Appendix A. Search strategy

I. Primary Studies:

Database: Ovid MEDLINE(R) <1996 to October Week 5 2009>
Search Strategy:
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1 exp Gastroesophageal Reflux/ (10877)
2 gastro?esophageal reflux.tw. (7093)
3 gastro-esophageal reflux.tw. (474)
4 gastro-oesophageal reflux.tw. (1977)
5 exp esophagitis/ (3248)
6 esophagitis.tw. (3877)
7 oesophagitis.tw. (1161)
8 (GERD or GORD).tw. (3695)
9 bile reflux/ (210)
10 heartburn/ (791)
11 heartburn.tw. (2122)
12 (acid adj5 reflux).tw. (1496)
13 exp dyspepsia/ (3469)
14 dyspep$.tw. (5288)
15 or/1-14 (22229)
16 limit 15 to human (21510)
17 limit 16 to english language (18093)
18 limit 17 to "all adult (19 plus years)" (10095)
19 17 not 18 (7998)
20 limit 19 to "all child (0 to 18 years)" (2307)
21 17 not 20 (15786)
22 follow-up studies/ (221986)
23 (follow-up or followup).tw. (287251)
24 exp cohort studies/ (469036)
25 cohort.tw. (108161)
26 exp Case-Control Studies/ (336457)

27 (case adj20 control).tw. (45125)
28 exp Longitudinal Studies/ (410361)
29 longitudinal.tw. (57455)
30 (random$ or rct).tw. (327155)
31 exp Randomized Controlled Trials/ (54377)
32 exp random allocation/ (30873)
33 exp Double-Blind Method/ (57833)
34 exp Single-Blind Method/ (10625)
35 randomized controlled trial.pt. (180083)
36 clinical trial.pt. (250829)
37 controlled clinical trials/ (0)
38 (clin$ adj trial$).tw. (98722)
39 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw. (55283)
40 exp Research Design/ (161832)
41 exp Evaluation Studies/ (123323)
42 exp Prospective Studies/ (188292)
43 exp Comparative Study/ (721897)
44 or/22-41 (1499433)
45 21 and 44 (7443)
46 limit 45 to (addresses or bibliography or biography or case reports or congresses or consensus development conference or consensus development conference, nih or dictionary or directory or editorial or festschrift or government publications or interview or lectures or legal cases or legislation or letter or news or newspaper article or patient education handout or periodical index) (379)
47 45 not 46 (7064)
48 limit 47 to (guideline or meta analysis or practice guideline or "review" or review, academic or "review literature" or review, multicase or "review of reported cases" or review, tutorial) [Limit not valid in Ovid MEDLINE(R); records were retained] (852)
49 47 not 48 (6212)
50 limit 49 to yr="2004 -Current" (2928)

II. Systematic reviews:

Database: Ovid MEDLINE(R), CDSR, ACP Journal Club, DARE, CLHTA
Search Strategy:

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1 exp Gastroesophageal Reflux/ (10807)
2 gastro?esophageal reflux.tw. (7156)
3 gastro-esophageal reflux.tw. (484)
4 gastro-oesophageal reflux.tw. (2047)
5 exp esophagitis/ (3200)
6 esophagitis.tw. (3905)
7 oesophagitis.tw. (1215)
8 (GERD or GORD).tw. (3747)
9 bile reflux/ (207)
10 heartburn/ (773)
11 heartburn.tw. (2194)
12 (acid adj5 reflux).tw. (1532)
13 exp dyspepsia/ (3454)
14 dyspep$.tw. (5509)
15 or/1-14 (22501)
16 limit 15 to human [Limit not valid in CDSR,ACP Journal Club,DARE; records were retained] (21755)
17 limit 16 to english language [Limit not valid in CDSR,ACP Journal Club,DARE; records were retained] (18383)
18 limit 17 to "all adult (19 plus years)" [Limit not valid in CDSR,ACP Journal Club,DARE; records were retained] (10460)
19 17 not 18 (7923)
20 limit 19 to "all child (0 to 18 years)" [Limit not valid in CDSR,ACP Journal Club,DARE; records were retained] (2275)
21 17 not 20 (16108)
22 (systematic overview$ or systematic review$).tw. (29771)
23 systematic.tw. (75657)
24 meta analysis.pt. (19604)
25 meta-analys$.mp. [mp=ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct] (44489)
26 25 or 22 or 24 or 23 (106759)
27 limit 26 to "review" [Limit not valid in ACP Journal Club,DARE; records were retained] (45706)
28 27 and 21 (558)
29 atypical.mp. [mp=ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct] (40208)
30 28 and 29 (22)
31 cough.mp. [mp=ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct] (15531)
32 28 and 31 (46)

33 reflux laryngitis.mp. [mp=ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct] (50)
34 33 and 28 (4)
35 asthma.mp. [mp=ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct] (55294)
36 35 and 28 (41)
37 chest pain.mp. [mp=ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct] (12149)
38 28 and 37 (25)
39 esophageal impedance.mp. [mp=ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct] (32)
40 impedance.mp. [mp=ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct] (14376)
41 39 or 40 (14376)
42 28 and 41 (7)
43 42 or 38 or 32 or 34 or 36 or 30 (107)

II. Primary Study Search to Update to Systematic review on the treatment of Gastroesophageal Reflux Disease and Asthma. {Gibson, 2009 6253 /id}

Database: Ovid MEDLINE(R) 1950 to November Week 3 2009; EBM Reviews - Cochrane Central Register of Controlled Trials 4th Qtr 2009
Search Strategy:

1 exp Gastroesophageal Reflux/ (19436)
2 gastro?esophageal reflux.tw. (11324)
3 gastro-esophageal reflux.tw. (865)
4 gastro-oesophageal reflux.tw. (3583)
5 exp esophagitis/ (8814)
6 esophagitis.tw. (7896)
7 oesophagitis.tw. (2773)
8 (GERD or GORD).tw. (4568
9 ("reflux" or "ger" or "gerd" or "acid" or "esophagus").tw. (1027656)
10 bile reflux/ (651)
11 heartburn/ (1573)
12 heartburn.tw. (3651)
13 (acid adj5 reflux).tw. (2612)
14 exp dyspepsia/ (7196)

15 dyspep$.tw. (10273)
16 or/1-15 (1046853)
17 ("cimetidine" or "ranitidine" or "famotidine" or "nizatidine" or "omeprazole" or "pantoprazole" or "lansoprazole" or "rabeprazole" or "esomeprazole" or "surgery" or "Nissen" or "fundoplication" or "therapy" or "treatment").tw. (3401111)
18 exp anti-ulcer agents/ (43815)
19 exp histamine H2 antagonists/ (21081)
20 proton pump inhibitor$.tw. (6459)
21 ("prilosec" or "zegerid" or "pepcid" or "tagamet" or "tagemet" or "axid" or "zantac").mp. (286)
22 exp Digestive System Surgical Procedures/ (231485)
23 ("antireflux surger$" or "anti-reflux surger$" or "Belsey Mark" or "Hill gastropexy" or "Hill posterior" or "Hill repair" or "laproscop$" or "Rosetti" or "Toupet's" or "Woodward" or "Thal fundic" or "Allison's").tw. (2010)
24 or/17-23 (3561960)
25 asthma.mp. [mp=ti, ot, ab, nm, hw, ui, sh, kw] (127269)
26 randomized controlled trial.pt. (560951)
27 controlled clinical trial.pt. (161290)
28 randomized controlled trials/ (67115)
29 Random Allocation/ (88433)
30 Double-blind Method/ (194574)
31 Single-Blind Method/ (22534)
32 clinical trial.pt. (748591)
33 Clinical Trials.mp. or exp Clinical Trials/ (275706)
34 (clinic$ adj25 trial$).tw. (222717)
35 ((singl$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$)).tw. (219302)
36 Placebos/ (48648)
37 placebo$.tw. (230781)
38 random$.tw. (743435)
39 trial$.tw. (580232)
40 (randomized control trial or clinical control trial).sd. (227662)
41 (latin adj square).tw. (3535)
42 Comparative Study.tw. or Comparative Study.pt. (1641309)
43 exp Evaluation studies/ (149648)
44 Follow-Up Studies/ (437652)
45 Prospective Studies/ (331593)

46 (control$ or prospectiv$ or volunteer$).tw. (2460246)
47 Cross-Over Studies/ (45716)
48 or/26-47 (4912825)
49 16 and 24 and 25 and 48 (885)
50 remove duplicates from 49 (710)
51 limit 50 to english language [Limit not valid in CCTR; records were retained] (604)
52 limit 51 to humans [Limit not valid in CCTR; records were retained] (568)
53 limit 52 to yr="2002 -Current" (277)

III. PPI use (GERD and non-GERD indications) and fracture

Database: Ovid MEDLINE(R), Ovid MEDLINE(R) In-Process
Search Strategy:
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1 Bone Density/ (31259)
2 exp Osteoporosis/ (36259)
3 ((bone$ or plate$) adj3 mineral$).tw. (29932)
4 (bone adj2 (loss or turnover or densi$)).tw. (41898)
5 (Skelet$ adj2 (mineral$ or development$)).tw. (3069)
6 mineralization defect$.tw. (202)
7 Mineral$ content$.tw. (6959)
8 BMC.tw. (3768)
9 Osteoporo$.tw. (38113)
10 Osteomalac$.tw. (3663)
11 (Osteopath$ or osteopenia).tw. (8678)
12 Bone Development/ (10526)
13 Osteogenesis/ (14232)
14 fracture$.tw. (133687)
15 Accidental Falls/ (10664)
16 falls.tw. (21363)
17 exp "Bone and Bones"/ (409010)
18 exp PHOTON ABSORPTIOMETRY/ (13051)
19 or/1-18 (581027)

20 exp Gastroesophageal Reflux/ (18164)
21 gastro?esophageal reflux.tw. (10881)
22 gastro-esophageal reflux.tw. (824)
23 gastro-oesophageal reflux.tw. (3010)
24 exp esophagitis/ (8241)
25 esophagitis.tw. (7506)
26 oesophagitis.tw. (2250)
27 (GERD or GORD).tw. (4293)
28 bile reflux/ (632)
29 heartburn/ (1344)
30 heartburn.tw. (3056)
31 (acid adj5 reflux).tw. (2366)
32 exp dyspepsia/ (6415)
33 dyspep$.tw. (8744)
34 or/20-33 (40966)
35 limit 34 to human (37684)
36 limit 35 to english language (29047)
37 limit 36 to "all adult (19 plus years)" (16156)
38 36 not 37 (12891)
39 limit 38 to "all child (0 to 18 years)" (3847)
40 36 not 39 (25200)
41 exp anti-ulcer agents/ (36323)
42 exp omeprazole/ (7626)
43 omeprazole.mp. (9064)
44 lansoprazole.mp. (1972)
45 pantoprazole.mp. (1054)
46 rabeprazole.mp. (757)
47 esomeprazole.mp. (595)
48 dexlansoprazole.mp. (24)
49 exp histamine H2 antagonists/ (17528)
50 cimetidine/ (8937)
51 cimetidine.mp. (11917)
52 exp ranitidine/ (4802)

53 ranitidine.mp. (6225)
54 exp famotidine/ (1351)
55 famotidine.mp. (1783)
56 exp nizatidine/ (290)
57 nizatidine.mp. (374)
58 exp domperidone/ (1428)
59 domperidone.mp. (2041)
60 exp metoclopramide/ (4293)
61 metoclopramide.mp. (5860)
62 prokinetic$.tw. (1665)
63 proton pump inhibitor$.tw. (5868)
64 prilosec.mp. (43)
65 zegerid.mp. (5)
66 pepcid.mp. (12)
67 (tagamet or tagemet).mp. (94)
68 axid.mp. (11)
69 (zantac or protonix or nexium or prevacid or aciphex).mp. (111)
70 or/41-69 (53552)
71 19 and 70 (314)
72 19 and (40 or 70) (550)
73 limit 72 to (english language and humans) (413)
74 limit 73 to (addresses or bibliography or biography or case reports or letter or news or "review") (163)
75 73 not 74 (250)

Appendix B.

