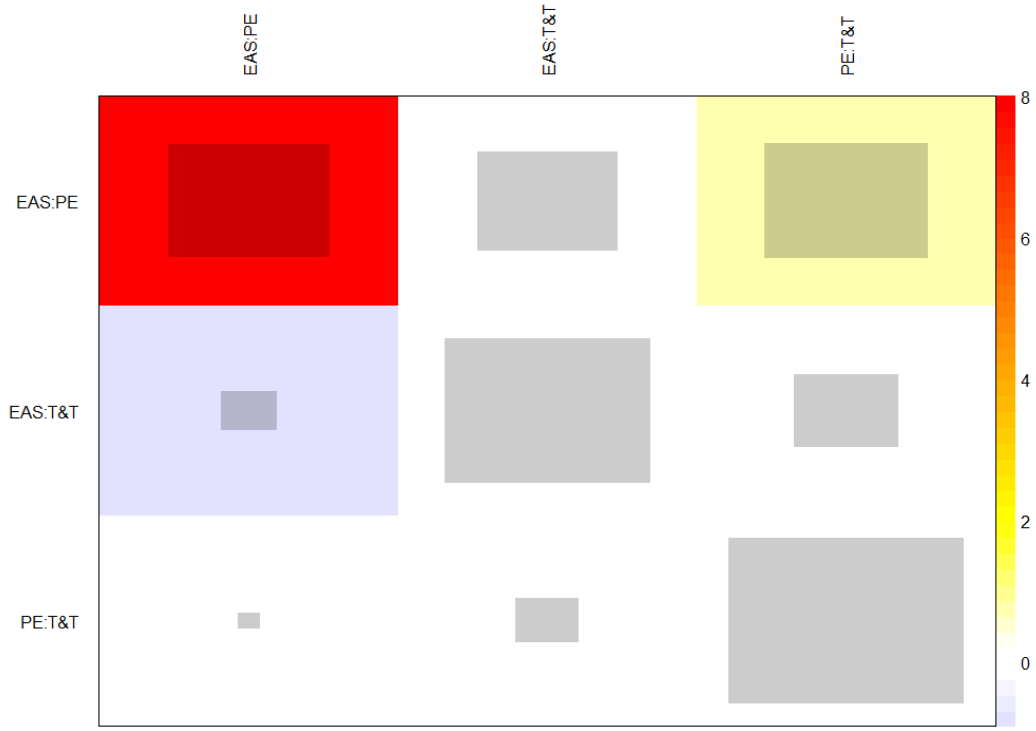
Legend			
Intervention	**Abbreviation**	**Number of trial arms**	**Number of participants**
"Test and scope"	A	1	199
"Test and treat"	B	5	1044
Prompt endoscopy	C	5	984
Empirical acid suppression	D	3	591

Supplementary Figure 15. Forest Plot for Participant Dissatisfaction with Management.



Note: The P-score is the probability of each treatment being ranked as best in the network analysis. A higher score equates to a greater probability of being ranked first.

Supplementary Figure 16. Network Heat Plot for Participant Dissatisfaction with Management.



Legend	
Intervention	**Abbreviation**
Prompt endoscopy	PE
Empirical acid suppression	EAS
"Test and treat"	T&T