I. Primary studies on GERD

Pubmed ID	Author	Title	Reasons for rejection
19129015	Abdel-Raouf El-Geidie A;Gadel-Hak N;Fathi O;	Secondary antireflux surgery	Not relevant, study assesses causes and some outcomes of secondary antireflux surgeries to correct original surgery but purpose wasn't to make comparisons
19363692	Agrawal S;Shapey I;Peacock A;Ali A;Super P;	Prospective study of routine day-case laparoscopic modified Lind partial fundoplication	FU < 5 years
19641320	Bajbouj M;Becker V;Phillip V;Wilhelm D;Schmid RM;Meining A;	High-dose esomeprazole for treatment of symptomatic refractory gastroesophageal reflux disease--a prospective pH-metry/impedance-controlled study	Prospective non-comparative medical treatment cohort
16315125	Bajbouj M;Reichenberger J;Neu B;Prinz C;Schmid RM;Rosch T;Meining A;	A prospective multicenter clinical and endoscopic follow-up study of patients with gastroesophageal reflux disease	no intervention of interest
16506382	Bataille D;Simoens C;Mendes da CP;	Laparoscopic revision for failed anti-reflux surgery. Preliminary results	Previous antireflux surgeries
16187196	Bautista JM;Wong WM;Pulliam G;Esquivel RF;Fass R;	The value of ambulatory 24 hr esophageal pH monitoring in clinical practice in patients who were referred with persistent gastroesophageal reflux disease (GERD)-related symptoms while on standard dose anti-reflux medications	Not relevant, study assesses value of pH testing in failed PPI vs failed H2RA pts
19491837	Beaumont H;	Does the presence of a hiatal hernia affect the efficacy of the reflux inhibitor baclofen during add-on therapy?	GABA agonist baclofen is not Tx of interest
19491837	Beaumont H;Boeckxstaens GE;	Does the presence of a hiatal hernia affect the efficacy of the reflux inhibitor baclofen during add-on therapy?	no comparison of interest; duration <4 weeks
17900268	Becker V;Bajbouj M;Waller K;Schmid RM;Meining A;	Clinical trial: persistent gastro-oesophageal reflux symptoms despite standard therapy with proton pump inhibitors - a follow-up study of intraluminal-impedance guided therapy	Not relevant, study assesses utility of ph monitoring in identifying pts to modify ppi therapy

Pubmed ID	Author	Title	Reasons for rejection
15813833	Bergman MP;Klinkenberg-Knol EC;Faller G;Aar A;Lakhai W;Vandenbroucke-Grauls CM;Kuipers EJ;Appelmelk BJ;	Long-term acid suppression by omeprazole in gastro-oesophageal reflux disease patients does not lead to anti-gastric autoantibody production	sample size <100 for KQ3
18757375	Bergman S;Mikami DJ;Hazey JW;Roland JC;Dettorre R;Melvin WS;	Endolumenal fundoplication with EsophyX: the initial North American experience	N<10
17111285	Biertho L;Dallemagne B;Dewandre JM;Jehaes C;Markiewicz S;Monami B;Wahlen C;Weerts J;	Laparoscopic treatment of Barrett's esophagus: long-term results	100% Barrett's
16508818	Biertho L;Sebajang H;Anvari M;	Effects of laparoscopic Nissen fundoplication on esophageal motility: long-term results	condition excluded in this review
16181303	Bigard MA;Genestin E;	Treatment of patients with heartburn without endoscopic evaluation: on-demand treatment after effective continuous administration of lansoprazole 15 mg	PPI vs placebo is excluded
18814008	Birk J;	The Plicator procedure for the treatment of gastroesophageal reflux disease: a registry study	NDO device excluded
18814008	Birk J;Pruitt R;Haber G;Raijman I;Baluyut A;Meiselman M;Sedghi S;	The Plicator procedure for the treatment of gastroesophageal reflux disease: a registry study	NDO device excluded
16948806	Bjornsson E;Abrahamsson H;Simren M;Mattsson N;Jensen C;Agerforz P;Kilander A;	Discontinuation of proton pump inhibitors in patients on long-term therapy: a double-blind, placebo-controlled trial	discontinuation of PPIs in long-term PPI users
19074947	Blazeby JM;Barham CP;Donovan JL;	Commentary: Randomised trials of surgical and non-surgical treatment: a role model for the future.[comment]	commentary
18057058	Blondeau K;Mertens V;Vanaudenaerde BA;Verleden GM;Van Raemdonck DE;Sifrim D;Dupont LJ;	Gastro-oesophageal reflux and gastric aspiration in lung transplant patients with or without chronic rejection	lung transplant patients
18005786	Bochkarev V;Iqbal A;Lee YK;Vitamvas M;Oleynikov D;	One hundred consecutive laparoscopic Nissen's without the use of a bougie	follow-up <5 years
18553196	Bochkarev V;Lee YK;Vitamvas M;Oleynikov D;	Short esophagus: how much length can we get?	follow-up <5 years; intervention not of interest (extended transhiatal mediastinal dissection to elongate short esophagus)

Pubmed ID	Author	Title	Reasons for rejection
15793667	Bocskei C;Viczian M;Bocskei R;Horvath I;	The influence of gastroesophageal reflux disease and its treatment on asthmatic cough	atypical GERD
17972135	Boddy AP;Mehta S;Bennett J;Lowndes R;Mahon D;Rhodes M;	Postoperative esophageal physiology studies may help to predict long-term symptoms following laparoscopic Nissen fundoplication	surgical cohort N<100; surgical arm from a RCT (Mahon, 2005 in our 2005 report)
18938747	Bogte A;Bredenoord AJ;Smout AJ;	Diagnostic yield of oesophageal pH monitoring in patients with chronic unexplained cough	no treatment
19495892	Boiron M;Benchellal Z;Huten N;	Study of swallowing sound at the esophagogastric junction before and after fundoplication	< 100 patients and FU < 5 yrs
18846406	Bonavina L;Saino GI;Bona D;Lipham J;Ganz RA;Dunn D;DeMeester T;	Magnetic augmentation of the lower esophageal sphincter: results of a feasibility clinical trial	N<100; follow-up <5 year
16059414	Bonnet G;Khan MI;Ong L;	Using quality-of-life instruments to measure outcome after laparoscopic fundoplication	surgical cohort N<100
16427926	Boolchand V;Faulx A;Das A;Zyzanski S;Isenberg G;Cooper G;Sivak MV;Chak A;	Primary care physician attitudes toward endoscopic screening for GERD symptoms and unsedated esophagoscopy	not relevant
15844695	Bove M;Vieth M;Casselbrant A;Ny L;Lundell L;Ruth M;	Acid challenge to the esophageal mucosa: effects on local nitric oxide formation and its relation to epithelial functions	healthy pts
18477258	Bozikas A;Marsman WA;Rosmolen WD;van Baal JW;Kulik W;ten Kate FJ;Krishnadath KK;Bergman JJ;	The effect of oral administration of ursodeoxycholic acid and high-dose proton pump inhibitors on the histology of Barrett's esophagus	BE pts
15827858	Braghetto I;Korn O;Debandi A;Burdiles P;Valladares H;Csendes A;	Laparoscopic cardial calibration and gastropexy for treatment of patients with reflux esophagitis: pathophysiological basis and result	N<100; follow-up <5 year
16045573	Braghetto I;Papapietro K;Csendes A;Gutierrez J;Fagalde P;Diaz E;Rodriguez A;Undurraga F;	Nonesophageal side-effects after antireflux surgery plus acid-suppression duodenal diversion surgery in patients with long-segment Barrett's esophagus*	BE pts
14997925	Brandt MG;Darling GE;Miller L;	Symptoms, acid exposure and motility in patients with Barrett's esophagus	no intervention of interest
19697277	Bredenoord AJ;	Lesogaberan, a GABA(B) agonist for the potential treatment of gastroesophageal reflux disease	GABA agonist not Tx of interest

Pubmed ID	Author	Title	Reasons for rejection
18963650	Bretagne JF;Honnorat C;Richard-Molard B;Soufflet C;Barthelemy P;	Management of gastroesophageal reflux disease by primary care physicians and gastroenterologists: a prospective study of patients' records	not relevant
15886080	Bretagne JF;Rey JF;Caekaert A;Barthelemy P;	Routine management of gastro-oesophageal reflux disease by gastroenterologists in France: a prospective observational study	cross-sectional study on prevalence and treatment practices of GERD
18043104	Bright T;Watson DI;Tam W;Game PA;Astill D;Ackroyd R;Wijnhoven BP;Devitt PG;Schoeman MN;	Randomized trial of argon plasma coagulation versus endoscopic surveillance for barrett esophagus after antireflux surgery: late results	all patients with Barrett's
15997449	Byrne JP;Smithers BM;Nathanson LK;Martin I;Ong HS;Gotley DC;	Symptomatic and functional outcome after laparoscopic reoperation for failed antireflux surgery	intervention not considered in this review
18318084	Byrne PJ;Ravi N;Al-Sarraf N;Rowley S;Moran T;Reynolds JV;	The Rossetti-Nissen fundoplication--effective in managing gastro-oesophageal reflux disease	follow-up <5 years
16990197	Bytzer P;Morocutti A;Kennerly P;Ravic M;Miller N;ROSE T;	Effect of rabeprazole and omeprazole on the onset of gastro-oesophageal reflux disease symptom relief during the first seven days of treatment	RCT <4 wk but had AE data
18071818	Cadiere GB;Rajan A;Germay O;Himpens J;	Endoluminal fundoplication by a transoral device for the treatment of GERD: A feasibility study	follow up <5 years
17190659	Cadiere GB;Rajan A;Rqibate M;Germay O;Dapri G;Himpens J;Gawlicka AK;	Endoluminal fundoplication (ELF)--evolution of EsophyX, a new surgical device for transoral surgery	results published in another paper (Cadiere 2008 18443855)
17985242	Cai Q;Barrie M;Olejeme H;Rosenberg MD;	A pilot study of efficacy and safety of continuous intravenous infusion of pantoprazole in the treatment of severe erosive esophagitis	med vs med < 4 weeks' duration
15793885	Calabrese C;Fabbri A;Bortolotti M;Cenacchi G;Carlo S;Zahlane D;Miglioli M;Di FG;	Effect of omeprazole on symptoms and ultrastructural esophageal damage in acid bile reflux	N<100
18485128	Calabrese C;Liguori G;Gabusi V;Gionchetti P;Rizzello F;Straforini G;Brugnera R;Di FG;	Ninety-six-hour wireless oesophageal pH monitoring following proton pump inhibitor administration in NERD patients	med vs med < 4 weeks' duration
19248192	Calabrese C;Trere D;Liguori G;Gabusi V;Vici M;Cenacchi G;Derenzini M;Di FG;	Esophageal cell proliferation in gastroesophageal reflux disease: clinical-morphological data before and after pantoprazole	N<100

Pubmed ID	Author	Title	Reasons for rejection
15064622	Carrau RL;Khidr A;Crawley JA;Hillson EM;Davis JK;Pashos CL;	The impact of laryngopharyngeal reflux on patient-reported quality of life	not relevant
16702854	Casburn-Jones AC;Murray LS;Gillen D;McColl KE;	Endoscopy has minimal impact on mortality from upper gastrointestinal cancer in patients older than 55 years with uncomplicated dyspepsia	not population of interest
18774726	Casson AG;Madani K;Mann S;Zhao R;Reeder B;Lim HJ;	Does previous fundoplication alter the surgical approach to esophageal adenocarcinoma?	population: patients with esophageal cancer
15948814	Castell D;Bagin R;Goldlust B;Major J;Hepburn B;	Comparison of the effects of immediate-release omeprazole powder for oral suspension and pantoprazole delayed-release tablets on nocturnal acid breakthrough in patients with symptomatic gastro-oesophageal reflux disease	<4 wk dose
16737416	Castro FM;Garcia DE;Larraona JL;Rodriguez Hornillo MC;Lamas RE;Nunez HD;Pallares QM;	Efficacy of low-dose lansoprazole in the treatment of non-erosive gastrooesophageal reflux disease. Influence of infection by Helicobacter pylori	single arm study, Tx for 2 weeks only (<4 wk dose), no adverse events data
19521090	Ceccarelli G;Patriti A;Biancafarina A;Spaziani A;Bartoli A;Bellochi R;Casciola L;	Intraoperative and postoperative outcome of robot-assisted and traditional laparoscopic Nissen fundoplication	follow up <5 years
19521090	Ceccarelli G;Patriti A;Biancafarina A;Spaziani A;Bartoli A;Bellochi R;Casciola L;	Intraoperative and postoperative outcome of robot-assisted and traditional laparoscopic Nissen fundoplication	comparison not of interest; FU <5 years
17161211	Celik A;Loux TJ;Harmon CM;Saito JM;Georgeson KE;Barnhart DC;	Revision Nissen fundoplication can be completed laparoscopically with a low rate of complications: a single-institution experience with 72 children	pediatric patients
17345143	Chang EY;Minjarez RC;Kim CY;Seltman AK;Gopal DV;Diggs B;Davila R;Hunter JG;Jobe BA;	Endoscopic ultrasound for the evaluation of Nissen fundoplication integrity: a blinded comparison with conventional testing	not relevant
15242497	Chen CL;Orr WC;	Autonomic responses to heartburn induced by esophageal acid infusion	not relevant
16633101	Chen CL;Reif ME;Orr WC;	Effect of laparoscopic Nissen fundoplication on symptoms and gastric myoelectric activity in gastroesophageal reflux disease	N<100; follow up <5 years
16197532	Chen LQ;Ferraro P;Martin J;Duranceau AC;	Antireflux surgery for Barrett's esophagus: comparative results of the Nissen and Collis-Nissen operations	comparisons of surgical techniques: N<100

Pubmed ID	Author	Title	Reasons for rejection
19125799	Chin KF;Myers JC;Jamieson GG;Devitt PG;	Symptoms experienced during 24-h pH monitoring and their relationship to outcome after laparoscopic total fundoplication	predictor not of interest
15647177	Cicala M;Gabbrielli A;Emerenziani S;Guarino MP;Ribolsi M;Caviglia R;Costamagna G;	Effect of endoscopic augmentation of the lower oesophageal sphincter (Gatekeeper reflux repair system) on intraoesophageal dynamic characteristics of acid reflux.[see comment]	This technology is not in use in the US
16843863	Ciovica R;Gadenstatter M;Klingler A;Lechner W;Riedl O;Schwab GP;	Quality of life in GERD patients: medical treatment versus antireflux surgery	follow up <5 years
15862256	Ciovica R;Gadenstatter M;Klingler A;Neumayer C;Schwab GP;	Laparoscopic antireflux surgery provides excellent results and quality of life in gastroesophageal reflux disease patients with respiratory symptoms	Atypical GERD patients
19169748	Ciovica R;Riedl O;Neumayer C;Lechner W;Schwab GP;Gadenstatter M;	The use of medication after laparoscopic antireflux surgery	FU < 5 years
19737849	Comte L;Vansteelandt S;Tousset E;Baxter G;Vrijens B;	Linear and loglinear structural mean models to evaluate the benefits of an on-demand dosing regimen	Paper describes various mathematical models; no data on proportion of patients who are GERD and those who are dyspeptic patients, no data on outcomes
17555422	Conchillo JM;Schwartz MP;Selimah M;Samsom M;Arts J;Tack J;Sifrim D;Smout AJ;	Role of intra-oesophageal impedance monitoring in the evaluation of endoscopic gastroplication for gastro-oesophageal reflux disease	not relevant - Use of impedance monitoring as an evaluation tool
14674675	Contini S;Scarpignato C;	Endoscopic treatment of gastro-oesophageal reflux disease (GORD): a systematic review	SR of enoluminal procedures, all studies included are pre-2005
15852426	Cookson R;Flood C;Koo B;Mahon D;Rhodes M;	Short-term cost effectiveness and long-term cost analysis comparing laparoscopic Nissen fundoplication with proton-pump inhibitor maintenance for gastro-oesophageal reflux disease	cost-effectiveness analysis of surgical vs. ppi
17311604	Cote GA;Ferreira MR;Rozenberg-Ben-Dror K;Howden CW;	Programme of stepping down from twice daily proton pump inhibitor therapy for symptomatic gastro-oesophageal reflux disease associated with a formulary change at a VA medical center	< 5 years FU
17950091	Cowgill SM;Arnaoutakis D;Villadolid D;Rosemurgy AS;	'Redo' fundoplications: satisfactory symptomatic outcomes with higher cost of care	N<100

Pubmed ID	Author	Title	Reasons for rejection
16364717	Csendes A;Bragheto I;Burdiles P;Smok G;Henriquez A;Parada F;	Regression of intestinal metaplasia to cardiac or fundic mucosa in patients with Barrett's esophagus submitted to vagotomy, partial gastrectomy and duodenal diversion. A prospective study of 78 patients with more than 5 years of follow up.[see comment]	all patients with Barrett's
16455459	Csendes A;Burgos AM;Smok G;Burdiles P;Henriquez A;	Effect of gastric bypass on Barrett's esophagus and intestinal metaplasia of the cardia in patients with morbid obesity	Population (morbidly obese) and intervention (gastric bypass) are not relevant
18019869	Dachs R;rby-Stewart A;Graber M;	Choosing one PPI treatment over another	review paper
16125065	D'Alessio MJ;Rakita S;Bloomston M;Chambers CM;Zervos EE;Goldin SB;Poklepovic J;Boyce HW;Rosemurgy AS;	Esophagography predicts favorable outcomes after laparoscopic Nissen fundoplication for patients with esophageal dysmotility	Makes no distinction b/n GERD and hiatus hernia patients
19565992	Dan D;Seetahal S;Naraynsingh V;	Laparoscopic Nissen fundoplication for improved gastrointestinal symptoms and quality of life	N<100
16208110	Davis RE;Iqbal A;Gerhardt JD;Welch RA;Turaga K;Tierney B;Haider M;Filipi CJ;	A long-term comparison of plication configurations for endoluminal gastroplication: circumferential versus helical	surg comparison (circumferential vs. helical) but <50 per arm, <5 y f/u
16990199	de Boer W;de WN;Geldof H;Hazelhoff B;Bergmans P;Smout A;Tytgat G;	Does Helicobacter pylori infection influence response rate or speed of symptom control in patients with gastroesophageal reflux disease treated with rabeprazole?	<4 wk Rx
15072663	de J;van RB;Timmer R;Gooszen HG;Smout AJ;	The influence of laparoscopic adjustable gastric banding on gastroesophageal reflux	not relevant
16417759	de J;van RB;Timmer R;Gooszen HG;Smout AJ;	Effect of laparoscopic gastric banding on esophageal motility	not relevant
18384663	De Jonge PJ;Siersema PD;Van Breda SG;Van Zoest KP;Bac DJ;Leeuwenburgh I;Ouwendijk RJ;Van DH;Kusters JG;Kuipers EJ;	Proton pump inhibitor therapy in gastro-oesophageal reflux disease decreases the oesophageal immune response but does not reduce the formation of DNA adducts	no outcome of interest (cellular immune response; oxidative DNA damage)
16866863	de Souza CM;Ferrari AP;Ciconelli R;Ferraz MB;Moraes-Filho JP;	Evaluation of health-related quality of life in gastroesophageal reflux disease patients before and after treatment with pantoprazole	not RCT med rx; N<100

Pubmed ID	Author	Title	Reasons for rejection
17345934	del Genio G;Rossetti G;Brusciano L;Maffettone V;Napolitano V;Pizza F;Tolone S;del GA;Di MM;	Laparoscopic Nissen-Rossetti fundoplication is effective to control gastro-oesophageal and pharyngeal reflux detected using 24-hour oesophageal impedance and pH monitoring (MII-pH)	duplicate publication: same population as del Genio 2007
18612705	del Genio G;Tolone S;del GF;Aggarwal R;d'Alessandro A;Allaria A;Rossetti G;Brusciano L;del GA;	Prospective assessment of patient selection for antireflux surgery by combined multichannel intraluminal impedance pH monitoring	Evaluation of the use of multichannel intraluminal impedance pH monitoring (MII-pH) for patient selection in anti-reflux surgery
18025830	del Genio G;Tolone S;Rossetti G;Brusciano L;del GF;Pizza F;Russo F;Di MM;Napolitano V;del GA;	Total fundoplication does not obstruct the esophageal secondary peristalsis: investigation with pre- and postoperative 24-hour pH-multichannel intraluminal impedance	N<100; follow up <5 years
18564168	del Genio G;Tolone S;Rossetti G;Brusciano L;Pizza F;del GF;Russo F;Di MM;Lucido F;Barra L;Maffettone V;Napolitano V;del GA;	Objective assessment of gastroesophageal reflux after extended Heller myotomy and total fundoplication for achalasia with the use of 24-hour combined multichannel intraluminal impedance and pH monitoring (MII-pH)	achalasia not considered in this review
18184117	Dent J;Kahrilas PJ;Hatlebakk J;Vakil N;Denison H;Franzen S;Lundborg P;	A randomized, comparative trial of a potassium-competitive acid blocker (AZD0865) and esomeprazole for the treatment of patients with nonerosive reflux disease	AZD0865 was discontinued from clinical development after analysis showed that AZD0865 did not show additional clinical efficacy compared to PPI treatment AZD0865 was being developed for acid related GI disease. Drug was discontinued in 2005. http://www.as
16688803	des Varannes SB;Sacher-Huvelin S;Vavasseur F;Masliah C;Le RM;Aygalenq P;Bonnot-Marlier S;Lequeux Y;Galmiche JP;	Rabeprazole test for the diagnosis of gastro-oesophageal reflux disease: results of a study in a primary care setting	not relevant
16783042	Dettmar PW;Hampson FC;Jain A;Choubey S;Little SL;Baxter T;	Administration of an alginate based gastric reflux suppressant on the bioavailability of omeprazole.[see comment]	Assesses drug interaction between 10 per cent w/v liquid alginate suspension and omeprazole
17681004	Dettmar PW;Hampson FC;Taubel J;Lorch U;Johnstone LM;Sykes J;Berry PJ;	The suppression of gastro-oesophageal reflux by alginates	not GERD patients

Pubmed ID	Author	Title	Reasons for rejection
16494641	Dettmar PW;Sykes J;Little SL;Bryan J;	Rapid onset of effect of sodium alginate on gastro-oesophageal reflux compared with ranitidine and omeprazole, and relationship between symptoms and reflux episodes	med vs med < 4 weeks' duration
16167971	Dickman R;Emmons S;Cui H;Sewell J;Hernandez D;Esquivel RF;Fass R;	The effect of a therapeutic trial of high-dose rabeprazole on symptom response of patients with non-cardiac chest pain: a randomized, double-blind, placebo-controlled, crossover trial	Outcome is Atypical GERD - non-cardiac chest pain
15800686	Diculescu M;Iacob R;Chira C;Mihaila D;Iacob S;	Esomeprazole in the treatment of patients with heartburn and other upper gastrointestinal symptoms, referred to primary care -- results of the in-practice evaluation program in Romania.[see comment]	med cohort with no AE reported
17714057	Dotan E;Katz R;Bratcher J;Wasserman C;Liebman M;Panagopoulos G;Spaccavento C;	The prevalence of pantoprozole associated thrombocytopenia in a community hospital	no information on patient's diagnoses
17058295	Draaisma WA;Ruurda JP;Scheffer RC;Simmermacher RK;Gooszen HG;Rijnhart-De Jong HG;Buskens E;Broeders IA;	Randomized clinical trial of standard laparoscopic versus robot-assisted laparoscopic Nissen fundoplication for gastro-oesophageal reflux disease	follow up <5 years
19845420	Duh MS;Gosselin A;Luo R;Lohoues H;Lewis BE;Crawley JA;	Impact of compliance with proton pump inhibitors on NSAID treatment	Cointervention being assessed (NSAID Rx) is not of interest
19568229	El-Serag HB;Fitzgerald S;Richardson P;	The extent and determinants of prescribing and adherence with acid-reducing medications: a national claims database study	retrospective cohort study of PI and H2RA prescribing practices and compliance
19568229	El-Serag HB;Fitzgerald S;Richardson P;	The extent and determinants of prescribing and adherence with acid-reducing medications: a national claims database study	PPI prescription patterns are not of interest
18363892	El-Serag HB;Wieman M;Richardson P;	The use of acid-decreasing medication in veteran patients with gastro-oesophageal reflux disorder with and without Barrett's oesophagus	not relevant; retrospective cohort study on the extent of PPI use in patients with newly diagnosed GERD with and without BO and to examine other potential determinants of PPI use in these patients.

Pubmed ID	Author	Title	Reasons for rejection
17954090	el-Sherif AE;Adusumilli PS;Pettiford BL;d'Amato TA;Schuchert MJ;Clark A;DiRenzo C;Landreneau JP;Luketich JD;Landreneau RJ;	Laparoscopic clam shell partial fundoplication achieves effective reflux control with reduced postoperative dysphagia and gas bloating	adverse events: not the primary outcome
17453284	Engstrom C;Lonroth H;Mardani J;Lundell L;	An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial	no comparions of interest; subjects <100
15773839	Engstrom C;Ruth M;Lonroth H;Lundell L;	Manometric characteristics of the gastroesophageal junction after anterior versus posterior partial fundoplication	N<50; follow-up<5 year
19654097	Epstein D;	Laparoscopic fundoplication compared with medical management for gastro-oesophageal reflux disease: cost effectiveness study	cost effectiveness study
19654097	Epstein D;Bojke L;Sculpher MJ;REFLUX trial group;	Laparoscopic fundoplication compared with medical management for gastro-oesophageal reflux disease: cost effectiveness study.[see comment]	cost-effectiveness analysis
15569119	Fallone CA;Guyatt GH;Armstrong D;Wiklund I;Degl'innocenti A;Heels-Ansdell D;Barkun AN;Chiba N;Zanten SJ;El-Dika S;Austin P;Tanser L;Schunemann HJ;	Do physicians correctly assess patient symptom severity in gastro-oesophageal reflux disease?	not relevant
18235928	Farah JF;Grande JC;Goldenberg A;Martinez JC;Lupinacci RA;Matone J;	Randomized trial of total fundoplication and fundal mobilization with or without division of short gastric vessels: a short-term clinical evaluation	<50 per arm, <5 y f/u
CN-00688	Farup PG HM;	Alternative vs. conventional treatment given on-demand for gastroesophageal reflux disease: a randomised controlled trial	pectin-based, raft-forming, natural, anti-reflux agent (PRA) is not a medication iof interest
19236727	Farup PG;Heibert M;Hoeg V;	Alternative vs. conventional treatment given on-demand for gastroesophageal reflux disease: a randomised controlled trial	Rejected after extraction after consultation with Peter as PRA is akin to an antacid and not a drug that we are interested in

Pubmed ID	Author	Title	Reasons for rejection
18729549	Feng L;Tan CH;Merchant RA;Ng TP;	Association between depressive symptoms and use of HMG-CoA reductase inhibitors (statins), corticosteroids and histamine H(2) receptor antagonists in community-dwelling older persons: cross-sectional analysis of a population-based cohort	not relevant
16926745	Fennerty MB;Johnson DA;	Heartburn severity does not predict disease severity in patients with erosive esophagitis	5 separate RCTs
16337389	Foroulis CN;Thorpe JA;	Photodynamic therapy (PDT) in Barrett's esophagus with dysplasia or early cancer	Population: Barrett's esophagus complicated with high-grade dysplasia and/or early esophageal adenocarcinoma
18924018	Franke A;Hepp C;Harder H;Beglinger C;Singer MV;	Esomeprazole reduces gastroesophageal reflux after beer consumption in healthy volunteers	Population: healthy volunteers without a history of GERD
16709355	Frantzides CT;Carlson MA;Zografakis JG;Moore RE;Zeni T;Madan AK;	Postoperative gastrointestinal complaints after laparoscopic Nissen fundoplication	follow-up <5 years
16334434	Franzen T;Anderberg B;Wiren M;Johansson KE;	Long-term outcome is worse after laparoscopic than after conventional Nissen fundoplication	f/u <5 years
17379591	Frazzoni M;Manno M;De ME;Savarino V;	Efficacy in intra-oesophageal acid suppression may decrease after 2-year continuous treatment with proton pump inhibitors	patients with Barrett's esophagus or severe reflux oesophagitis
16289976	Frazzoni M;Manno M;De ME;Savarino V;	Intra-oesophageal acid suppression in complicated gastro-oesophageal reflux disease: esomeprazole versus lansoprazole	patients with Barrett's esophagus or ulcerative reflux oesophagitis
18049392	Frezza EE;Dissanaike S;Wachtel MS;	Laparoscopic highly selective vagotomy with nissen fundoplication: is there any role?	N<100; follow-up <5 yr
15235916	Fuchs KH;Breithaupt W;Fein M;Maroske J;Hammer I;	Laparoscopic Nissen repair: indications, techniques and long-term benefits	review
18071800	Funch-Jensen P;Bendixen A;Iversen MG;Kehlet H;	Complications and frequency of redo antireflux surgery in Denmark: a nationwide study, 1997-2005	Primary fundoplication group not homogenous GERD population--unable to distinguish b/w surgery for GERD or paraesophageal hernia
16334770	Gad El-Hak N;Abo ZM;Aboelenen A;Fouad A;Abd AT;El-Shoubary M;Kandel T;Hamdy E;Abdel WM;Fathy O;El-ebidy G;Sultan A;Elfiky A;Elghwalby N;Ezzat F;	Short gastric vessels division in Laparoscopic Nissen Fundoplication	follow-up <5 years

Pubmed ID	Author	Title	Reasons for rejection
16785284	Garcia Rodriguez LA;Lagergren J;Lindblad M;	Gastric acid suppression and risk of oesophageal and gastric adenocarcinoma: a nested case control study in the UK.[see comment]	not population of interest
18054750	Garcia Rodriguez LA;Ruigomez A;Panes J;	Use of acid-suppressing drugs and the risk of bacterial gastroenteritis.[see comment]	not GERD patients
19222532	Garg N;Yano F;Filipi CJ;Mittal SK;	Long-term symptomatic outcomes after Collis gastroplasty with fundoplication	< 100 patients
16630752	Geevasinga N;Coleman PL;Webster AC;Roger SD;	Proton pump inhibitors and acute interstitial nephritis.[see comment]	not GERD patients
19368103	Ghosh A;Halder S;Mandal S;Mandal A;Basu M;Dabholkar P;	Rabeto plus: a valuable drug for managing functional dyspepsia	Med pre- and post trial, <4wk, itopride is not of interest, not sure what is "rabeto plus"?
18569981	Ghoshal UC;Chourasia D;Tripathi S;Misra A;Singh K;	Relationship of severity of gastroesophageal reflux disease with gastric acid secretory profile and esophageal acid exposure during nocturnal acid breakthrough: a study using 24-h dual-channel pH-metry	not relevant
18403945	Gillies RS;Stratford JM;Booth MI;Dehn TC;	Does laparoscopic antireflux surgery improve quality of life in patients whose gastro-oesophageal reflux disease is well controlled with medical therapy?	N<100; follow up <5 years
19573227	Gisbert JP;Cooper A;Karagiannis D;Hatlebakk J;Agreus L;Jablonowski H;Zapardiel J;	Impact of gastroesophageal reflux disease on patients' daily lives: a European observational study in the primary care setting	Not relevant; crosssectional study
17187611	Goessler A;Huber-Zeyringer A;Hoellwarth ME;	Recurrent gastroesophageal reflux in neurologically impaired patients after fundoplication	Population: mentally retarded children
18373118	Granderath FA;Granderath UM;Pointner R;	Laparoscopic revisional fundoplication with circular hiatal mesh prosthesis: the long-term results	Population: previous anti-reflux surgery
17306636	Granderath FA;Kamolz T;Granderath UM;Pointner R;	Gas-related symptoms after laparoscopic 360 degrees Nissen or 270 degrees Toupet fundoplication in gastrooesophageal reflux disease patients with aerophagia as comorbidity.[see comment]	no comparator of interest

Pubmed ID	Author	Title	Reasons for rejection
16847231	Granderath FA;Kamolz T;Schweiger UM;Pointner R;	Impact of laparoscopic nissen fundoplication with prosthetic hiatal closure on esophageal body motility: Results of a prospective randomized trial.[see comment][erratum appears in Arch Surg. 2007 Jun;142(6):579]	no intervention of interest: laparoscopic Nissen fundoplication with prosthetic hiatal closure/with simple sutured hiatal closure
15655204	Granderath FA;Schweiger UM;Kamolz T;Asche KU;Pointner R;	Laparoscopic Nissen fundoplication with prosthetic hiatal closure reduces postoperative intrathoracic wrap herniation: preliminary results of a prospective randomized functional and clinical study	no intervention of interest: laparoscopic Nissen fundoplication with prosthetic hiatal closure/with simple sutured hiatal closure
16206005	Granderath FA;Schweiger UM;Kamolz T;Pointner R;	Dysphagia after laparoscopic antireflux surgery: a problem of hiatal closure more than a problem of the wrap.[see comment]	Identification of the morphologic cause of dysphagia after laparoscopic antireflux surgery
17103275	Granderath FA;Schweiger UM;Pointner R;	Laparoscopic antireflux surgery: tailoring the hiatal closure to the size of hiatal surface area.[see comment]	Evaluating different methods of crural closure by the size of the hiatal defect
18796263	Grant A;Wileman S;Ramsay C;Bojke L;Epstein D;Sculpher M;Macran S;Kilonzo M;Vale L;Francis J;Mowat A;Krukowski Z;Heading R;Thursz M;Russell I;Campbell M;REFLUX trial group;	The effectiveness and cost-effectiveness of minimal access surgery amongst people with gastro-oesophageal reflux disease - a UK collaborative study. The REFLUX trial	Duplicate (UI 19074946)
18719508	Grigolon A;Cantu P;Savojardo D;Conte D;Penagini R;	Esophageal acid exposure on proton pump inhibitors in unselected asymptomatic gastroesophageal reflux disease patients	non-RCT med comparison; N<100
18095025	Grotenhuis BA;Wijnhoven BP;Bessell JR;Watson DI;	Laparoscopic antireflux surgery in the elderly	study not specific for adverse events
17704884	Guerin E;Betroune K;Closset J;Mehdi A;Lefebvre JC;Houben JJ;Gelin M;Vaneukem P;El N;	Nissen versus Toupet fundoplication: results of a randomized and multicenter trial	follow up <5 yr
18350759	Guirguis-Blake J;	Medical treatments in the short-term management of reflux esophagitis	Cochrane briefs
16137589	Gutschow CA;Collet P;Prenzel K;Holscher AH;Schneider PM;	Long-term results and gastroesophageal reflux in a series of laparoscopic adjustable gastric banding	The population studied as well as the intervention used is not relevant
17122976	Hakanson BS;Thor KB;Thorell A;Ljungqvist O;	Open vs laparoscopic partial posterior fundoplication. A prospective randomized trial	follow up <5 yr

Pubmed ID	Author	Title	Reasons for rejection
15683433	Hamamoto N;Hashimoto T;Adachi K;Hirakawa K;Ishihara S;Inoue H;Taniura H;Niigaki M;Sato S;Kushiyama Y;Suetsugu H;Miyake T;Kinoshita Y;	Comparative study of nizatidine and famotidine for maintenance therapy of erosive esophagitis	H2RA vs H2RA not comparator of interest
18027060	Hartmann J;Jacobi CA;Menenakos C;Ismail M;Braumann C;	Surgical treatment of gastroesophageal reflux disease and upside-down stomach using the Da Vinci robotic system. A prospective study	system experimental, follow up <5 yr
19115245	Hartmann J;Menenakos C;Ordemann J;Nocon M;Raue W;Braumann C;	Long-term results of quality of life after standard laparoscopic vs. robot-assisted laparoscopic fundoplications for gastro-oesophageal reflux disease. A comparative clinical trial	system experimental, follow up <5 yr
15842575	Hawkey C;Talley NJ;Yeomans ND;Jones R;Sung JJ;Langstrom G;Naesdal J;Scheiman JM;Study Group;	Improvements with esomeprazole in patients with upper gastrointestinal symptoms taking non-steroidal antiinflammatory drugs, including selective COX-2 inhibitors	The study population included people with chronic conditions who were chronic (>7 months) continuous users of NSAID; not GERD patients.
17318044	Heemskerk J;van Gemert WG;Greve JW;Bouvy ND;	Robot-assisted versus conventional laparoscopic Nissen fundoplication: a comparative retrospective study on costs and time consumption	non-RCT surgical tx, N<100
17593070	Hogan D;Pratha V;Riff D;Ducker S;Schwartz H;Soffer E;Wang W;Rath N;Comer GM;	Oral pantoprazole in the form of granules or tablets are pharmacodynamically equivalent in suppressing acid output in patients with gastro-oesophageal reflux disease and a history of erosive oesophagitis	no clinical outcome of interest
18600389	Hongo M;Kinoshita Y;Haruma K;	A randomized, double-blind, placebo-controlled clinical study of the histamine H2-receptor antagonist famotidine in Japanese patients with nonerosive reflux disease	H2RA vs placebo not comparator of interest
19107335	Hongo M;Kinoshita Y;Miwa H;Ashida K;	The demographic characteristics and health-related quality of life in a large cohort of reflux esophagitis patients in Japan with reference to the effect of lansoprazole: the REQUEST study	Not focused on AE
17944742	Horowitz N;Moshkowitz M;Leshno M;Ribak J;Birkenfeld S;Kenet G;Halpern Z;	Clinical trial: evaluation of a clinical decision-support model for upper abdominal complaints in primary-care practice	study intervention was a medical algorithm, which is not of interest

Pubmed ID	Author	Title	Reasons for rejection
16328397	Horstmann R;Classen C;Rottgermann S;Langer M;Palmes D;	Long-term experience of treating 185 patients with gastroesophageal reflux disease (GERD) by anti-reflux surgery respecting the functional-morphological restoration of the esophagus	intervention not of interest, f/u<5 yr
18758373	Howden CW BEKFGTBR;	Control of 24-hour intragastric acidity with morning dosing of immediate-release and delayed-release proton pump inhibitors in patients with GERD	Tx period < 4 weeks
18758373	Howden CW;Ballard ED;Koch FK;Gautille TC;Bagin RG;	Control of 24-hour intragastric acidity with morning dosing of immediate-release and delayed-release proton pump inhibitors in patients with GERD	med vs med < 4 weeks' duration
17364152	Hubbard N;Velanovich V;	Endoscopic endoluminal radiofrequency ablation of Barrett's esophagus in patients with fundoplications	patients with fundoplication and Barrett's esophagus
19281670	Hughes JD;Tanpurekul W;Keen NC;Ee HC;	Reducing the cost of proton pump inhibitors by adopting best practice	Descriptive study of prescribing characteristics as well as cost; no data on effect of PPI
18445141	Hunt RH;Armstrong D;Yaghoobi M;James C;Chen Y;Leonard J;Shin JM;Lee E;Tang-Liu D;Sachs G;	Predictable prolonged suppression of gastric acidity with a novel proton pump inhibitor, AGN 201904-Z	Not a population of interest - healthy male volunteers
15942709	Inamori M;Togawa J;Iwasaki T;Ozawa Y;Kikuchi T;Muramatsu K;Chiguchi G;Matsumoto S;Kawamura H;Abe Y;Kirikoshi H;Kobayashi N;Shimamura T;Kubota K;Sakaguchi T;Saito S;Ueno N;Nakajima A;	Early effects of lafutidine or rabeprazole on intragastric acidity: which drug is more suitable for on-demand use?[see comment]	Population: healthy male volunteers
18855057	Jensen CD;Gilliam AD;Horgan LF;Bawa S;Attwood SE;	Day-case laparoscopic Nissen fundoplication	f/u <5 years
18502362	Jeske HC;Borovicka J;von GA;Tiefenthaler W;Hohlrieder M;Heidegger T;Benzer A;	Preoperative administration of esomeprazole has no influence on frequency of refluxes	Enrolled healthy volunteers; Not the population of interest
16011671	Johnson DA;Stacy T;Ryan M;Wootton T;Willis J;Hornbuckle K;Brooks W;Doviak M;	A comparison of esomeprazole and lansoprazole for control of intragastric pH in patients with symptoms of gastro-oesophageal reflux disease	med vs med < 4 weeks' duration

Pubmed ID	Author	Title	Reasons for rejection
16301023	Johnston MH;Eastone JA;Horwhat JD;Cartledge J;Mathews JS;Foggy JR;	Cryoablation of Barrett's esophagus: a pilot study.[see comment]	patients with Barrett's esophagus
19166433	Jones R;Patrikios T;	The effectiveness of esomeprazole 40 mg in patients with persistent symptoms of gastro-oesophageal reflux disease following treatment with a full dose proton pump inhibitor	med cohort N<100
17950677	Kahrilas PJ;Dent J;Lauritsen K;Malfertheiner P;Denison H;Franzen S;Hasselgren G;	A randomized, comparative study of three doses of AZD0865 and esomeprazole for healing of reflux esophagitis	AZD0865 was discontinued from clinical development after analysis showed that AZD0865 did not show additional clinical efficacy compared to PPI treatment AZD0865 was being developed for acid related GI disease. Drug was discontinued in 2005. http://www.as
16240208	Kahrilas PJ;Miner P;Johanson J;Mao L;Jokubaitis L;Sloan S;	Efficacy of rabeprazole in the treatment of symptomatic gastroesophageal reflux disease	PPI vs placebo is excluded
16093871	Kaspari S;Kupcinskas L;Heinze H;Berghofer P;	Pantoprazole 20 mg on demand is effective in the long-term management of patients with mild gastro-oesophageal reflux disease	PPI vs placebo is excluded
17229243	Katz PO;Koch FK;Ballard ED;Bagin RG;Gautille TC;Checani GC;Hogan DL;Pratha VS;	Comparison of the effects of immediate-release omeprazole oral suspension, delayed-release lansoprazole capsules and delayed-release esomeprazole capsules on nocturnal gastric acidity after bedtime dosing in patients with night-time GERD symptoms	RCT < 4 wk
17903731	Kelly JJ;Watson DI;Chin KF;Devitt PG;Game PA;Jamieson GG;	Laparoscopic Nissen fundoplication: clinical outcomes at 10 years	f/u <5 years
19460767	Keywood C;Wakefield M;Tack J;	A proof-of-concept study evaluating the effect of ADX10059, a metabotropic glutamate receptor-5 negative allosteric modulator, on acid exposure and symptoms in gastro-oesophageal reflux disease	med vs med < 4 weeks' duration
19797106	Khajanchee YS;Dunst CM;Swanstrom LL;	Outcomes of Nissen fundoplication in patients with gastroesophageal reflux disease and delayed gastric emptying	follow-up < 5 years
19255848	Khan A;Cho I;Traube M;	Patients with throat symptoms on Acid suppressive therapy: do they have reflux?	Data for our purposes not available?

Pubmed ID	Author	Title	Reasons for rejection
19052958	Khan MA;Smythe A;Globe J;Stoddard CJ;Ackroyd R;	Randomized controlled trial of laparoscopic Nissen versus Lind fundoplication for gastro-oesophageal reflux disease	follow-up < 5 years
19467139	Kim JH;Sinn DH;Son HJ;Kim JJ;Rhee JC;Rhee PL;	Comparison of one-week and two-week empirical trial with a high-dose rabeprazole in non-cardiac chest pain patients	No comparator, Trial < 4 weeks, PPI used as diagnositic tool for GERD-related NCCP; Only 38% of pts with GERD
16868803	Kinoshita Y;Kobayashi T;Kato M;Asahina K;Haruma K;Shimatani T;Inoue S;Kabemura T;Kurosawa S;Kuwayama H;Ashida K;Hirayama M;Kiyama S;Yamamoto M;Suzuki J;Suzuki H;Matsumoto K;Aoshima M;	The pharmacodynamic effect of omeprazole 10 mg and 20 mg once daily in patients with nonerosive reflux disease in Japan	med vs med < 4 weeks' duration
18812271	Kornmo TS;Ruud TE;	Long-term results of laparoscopic Nissen fundoplication due to gastroesophageal reflux disease. A ten year follow-up in a low volume center	N<100
17103281	Kundhal PS;Harnish JL;Urbach DR;	Effect of surgeon on outcome of antireflux surgery	no modifier of interest; N<100
19280541	Kunsch S;Neesse A;Linhart T;Steinkamp M;Fensterer H;Adler G;Gress TM;Ellenrieder V;	Impact of pantoprazole on duodeno-gastro-esophageal reflux (DGER)	condition not considered in this review
17385034	Kusano M;Shimoyama Y;Kawamura O;Maeda M;Kuribayashi S;Nagoshi A;Zai H;Moki F;Horikoshi T;Toki M;Sugimoto S;Mori M;	Proton pump inhibitors improve acid-related dyspepsia in gastroesophageal reflux disease patients	PPIs (rabeprazole+lansoprazole+omeprazole)
18465242	Kusano M;Shirai N;Yamaguchi K;Hongo M;Chiba T;Kinoshita Y;Acid-Related Symptom (ARS) Research Group;	It is possible to classify non-erosive reflux disease (NERD) patients into endoscopically normal groups and minimal change groups by subjective symptoms and responsiveness to rabeprazole -- a report from a study with Japanese patients	classification of non-erosive reflux disease patients
19641272	Kushner PR;Snoddy AM;Gilderman L;Peura DA;	Lansoprazole 15 mg once daily for 14 days is effective for treatment of frequent heartburn: results of 2 randomized, placebo-controlled, double-blind studies	med vs med < 4 weeks' duration

Pubmed ID	Author	Title	Reasons for rejection
17029609	Labenz J;Nocon M;Lind T;Leodolter A;Jaspersen D;Meyer-Sabellek W;Stolte M;Vieth M;Willich SN;Malfertheiner P;	Prospective follow-up data from the ProGERD study suggest that GERD is not a categorial disease.[see comment]	progression or regression of GERD under routine care
17171490	Lagergren J;Viklund P;	Is esophageal adenocarcinoma occurring late after antireflux surgery due to persistent postoperative reflux?[see comment]	case-contol study of esophageal adenocarcinoma
18777121	Lamb PJ;Myers JC;Thompson SK;Jamieson GG;	Laparoscopic fundoplication in patients with a hypertensive lower esophageal sphincter	N<100
CN-00722	Lazebnik LB DVKV;	[Efficiency of famotidin in prophylaxis of NSAIDs-induced gastropathy: result of multicenter research ZASLON-1 (protection of gastric mucosa from non-steroidal anti-inflammatory drugs]	Not GERD nor GERD tx (NSAID)? Article in Russian
19349130	Lecuyer M;Cousin T;Monnot MN;Coffin B;	Efficacy of an activated charcoal-simethicone combination in dyspeptic syndrome: results of a randomized prospective study in general practice	not treatment of interest
19392871	Lee ES;Kim N;Lee SH;Park YS;Kim JW;Jeong SH;Lee DH;Jung HC;Song IS;	Comparison of risk factors and clinical responses to proton pump inhibitors in patients with erosive oesophagitis and non-erosive reflux disease	comparison not of interest-no individual data by drug
17227313	Lindeboom MY;Ringers J;Straathof JW;van Rijn PJ;Neijenhuis P;Masclee AA;	The effect of laparoscopic partial fundoplication on dysphagia, esophageal and lower esophageal sphincter motility	sample size <100 for KQ3
19755967	Lippmann QK;Crockett SD;Dellon ES;Shaheen NJ;	Quality of life in GERD and Barrett's esophagus is related to gender and manifestation of disease	No treatments
17393309	Lu M;Malladi V;Agha A;Abudayyeh S;Han C;Siepman N;Graham DY;	Failures in a proton pump inhibitor therapeutic substitution program: lessons learned	no modifiers of interest: sequence effect (LAN-RAB-LAN-RAB vs. RAB-LAN-RAB-LAN)
17033907	Macran S;Wileman S;Barton G;Russell I;REFLUX trial group;	The development of a new measure of quality of life in the management of gastro-oesophageal reflux disease: the Reflux questionnaire	development of a new measure of quality of life: the Reflux questionnaire
17051602	Mainie I;Tutuian R;Agrawal A;Adams D;Castell DO;	Combined multichannel intraluminal impedance-pH monitoring to select patients with persistent gastro-oesophageal reflux for laparoscopic Nissen fundoplication	<100 patients, <5yrs FU
18496394	Mainie I;Tutuian R;Castell DO;	Addition of a H2 receptor antagonist to PPI improves acid control and decreases nocturnal acid breakthrough	non-RCT of med; follow-up<4 wk; no adverse events

Pubmed ID	Author	Title	Reasons for rejection
16917401	Mainie I;Tutuian R;Castell DO;	Comparison between the combined analysis and the DeMeester Score to predict response to PPI therapy	predictor not considered in this review
16556669	Mainie I;Tutuian R;Shay S;Vela M;Zhang X;Sifrim D;Castell DO;	Acid and non-acid reflux in patients with persistent symptoms despite acid suppressive therapy: a multicentre study using combined ambulatory impedance-pH monitoring.[see comment]	Study of association between reflux episodes and GORD symptioms
17693266	Mariette C;Piessen G;Balon JM;Guidat A;Lebuffe G;Triboulet JP;	The safety of the same-day discharge for selected patients after laparoscopic fundoplication: a prospective cohort study	sample size <100 for KQ3
18027047	Mark LA;Okrainec A;Ferri LE;Feldman LS;Mayrand S;Fried GM;	Comparison of patient-centered outcomes after laparoscopic Nissen fundoplication for gastroesophageal reflux disease or paraesophageal hernia	Population not of interest
17219264	Masqusi S;Velanovich V;	Pyloroplasty with fundoplication in the treatment of combined gastroesophageal reflux disease and bloating	Intervention/Outcome not of interest
18973468	Mathavan VK;Yuh JN;Marks JM;	Long-term evaluation of patients undergoing laparoscopic antireflux surgery without bougie placement	follow up less than 5 years
18199712	Mathes RW;Malone KE;Daling JR;Porter PL;Li CI;	Relationship between histamine2-receptor antagonist medications and risk of invasive breast cancer	not population of interest
18506466	McGlashan JA JLS;	The value of a liquid alginate suspension (Gaviscon Advance) in the management of laryngopharyngeal reflux	LPR (only 6% GORD)--Include for AG? Not a review
18506466	McGlashan JA;Johnstone LM;Sykes J;Strugala V;Dettmar PW;	The value of a liquid alginate suspension (Gaviscon Advance) in the management of laryngopharyngeal reflux	Atypical GERD outcomes
17382741	McVary KT;Roehrborn CG;Kaminetsky JC;Auerbach SM;Wachs B;Young JM;Esler A;Sides GD;Denes BS;	Tadalafil relieves lower urinary tract symptoms secondary to benign prostatic hyperplasia	not relevant
18512110	Mejia-Rivas MA;Herrera-Lopez A;Hernandez-Calleros J;Herrera MF;Valdovinos MA;	Gastroesophageal reflux disease in morbid obesity: the effect of Roux-en-Y gastric bypass	Intervention (Roux-en-Y Gastric Bypass) is not of intrest

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16225490	Metz DC;Miner PB;Heuman DM;Chen Y;Sostek M;	Comparison of the effects of intravenously and orally administered esomeprazole on acid output in patients with symptoms of gastro-oesophageal reflux disease	med vs med < 4 weeks' duration
18398651	Mickevicius A;Endzinas Z;Kiudelis M;Jonaitis L;Kupcinskas L;Maleckas A;Pundzius J;	Influence of wrap length on the effectiveness of Nissen and Toupet fundoplication: a prospective randomized study	follow-up < 5yrs
17444849	Miyamoto M;Haruma K;Kuwabara M;Nagano M;Okamoto T;Tanaka M;	Long-term gastroesophageal reflux disease therapy improves reflux symptoms in elderly patients: five-year prospective study in community medicine	< 100 patients
18028348	Miyamoto M;Haruma K;Takeuchi K;Kuwabara M;	Frequency scale for symptoms of gastroesophageal reflux disease predicts the need for addition of prokinetics to proton pump inhibitor therapy.[see comment]	< 5 years of follow up
15256830	Monnikes H;Bardhan KD;Stanghellini V;Berghofer P;Bethke TD;Armstrong D;	Evaluation of GERD symptoms during therapy. Part II. Psychometric evaluation and validation of the new questionnaire ReQuest in erosive GERD	duplicate publication with Monnikes 2007 (refID 833)
17489031	Monnikes H;Bardhan KD;Stanghellini V;Berghofer P;Bethke TD;Armstrong D;	Evaluation of GERD symptoms during therapy. Part II. Psychometric evaluation and validation of the new questionnaire ReQuest in erosive GERD	Non-comparative Non-RCT for medical tx
17489034	Monnikes H;Pfaffenberger B;Gatz G;Hein J;Bardhan KD;	Novel measurement of rapid treatment success with ReQuest: first and sustained symptom relief as outcome parameters in patients with endoscopy-negative GERD receiving 20 mg pantoprazole or 20 mg esomeprazole	RCT < 4 wk
19383986	Moretzsohn LD CEFJSMBEB;	Control of esophageal and intragastric pH with compounded and manufactured omeprazole in patients with reflux esophagitis: a pilot study	Treatment arms < 10
19383986	Moretzsohn LD;Carvalho EB;Franco JD;Soares MP;Brito EM;Belarmino K;Coelho LG;	Control of esophageal and intragastric pH with compounded and manufactured omeprazole in patients with reflux esophagitis: a pilot study	med vs med < 4 weeks' duration
16552744	Morino M;Pellegrino L;Giaccone C;Garrone C;Rebecchi F;	Randomized clinical trial of robot-assisted versus laparoscopic Nissen fundoplication	no comparison or outcome of interest
16703443	Morton JM;Galanko JA;Soper NJ;Low DE;Hunter J;Traverso LW;	NIS vs SAGES: a comparison of national and voluntary databases	not focused on GERD population

Pubmed ID	Author	Title	Reasons for rejection
19178902	Muller-Stich BP;Koninger J;Muller-Stich BH;Schafer F;Warschkow R;Mehrabi A;Gutt CN;	Laparoscopic mesh-augmented hiatoplasty as a method to treat gastroesophageal reflux without fundoplication: single-center experience with 306 consecutive patients	follow up < 5 years
18353273	Muller-Stich BP;Linke GR;Borovicka J;Marra F;Warschkow R;Lange J;Mehrabi A;Koninger J;Gutt CN;Zerz A;	Laparoscopic mesh-augmented hiatoplasty as a treatment of gastroesophageal reflux disease and hiatal hernias-preliminary clinical and functional results of a prospective case series	less than 100 patients and follow up < 5 years
19165497	Muller-Stich BP;Reiter MA;Mehrabi A;Wente MN;Fischer L;Koninger J;Gutt CN;	No relevant difference in quality of life and functional outcome at 12 months' follow-up-a randomised controlled trial comparing robot-assisted versus conventional laparoscopic Nissen fundoplication	no comparisonof interest; follow-up<5 yr
17353978	Muller-Stich BP;Reiter MA;Wente MN;Bintintan VV;Koninger J;Buchler MW;Gutt CN;	Robot-assisted versus conventional laparoscopic fundoplication: short-term outcome of a pilot randomized controlled trial	no comparison or outcome of interest
19796556	Muro Y;Sugiura K;Nitta Y;Mitsuma T;Hoshino K;Usuda T;Hayashi K;Murase Y;Shimizu M;Matsuo H;	Scoring of reflux symptoms associated with scleroderma and the usefulness of rabeprazole	No comparator-RBZ only
17760657	Myers JC;Jamieson GG;Wayman J;King DR;Watson DI;	Esophageal ileus following laparoscopic fundoplication	sample size <100 for KQ3
16736336	Nakadi IE;Melot C;Closset J;DeMoor V;Betroune K;Feron P;Lingier P;Gelin M;	Evaluation of da Vinci Nissen fundoplication clinical results and cost minimization	comparison not of interest; N<100
15943842	Nakamura T;Shirakawa K;Masuyama H;Sugaya H;Hiraishi H;Terano A;	Minimal change oesophagitis: a disease with characteristic differences to erosive oesophagitis	no clear definition of symptoms
15549628	Neumayer C;Ciovica R;Gadenstatter M;Erd G;Leidl S;Lehr S;Schwab G;	Significant weight loss after laparoscopic Nissen fundoplication	follow up < 5 years
19837071	Ng FH;Wong SY;Lam KF;Chu WM;Chan P;Ling YH;Kng C;Yuen WC;Lau YK;Kwan A;Wong BC;	Famotidine is inferior to pantoprazole in preventing recurrence of aspirin-related peptic ulcers or erosions	Not GERD population
18194508	Nojkov B;Rubenstein JH;Adlis SA;Shaw MJ;Saad R;Rai J;Weinman B;Chey WD;	The influence of co-morbid IBS and psychological distress on outcomes and quality of life following PPI therapy in patients with gastro-oesophageal reflux disease	follow up < 5 years

Pubmed ID	Author	Title	Reasons for rejection
16187198	Oda K;Iwakiri R;Hara M;Watanabe K;Danjo A;Shimoda R;Kikkawa A;Ootani A;Sakata H;Tsunada S;Fujimoto K;	Dysphagia associated with gastroesophageal reflux disease is improved by proton pump inhibitor	less than 100 patients and follow up < 5 years
17285394	Ogut F;Ersin S;Engin EZ;Kirazli T;Midilli R;Unsal G;Bor S;	The effect of laparoscopic Nissen fundoplication on laryngeal findings and voice quality	Crosssectional study of Atypical GERD; no intervention
17072714	Omura N;Kashiwagi H;Yano F;Tsuboi K;Ishibashi Y;Kawasaki N;Suzuki Y;Yanaga K;	Therapeutic effects of laparoscopic fundoplication for nonerosive gastroesophageal reflux disease	less than 100 patients and follow up < 5 years
18080197	Oridate N;Takeda H;Asaka M;Nishizawa N;Mesuda Y;Mori M;Furuta Y;Fukuda S;	Acid-suppression therapy offers varied laryngopharyngeal and esophageal symptom relief in laryngopharyngeal reflux patients	Atypical GERD - LPR - patients
18648738	Oridate N;Takeda H;Mesuda Y;Nishizawa N;Furuta Y;Asaka M;Fukuda S;	Evaluation of upper abdominal symptoms using the Frequency Scale for the Symptoms of Gastroesophageal Reflux Disease in patients with laryngopharyngeal reflux symptoms	Atypical GERD - LPR - patients
17296648	Orr WC;Craddock A;Goodrich S;	Acidic and non-acidic reflux during sleep under conditions of powerful acid suppression	med vs med < 4 weeks' duration
15679759	Orr WC;Goodrich S;Robert J;	The effect of acid suppression on sleep patterns and sleep-related gastro-oesophageal reflux.[see comment]	med vs med < 4 weeks' duration
19968010	Orr WC;Robert JJ;Houck JR;Giddens CL;Tawk MM;	The effect of acid suppression on upper airway anatomy and obstruction in patients with sleep apnea and gastroesophageal reflux disease	Medical cohort
19440812	Ozawa S;Kumai K;Higuchi K;Arakawa T;Kato M;Asaka M;Katada N;Kuwano H;Kitajima M;	Short-term and long-term outcome of endoluminal gastroplication for the treatment of GERD: the first multicenter trial in Japan	N<100; follow-up <5 year
16362470	Ozmen V;Oran ES;Gorgun E;Asoglu O;Igci A;Kecer M;Dizdaroglu F;	Histologic and clinical outcome after laparoscopic Nissen fundoplication for gastroesophageal reflux disease and Barrett's esophagus	Patients with Barretts Oespphagus
19960567	Pace F;Pallotta S;Manes G;de LA;Zentilin P;Russo L;Savarino V;Neri M;Grossi E;Cuomo R;	Outcome of nonerosive gastro-esophageal reflux disease patients with pathological acid exposure	no treatment of interest

Pubmed ID	Author	Title	Reasons for rejection
19875392	Pandeya N;Webb PM;Sadeghi S;Green AC;Whiteman DC;Australian CS;	Gastro-oesophageal reflux symptoms and the risks of oesophageal cancer: are the effects modified by smoking, NSAIDs or acid suppressants?	not all GERD pts
15995512	Park W;Hicks DM;Khandwala F;Richter JE;Abelson TI;Milstein C;Vaezi MF;	Laryngopharyngeal reflux: prospective cohort study evaluating optimal dose of proton-pump inhibitor therapy and pretherapy predictors of response	Pts w. atypical gerd
CN-00681	Peterson KA SWRDYDTKH;	The role of gastroesophageal reflux in exercise-triggered asthma: a randomized controlled trial	Atypical GERD; included in Asthma update
16531138	Pidoto RR;Fama' F;Giacobbe G;Gioffre' Florio MA;Cogliandolo A;	Quality of life and predictors of long-term outcome in patients undergoing open Nissen fundoplication for chronic gastroesophageal reflux	surgical cohort N<100
17180259	Pleskow D;Rothstein R;Kozarek R;Haber G;Gostout C;Lembo A;	Endoscopic full-thickness plication for the treatment of GERD: long-term multicenter results	NDO device excluded
18027032	Pleskow D;Rothstein R;Kozarek R;Haber G;Gostout C;Lo S;Hawes R;Lembo A;	Endoscopic full-thickness plication for the treatment of GERD: Five-year long-term multicenter results	NDO device excluded
16927137	Pratha V;Hogan DL;Lynn RB;Field B;Metz DC;	Intravenous pantoprazole as initial treatment in patients with gastroesophageal reflux disease and a history of erosive esophagitis: a randomized clinical trial	<4 wk Rx
16441474	Puhan MA;Guyatt GH;Armstrong D;Wiklund I;Fallone CA;Heels-Ansdell D;Degl'Innocenti A;Veldhuyzen van Zanten SJ;Tanser L;Barkun AN;Chiba N;Austin P;El-Dika S;Schunemann HJ;	Validation of a symptom diary for patients with gastro-oesophageal reflux disease	explores validity of a symptom diary as HRQL measurement instrument for GERD
19018854	Radajewski R;	Short-term symptom and quality-of-life comparison between laparoscopic Nissen and Toupet fundoplications	f/u<5yr for surgical study
19018854	Radajewski R;Hazebroek EJ;Berry H;Leibman S;Smith GS;	Short-term symptom and quality-of-life comparison between laparoscopic Nissen and Toupet fundoplications	follow up <5 years

Pubmed ID	Author	Title	Reasons for rejection
16553119	Rakita S;Villadolid D;Thomas A;Bloomston M;Albrink M;Goldin S;Rosemurgy A;	Laparoscopic Nissen fundoplication offers high patient satisfaction with relief of extraesophageal symptoms of gastroesophageal reflux disease	Pts w. atypical gerd
16454822	Rantanen TK;Rasanen JV;Sihvo EI;Ahotupa MO;Farkkila MA;Salo JA;	The impact of antireflux surgery on oxidative stress of esophageal mucosa caused by gastroesophageal reflux disease: 4-yr follow-up study	follow up <5 years
17156140	Rantanen TK;Sihvo EI;Rasanen JV;Salo JA;	Gastroesophageal reflux disease as a cause of death is increasing: analysis of fatal cases after medical and surgical treatment.[see comment]	no usable data
17943478	Rasanen JV;Sihvo EI;Rantanen TK;Ahotupa MO;Farkkila MA;Harjula A;Salo JA;	Gastroesophageal reflux patients' defective antioxidative capacity in the proximal esophageal mucosa before antireflux surgery and also after 4-year follow-up	N<100; follow up <5 years
17874274	Ravi N;Al-Sarraf N;Balfe P;Byrne PJ;Reynolds JV;	On-table endoscopy following laparoscopic fundoplication	follow up <5 years
18722223	Reichel O;Dressel H;Wiederanders K;Issing WJ;	Double-blind, placebo-controlled trial with esomeprazole for symptoms and signs associated with laryngopharyngeal reflux	Pts w. atypical gerd
19362552	Reimer C;	Proton-pump inhibitor therapy induces acid-related symptoms in healthy volunteers after withdrawal of therapy	not GERD patients
19362552	Reimer C;Sondergaard B;Hilsted L;Bytzer P;	Proton-pump inhibitor therapy induces acid-related symptoms in healthy volunteers after withdrawal of therapy.[see comment]	not population of interest, study looks at healthy subjects randomized to PPI or placebo
18293045	Reis GM;Savassi-Rocha PR;Nogueira AM;Lima MJ;de CS;Arantes V;Barros CA;Cancado OL;	Histological esophagitis before and after surgical treatment of morbid obesity (Capella technique): a prospective study	Gastric bypass for morbid obese with esophagitis
16238890	Remak E;Brown RE;Yuen C;Robinson A;	Cost-effectiveness comparison of current proton-pump inhibitors to treat gastro-oesophageal reflux disease in the UK	cost-effectiveness analysis
19888231	Richter JE;	Con: Impedance-pH testing does not commonly alter management of GERD. [Review] [22 refs]	not primary research, a commentary

Pubmed ID	Author	Title	Reasons for rejection
19370381	Riedl O;Gadenstatter M;Lechner W;Schwab G;Marker M;Ciovica R;	Preoperative lower esophageal sphincter manometry data neither impact manifestations of GERD nor outcome after laparoscopic Nissen fundoplication	f/u<5yr for surgical study
18584516	Rijnhart-De Jong HG;Draaisma WA;Smout AJ;Broeders IA;Gooszen HG;	The Visick score: a good measure for the overall effect of antireflux surgery?	no outcomes of interest
19797970	Rodriguez LA;Ruigomez A;Wallander MA;Johansson S;	Acid-suppressive drugs and community-acquired pneumonia	Pneumonia not considered atypical GERD
17054312	Roman S;Poncet G;Serraj I;Zerbib F;Boulez J;Mion F;	Characterization of reflux events after fundoplication using combined impedance-pH recording	follow up <5 years
16371737	Rossi M;Barreca M;de BN;Renzi C;Santi S;Gennai A;Bellini M;Costa F;Conio M;Marchi S;	Efficacy of Nissen fundoplication versus medical therapy in the regression of low-grade dysplasia in patients with Barrett esophagus: a prospective study.[see comment]	population: patients with Barrett esophagus and low-grade dysplasia
16952539	Rothstein R;Filipi C;Caca K;Pruitt R;Mergener K;Torquati A;Haber G;Chen Y;Chang K;Wong D;Deviere J;Pleskow D;Lightdale C;Ades A;Kozarek R;Richards W;Lembo A;	Endoscopic full-thickness plication for the treatment of gastroesophageal reflux disease: A randomized, sham-controlled trial.[see comment]	3 month FU
16952539	Rothstein R;Filipi C;Caca K;Pruitt R;Mergener K;Torquati A;Haber G;Chen Y;Chang K;Wong D;Deviere J;Pleskow D;Lightdale C;Ades A;Kozarek R;Richards W;Lembo A;	Endoscopic full-thickness plication for the treatment of gastroesophageal reflux disease: A randomized, sham-controlled trial	NDO device excluded
18320322	Sala E;Salminen P;Simberg S;Koskenvuo J;Ovaska J;	Laryngopharyngeal reflux disease treated with laparoscopic fundoplication	Pts w. atypical gerd
19736889	Salminen P;	The laparoscopic Nissen fundoplication--a better operation?. [Review] [33 refs]	review article
17450083	Salminen P;Sala E;Koskenvuo J;Karvonen J;Ovaska J;	Reflux laryngitis: a feasible indication for laparoscopic antireflux surgery?[see comment]	atypical GERD
17724407	Salyers WJ;Mansour A;El-Haddad B;Golbeck AL;Kallail KJ;	Lifestyle modification counseling in patients with gastroesophageal reflux disease	not relevant, article looks at lifestyle modifications for pts w/ gerd

Pubmed ID	Author	Title	Reasons for rejection
19900054	Sandbu R;Sundbom M;	Nationwide survey of long-term results of laparoscopic antireflux surgery in Sweden	f/u<5yr for surgical study
19848002	Sato K;Umeno H;Chitose S;Nakashima T;	Patterns of laryngopharyngeal and gastroesophageal reflux	Dx of atypical GERD
16032486	Schiefke I;Neumann S;Zabel-Langhennig A;Moessner J;Caca K;	Use of an endoscopic suturing device (the 'ESD') to treat patients with gastroesophageal reflux disease, after unsuccessful EndoCinch endoluminal gastroplication: another failure	endoscopic Suturing Device after faliure of EndoCinch
15731937	Schiefke I;Rogalski C;Zabel-Langhennig A;Witzigmann H;Mossner J;Hasenclever D;Caca K;	Are endoscopic antireflux therapies cost-effective compared with laparoscopic fundoplication?	cost-effectiveness analysis with no primary data
15731937	Schiefke I;Rogalski C;Zabel-Langhennig A;Witzigmann H;Mossner J;Hasenclever D;Caca K;	Are endoscopic antireflux therapies cost-effective compared with laparoscopic fundoplication?	Not primary study--cost effective comparison of endoscopic vs. surgery
15990817	Schilling D;Kiesslich R;Galle PR;Riemann JF;	Endoluminal therapy of GERD with a new endoscopic suturing device.[see comment]	surgical cohort; sample size <100 for KQ3
16642422	Schmitt C;Lightdale CJ;Hwang C;Hamelin B;	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	< 5 year fu
17227312	Schneider JH;Kramer KM;Konigsrainer A;Granderath FA;	The lower esophageal sphincter strength in patients with gastroesophageal reflux before and after laparoscopic Nissen fundoplication	< 5 year fu
18648896	Schneider JM;Brucher BL;Kuper M;Saemann K;Konigsrainer A;Schneider JH;	Multichannel intraluminal impedance measurement of gastroesophageal reflux in patients with different stages of morbid obesity	no treatment of interest
15586841	Schunemann HJ;Armstrong D;Degl'innocenti A;Wiklund I;Fallone CA;Tanser L;van Zanten SV;Heels-Ansdell D;El-Dika S;Chiba N;Barkun AN;Austin P;Guyatt GH;	A randomized multicenter trial to evaluate simple utility elicitation techniques in patients with gastroesophageal reflux disease	not relevant, study involves looking at ways to improve intruments measuring HRQL in GERD pts
18828350	Shahani S;Sawant P;Dabholkar P;	Rabeprazole plus domperidone: the answer for gastro-oesophageal reflux disease	non comparative study, <100 subjects, 4 weeks duration, no AE

Pubmed ID	Author	Title	Reasons for rejection
17985241	Shaheen NJ;Madanick RD;Alattar M;Morgan DR;Davis PH;Galanko JA;Spacek MB;Vaughn BV;	Gastroesophageal reflux disease as an etiology of sleep disturbance in subjects with insomnia and minimal reflux symptoms: a pilot study of prevalence and response to therapy	outcome not of interest
15726658	Shaheen NJ;Stuart E;Schmitz SM;Mitchell KL;Fried MW;Zacks S;Russo MW;Galanko J;Shrestha R;	Pantoprazole reduces the size of postbanding ulcers after variceal band ligation: a randomized, controlled trial	not GERD
17461474	Sharma B;Sharma M;Daga MK;Sachdev GK;Bondi E;	Effect of omeprazole and domperidone on adult asthmatics with gastroesophageal reflux	atypical GERD (this article is included in atypical GERD asthma update)
18356117	Sharma N;Agrawal A;Freeman J;Vela MF;Castell D;	An analysis of persistent symptoms in acid-suppressed patients undergoing impedance-pH monitoring.[see comment]	med cohort with no AE reported
19191851	Sharma P;Chey W;Hunt R;Laine L;Malfertheiner P;Wani S;	Endoscopy of the esophagus in gastroesophageal reflux disease: are we losing sight of symptoms? Another perspective	not primary research, a commentary
19888232	Shay S;	A balancing view: Impedance-pH testing in gerd-limited role for now, perhaps more helpful in the future. [Review] [14 refs]	not primary research, a commentary
19169148	Shim KN;Hong SJ;Sung JK;Park KS;Kim SE;Park HS;Kim YS;Lim SH;Kim CH;Park MJ;Yim JY;Cho KR;Kim D;Park SJ;Jee SR;Kim JI;Park JY;Song GA;Jung HY;Lee YC;Kim JG;Kim JJ;Kim N;Park SH;Jung HC;Chung IS;Study Group of Korean College of Helicobacter and Upper Gastr	Clinical spectrum of reflux esophagitis among 25,536 Koreans who underwent a health check-up: a nationwide multicenter prospective, endoscopy-based study	no treatment of interest
17211705	Shimatani T;Inoue M;Kuroiwa T;Moriwaki M;Xu J;Ikawa K;Morikawa N;Tazuma S;	Which has superior acid-suppressive effect, 10 mg omeprazole once daily or 20 mg famotidine twice daily? Effects of single or repeated administration in Japanese Helicobacter pylori-negative CYP2C19 extensive metabolizers	not population of interest

Pubmed ID	Author	Title	Reasons for rejection
16413249	Shimatani T;Inoue M;Kuroiwa T;Xu J;Mieno H;Nakamura M;Tazuma S;	Acid-suppressive effects of rabeprazole, omeprazole, and lansoprazole at reduced and standard doses: a crossover comparative study in homozygous extensive metabolizers of cytochrome P450 2C19	not population of interest, study compares PPI vs H2RA in healthy subjects with different metabolism genotypes
16778364	Shimizu Y;Dobashi K;Kobayashi S;Ohki I;Tokushima M;Kusano M;Kawamura O;Shimoyama Y;Utsugi M;Sunaga N;Ishizuka T;Mori M;	A proton pump inhibitor, lansoprazole, ameliorates asthma symptoms in asthmatic patients with gastroesophageal reflux disease	atypical GERD (this article is included in atypical GERD asthma update)
18794602	Smythe A;Troy GP;Ackroyd R;Bird NC;	Proton pump inhibitor influence on reflux in Barrett's oesophagus	100% Barrett's
16721220	Sontag SJ;Sonnenberg A;Schnell TG;Leya J;Metz A;	The long-term natural history of gastroesophageal reflux disease.[see comment]	no intervention
19438416	Spechler SJ;Barker PN;Silberg DG;	Clinical trial: intragastric acid control in patients who have Barrett's oesophagus--comparison of once- and twice-daily regimens of esomeprazole and lansoprazole	medical tx<4weeks
16713542	Spence GM;Watson DI;Jamiesion GG;Lally CJ;Devitt PG;	Single center prospective randomized trial of laparoscopic Nissen versus anterior 90 degrees fundoplication	follow-up < 5yrs
17229223	Stoltey J;Reeba H;Ullah N;Sabhaie P;Gerson L;	Does Barrett's oesophagus develop over time in patients with chronic gastro-oesophageal reflux disease?	no comparative Rx
15470328	Sugimoto M;Furuta T;Shirai N;Kajimura M;Hishida A;Sakurai M;Ohashi K;Ishizaki T;	Different dosage regimens of rabeprazole for nocturnal gastric acid inhibition in relation to cytochrome P450 2C19 genotype status	not population of interest, study looks to develop optimal dosage for rabeprazol in healthy subjects with different metabolism genotypes
16200654	Sundstrom A;Blomgren K;Alfredsson L;Wiholm BE;	Acid-suppressing drugs and gastroesophageal reflux disease as risk factors for acute pancreatitis--results from a Swedish Case-Control Study	pts w/ acute pancreatitis
18656731	Suurna MV;Welge J;Surdulescu V;Kushner J;Steward DL;	Randomized placebo-controlled trial of pantoprazole for daytime sleepiness in GERD and obstructive sleep disordered breathing	not GERD
16616347	Swoger J;Ponsky J;Hicks DM;Richter JE;Abelson TI;Milstein C;Qadeer MA;Vaezi MF;	Surgical fundoplication in laryngopharyngeal reflux unresponsive to aggressive acid suppression: a controlled study.[see comment]	atypical GERD

Pubmed ID	Author	Title	Reasons for rejection
15845561	Taghavi SA;Ghasedi M;Saberi-Firoozi M;izadeh-Naeeni M;Bagheri-Lankarani K;Kaviani MJ;Hamidpour L;	Symptom association probability and symptom sensitivity index: preferable but still suboptimal predictors of response to high dose omeprazole	< 5 year FU
16544080	Tharavej C;Hagen JA;Portale G;Hsieh CC;Gandamihardja TA;Lipham JC;Peters JH;DeMeester SR;Crookes PF;Bremner CG;DeMeester TR;	Bravo capsule induction of esophageal hypercontractility and chest pain	not relevant, not treatment for GERD, study looks at adverse effects of Bravo capsule, a monitoring system measuring esophageal acid exposure
CN-00726	Thompson SK CW;	Recurrent symptoms after fundoplication with a negative pH study--recurrent reflux or functional heartburn?	< 100 patients
18712573	Thompson SK;Cai W;Jamieson GG;Zhang AY;Myers JC;Parr ZE;Watson DI;Persson J;Holtmann G;Devitt PG;	Recurrent symptoms after fundoplication with a negative pH study--recurrent reflux or functional heartburn?	Association b/w heartburn and pt characteristics post fundoplicaiton
17468924	Thompson SK;Jamieson GG;Myers JC;Chin KF;Watson DI;Devitt PG;	Recurrent heartburn after laparoscopic fundoplication is not always recurrent reflux	N<100; follow-up <5 years
19597835	Tibbling L;Johansson M;Mjones AB;Franzen T;	Globus jugularis and dysphagia in patients with hiatus hernia	< 100 patients and FU < 5 yrs
17219292	Tierney B;Iqbal A;Haider M;Filipi C;	Effects of prior endoluminal gastroplication on subsequent laparoscopic Nissen fundoplication	only 6 pts
17556589	Tipnis NA;Rhee PL;Mittal RK;	Distension during gastroesophageal reflux: effects of acid inhibition and correlation with symptoms	effects of esomeprazole on Ger-induced distension of esophagus
15813832	Todd JA;Basu KK;de Caestecker JS;	Normalization of oesophageal pH does not guarantee control of duodenogastro-oesophageal reflux in Barrett's oesophagus	BE pts
16437281	Torquati A;Lutfi R;Khaitan L;Sharp KW;Richards WO;	Heller myotomy vs Heller myotomy plus Dor fundoplication: cost-utility analysis of a randomized trial	Pts w/ achalasia
16249975	Toruner M;Bektas M;Cetinkaya H;Soykan I;Ozden A;	The effect of rabeprazole alone or in combination with H2 receptor blocker on intragastric pH: a pilot study	not population of interest, study looks at PPI vs. PPI + H2RA in subjects with dyspectic sx
19397394	Tosato F;Monsellato I;Marano S;Leonardo G;Portale G;Bezzi M;	Functional evaluation at 1-year follow-up of laparoscopic Nissen-Rossetti fundoplication	1 yr fu

Pubmed ID	Author	Title	Reasons for rejection
19172353	Tsereteli Z;Sporn E;Astudillo JA;Miedema B;Eubanks WS;Thaler K;	Laparoscopic Nissen fundoplication is a good option in patients with abnormal esophageal motility	surgical study with <100 patients
15898520	Tucker LE;Blatt C;Richardson NL;Richardson DT;Cassat JD;Riechers TB;	Laparoscopic Nissen fundoplication in a community hospital: patient satisfaction survey.[see comment]	no outcomes of interest
17610010	Turkcapar A;Kepenekci I;Mahmoud H;Tuzuner A;	Laparoscopic fundoplication with prosthetic hiatal closure.[see comment][erratum appears in World J Surg. 2007 Nov;31(11):2168 Note: Turkcapar, Ahmet [added]; Mahmoud, Hatim [added]; Tuzuner, Acar [added]]	Comparison of hiatal closure methods with the same procedure (laparoscopic fundoplication) are not interventions of interest in this review
16899836	Tutuian R;Mainie I;Agrawal A;Adams D;Castell DO;	Nonacid reflux in patients with chronic cough on acid-suppressive therapy.[see comment]	association of cough and nonacid reflux
18445095	Tutuian R;Vela MF;Hill EG;Mainie I;Agrawal A;Castell DO;	Characteristics of symptomatic reflux episodes on Acid suppressive therapy	Not relevant--examines pt characteristics associated w/ symptomatic and non symptomatic reflux
16480404	Vakil N;Guda N;Partington S;	The effect of over-the-counter ranitidine 75 mg on night-time heartburn in patients with erosive oesophagitis on daily proton pump inhibitor maintenance therapy	med vs med < 4 weeks' duration
19150702	van Marrewijk CJ MSFGNMdWNMJvOMJJGDKJLR;	Effect and cost-effectiveness of step-up versus step-down treatment with antacids, H2-receptor antagonists, and proton pump inhibitors in patients with new onset dyspepsia (DIAMOND study): a primary-care-based randomised controlled trial	Dyspepsia is not disease of interest
17697200	van Zanten SV;Flook N;Talley NJ;Vakil N;Lauritsen K;Bolling-Sternevald E;Persson T;Bjorck E;Svedberg LE;STARS II Study Group;	One-week acid suppression trial in uninvestigated dyspepsia patients with epigastric pain or burning to predict response to 8 weeks' treatment with esomeprazole: a randomized, placebo-controlled study	Pts w dyspepsia
18996768	Varela JE;Hinojosa MW;Nguyen NT;	Laparoscopic fundoplication compared with laparoscopic gastric bypass in morbidly obese patients with gastroesophageal reflux disease	follow-up<5 years
17985190	Varga G;Kiraly A;Cseke L;Kalmar K;Horvath OP;	Effect of laparoscopic fundoplication on hypertensive lower esophageal sphincter associated with gastroesophageal reflux	surgical cohort N<100

Pubmed ID	Author	Title	Reasons for rejection
17066610	Victorzon M;Tolonen P;Vuorialho T;	Laparoscopic floppy Nissen fundoplication for gastro-oesophageal reflux disease is feasible as a day-case procedure	surgical cohort N<100
16769543	Vidal O;Lacy AM;Pera M;Valentini M;Bollo J;Lacima G;Grande L;	Long-term control of gastroesophageal reflux disease symptoms after laparoscopic Nissen-Rosetti fundoplication	follow-up<5 years
16393312	Vieth M;Kulig M;Leodolter A;Naucler E;Jaspersen D;Labenz J;Meyer-Sabellek W;Lind T;Willich S;Malfertheiner P;Stolte M;	Histological effects of esomeprazole therapy on the squamous epithelium of the distal oesophagus	no usable data
17760656	Violette A;Velanovich V;	Quality of life convergence of laparoscopic and open anti-reflux surgery for gastroesophageal reflux disease	f/u <5 y
18322871	von RD;Brey U;Riecken B;Caca K;	Endoscopic full-thickness plication (Plicator) with two serially placed implants improves esophagitis and reduces PPI use and esophageal acid exposure	NDO device excluded
18534586	von RD;Schiefke I;Fuchs KH;Raczynski S;Philipper M;Breithaupt W;Caca K;Neuhaus H;	Endoscopic full-thickness plication for the treatment of GERD by application of multiple Plicator implants: a multicenter study (with video).[see comment]	NDO device excluded
19440792	von RD;Schiefke I;Fuchs KH;Raczynski S;Philipper M;Breithaupt W;Caca K;Neuhaus H;	Endoscopic full-thickness plication for the treatment of gastroesophageal reflux disease using multiple Plicator implants: 12-month multicenter study results	NDO device excluded
19621668	Wada Y;Ito M;Takata S;Kitamura S;Takamura A;Tatsugami M;Imagawa S;Matsumoto Y;Tanaka S;Yoshihara M;Chayama K;	Little necessity of acid inhibition against proton pump inhibitor rebound effects and prior helicobacter pylori eradication therapy in gastric ulcer patients: a randomized prospective study	patients with gastric adenoma or early gastric cancer
17488137	Wahlqvist P;Guyatt GH;Armstrong D;Degl'innocenti A;Heels-Ansdell D;El-Dika S;Wiklund I;Fallone CA;Tanser L;Veldhuyzen van ZS;Austin P;Barkun AN;Chiba N;Schunemann HJ;	The Work Productivity and Activity Impairment Questionnaire for Patients with Gastroesophageal Reflux Disease (WPAI-GERD): responsiveness to change and English language validation	not relevant, primary objectives were test responsiveness of questionnaire in pts w/ gerd treated with PPI. No comparisons made.

Pubmed ID	Author	Title	Reasons for rejection
16498771	Walwaikar PP;Kulkarni SS;Bargaje RS;	Evaluation of new gastro-intestinal prokinetic (ENGIP-I) study	Med pre- and post trial, N<100
CN-00687	Wang R;	Burden of gastroesophageal reflux disease in Shanghai, China	no intervention
17270007	Warrington S;Baisley K;Lee D;Lomax K;Delemos B;Boyce M;Morocutti A;	Pharmacodynamic effects of single doses of rabeprazole 20 mg and pantoprazole 40 mg in patients with GERD and nocturnal heartburn	pharmacodynamic study
16643177	Watson DI;Jamieson GG;Bessell JR;Devitt PG;	Laparoscopic fundoplication in patients with an aperistaltic esophagus and gastroesophageal reflux	aperistaltic esophagus
18029886	Wehrli NE;Levine MS;Rubesin SE;Katzka DA;Laufer I;	Secondary achalasia and other esophageal motility disorders after laparoscopic Nissen fundoplication for gastroesophageal reflux disease	N<100
17827936	Weigt J;Monkemuller K;Peitz U;Malfertheiner P;	Multichannel intraluminal impedance and pH-metry for investigation of symptomatic gastroesophageal reflux disease	internvention not of interest
17309364	Wertheimer AI;Wilson JM;	Comparative drug effects: the case of GERD therapies	no details on intervention
16119436	Westbrook JI;Duggan AE;Duggan JM;Westbrook MT;	A 9 year prospective cohort study of endoscoped patients with upper gastrointestinal symptoms	non-specific dx of dyspepsia
17497194	Wieslaw T;Adam K;Artur B;Lech B;Krzysztof B;	Nissen fundoplication improves gastric myoelectrical activity characteristics and symptoms in gastroesophageal reflux patients: evaluation in transcutaneous electrogastrography	follow up < 5y
18070731	Wijnhoven BP;Watson DI;Devitt PG;Game PA;Jamieson GG;	Laparoscopic Nissen fundoplication with anterior versus posterior hiatal repair: long-term results of a randomized trial	no comparions of interest
16497615	Wiklund I;Carlsson R;Carlsson J;Glise H;	Psychological factors as a predictor of treatment response in patients with heartburn: a pooled analysis of clinical trials	secondary analysis
18479175	Wilder-Smith C;Backlund A;Eckerwall G;Lind T;Fjellman M;Rohss K;	Effect of increasing esomeprazole and pantoprazole doses on acid control in patients with symptoms of gastro-oesophageal reflux disease: a randomized, dose-response study	pharmacodynamic study
17327934	Wilder-Smith C;Lind T;Lundin C;Naucler E;Nilsson-Pieschl C;Rohss K;	Acid control with esomeprazole and lansoprazole: a comparative dose-response study	pharmacodynamic study

Pubmed ID	Author	Title	Reasons for rejection
19654570	Wilder-Smith CH;Wilder-Smith P;Kawakami-Wong H;Voronets J;Osann K;Lussi A;	Quantification of dental erosions in patients with GERD using optical coherence tomography before and after double-blind, randomized treatment with esomeprazole or placebo	no outcome of interest (dental erosion outcomes)
16025197	Wilkerson PM;Stratford J;Jones L;Sohanpal J;Booth MI;Dehn TC;	A poor response to proton pump inhibition is not a contraindication for laparoscopic antireflux surgery for gastro esophageal reflux disease	in Ip 2009 SR
18299944	Wong AS;Myers JC;Jamieson GG;	Esophageal pH profile following laparoscopic total fundoplication compared to anterior fundoplication	<100 pts @ 5 y f/u
16983477	Woodcock SA;Watson DI;Lally C;Archer S;Bessell JR;Booth M;Cade R;Cullingford GL;Devitt PG;Fletcher DR;Hurley J;Jamieson GG;Kiroff G;Martin CJ;Martin IJ;Nathanson LK;Windsor JA;International Society fir Disease of the Esophagus - Australasian Section;	Quality of life following laparoscopic anterior 90 degrees versus Nissen fundoplication: results from a multicenter randomized trial	f/u < 5 y
15711819	Wykypiel H;Gadenstaetter M;Klaus A;Klingler P;Wetscher GJ;	Nissen or partial posterior fundoplication: which antireflux procedure has a lower rate of side effects?	f/u < 5 y
18071793	Wykypiel H;Hugl B;Gadenstaetter M;Bonatti H;Bodner J;Wetscher GJ;	Laparoscopic partial posterior (Toupet) fundoplication improves esophageal bolus propagation on scintigraphy	<100 pts; f/u < 5 y
17623259	Yang H;Watson DI;Kelly J;Lally CJ;Myers JC;Jamieson GG;	Esophageal manometry and clinical outcome after laparoscopic Nissen fundoplication	no analysis of interest
19436275	Yang HB SBWSCHCWCW;	H. pylori eradication prevents the progression of gastric intestinal metaplasia in reflux esophagitis patients using long-term esomeprazole	No treatment of interest (triple therapy)
19102361	Yi CH;Chen CL;Kuo TB;Yang CC;	The effect of acid suppression on sleep and cardiac autonomic regulation in GERD	PPI vs placebo is excluded
19824113	Yoshikawa I;Nagato M;Yamasaki M;Kume K;Otsuki M;	Long-term treatment with proton pump inhibitor is associated with undesired weight gain	<100 patients
16960664	Youssef YK;Shekar N;Lutfi R;Richards WO;Torquati A;	Long-term evaluation of patient satisfaction and reflux symptoms after laparoscopic fundoplication with Collis gastroplasty	comparison not of interest

Pubmed ID	Author	Title	Reasons for rejection
16332481	Zaninotto G;Cassaro M;Pennelli G;Battaglia G;Farinati F;Ceolin M;Costantini M;Ruol A;Guirroli E;Rizzetto C;Portale G;Ancona E;Rugge M;	Barrett's epithelium after antireflux surgery.[see comment]	100% Barrett's
17619938	Zaninotto G;Portale G;Costantini M;Rizzetto C;Guirroli E;Ceolin M;Salvador R;Rampado S;Prandin O;Ruol A;Ancona E;	Long-term results (6-10 years) of laparoscopic fundoplication	patients with GERD mixed with patients with BE and Hiatal hernia, results are presented together
15580437	Zeman Z;Rozsa S;Tihanyi T;Tarko E;	Psychometric documentation of a quality-of-life questionnaire for patients undergoing antireflux surgery (QOLARS)	topic not of interest

II. Systematic reviews on extra-esophageal GERD

Pubmed ID	Author	Title	Reasons for rejection
16437694	Calabrese C;Fabbri A;Areni A;Scialpi C;Zahlane D;Di FG;	Asthma and gastroesophageal reflux disease: effect of long-term pantoprazole therapy	non-random selection
11182012	Coughlan JL;Gibson PG;Henry RL;	Medical treatment for reflux oesophagitis does not consistently improve asthma control: a systematic review.[see comment]. [Review] [44 refs]	SR has already been extracted
n/a	Gibson PG;Henry RL;Coughlan JL;	Gastro-oesophageal reflux treatment for asthma in adults and children.[update of Cochrane Database Syst Rev. 2000;(2):CD001496; PMID: 10796653]. [Review] [40 refs]	SR has already been included; this update search was conducted to add to this SR
17325553	Khoshoo V;Haydel R;	Effect of antireflux treatment on asthma exacerbations in nonatopic children	non-random; children
19274922	Sopo SM;Radzik D;Calvani M;	Does treatment with proton pump inhibitors for gastroesophageal reflux disease (GERD) improve asthma symptoms in children with asthma and GERD? A systematic review. [Review] [11 refs]	pediatric patients
16113133	Stordal K;Johannesdottir GB;Bentsen BS;Knudsen PK;Carlsen KC;Closs O;Handeland M;Holm HK;Sandvik L;	Acid suppression does not change respiratory symptoms in children with asthma and gastro-oesophageal reflux disease	pediatric patients and adoloscents
n/a	Susanto AD;Yanus F;Wiyono WH;Jusuf A;Lelosutan SAR;Prasetyo S;	Improved asthma symptoms and PEFR in moderate persistant asthma patients with GERD. The role of the proton pump inhibitor [Abstract]	conference proceedings, only abstract available
19357404	American Lung Association Asthma Clinical Research Center;Mastronarde JG;Anthonisen NR;Castro M;Holbrook JT;Leone FT;Teague WG;Wise RA;	Efficacy of esomeprazole for treatment of poorly controlled asthma.[see comment]	GERD dx not part of inclusion criteria--only 7% (29/402) of participants had GERD dx

III. Primary studies on PPI use and fracture risk

Pubmed ID	Author	Title	Reasons for rejection
19172761		Do PPIs have long-term side effects? Nexium and the other proton-pump inhibitors are great at reducing stomach acid, but that might have some unintended consequences	review
19885973		Proton pump inhibitors and fractures? Beware long-term use	unlikely to be a primary study
18797111	Iwakiri R;Fujimoto K;	Importance of vertebral fracture and body mass index in the pathogenesis of gastroesophageal reflux disease	review
18695170	Richards JB;Goltzman D;	Proton pump inhibitors: balancing the benefits and potential fracture risks	commentary
19931262	Targownik LE;Lix LM;Leung S;Leslie WD;	Proton-pump inhibitor use is not associated with osteoporosis or accelerated bone mineral density loss	no fracture outcomes
18703854	Yoshimura M;Nagahara A;Ohtaka K;Shimada Y;Asaoka D;Kurosawa A;Osada T;Kawabe M;Hojo M;Yoshizawa T;Watanabe S;	Presence of vertebral fractures is highly associated with hiatal hernia and reflux esophagitis in Japanese elderly people	not related to PPI use

First author: Anvari	**Year:** 2006	**UI: 16341568**

Modifying Factor(s): BMI

Study design: prospective cohort **Follow up duration:** 6 months Obese – 41.6 +/- 2.8 months Normal – 48.2 +/- 3.0 months	**Country:** Canada **Multicenter:** no	**Funding:** not reported

Interventions(s): Laparoscopic Nissen fundoplication

Primary outcome(s): symptoms score, esophageal manometry study, and pH study	**Other outcome(s):** (if reported)

Baseline characteristics:
GERD definition for the population included:
Age: 17-76 (normal - 43.9 +/- 1.5; obese 44.9 +/- 1.3)
Gender: normal - 55F, 15M; obese 55F, 15M
Race: not reported
BMI: normal – 24.2 +/- 0.2; obese – 38.4 +/- 0.5
Severity of symptoms: 6 symptoms scored 0-3: heartburn, regurgitation, epigastric or chest pain, epigastric fullness, dysphagia, cough
Duration of symptoms: not reported
Frequency of symptoms: 6 symptoms scored 0-4: same as above
Type of medications: PPI
Acid reflux (by pH study): yes. Abnormal: drop in pH < 4 off antireflux meds for 5 days
Abnormal manometry study: yes. Measured LES
Esophagitis by endoscopy: no

Significant baseline differences between GroupA and GroupB

Symptoms: GroupA (normal weight) and GroupB (obese) had similar preoperative reflux symptoms scores (38.8 +/- 1.8 vs 40.7 +/- 1.9)
EGD: not reported
EMS: basal baseline pressure was higher in GroupA as comparted to GroupB. 10.8+/-0.8 vs 6 +/- 0.6 (p<0.0001)
PH study: No difference. % time < pH 4. GroupA 7.5 +/- 0.7 vs GroupB 9.2 +/- 0.7
Hiatal hernia: not reported
Meds used in the groups: Not reported preoperatively

Other:

N enrolled per group:	GroupA: 70	GroupB: 70	
N completed per group:	GroupA: 70	GroupB: 69	

Outcomes (as reported in the Results)	**Results**		
	GroupA: *Normal (BMI<30)*	GroupB: *Obese (BMI >=35)*	Net difference (estimated)
Mean reflux score (off meds) after surgery (p < 0.0001)	38.79 +/- 1.8 to 4.87 +/- 0.69	40.69 +/- 1.89 to 12.41 +/- 1.46	Group A vs. B: -0.41 (95%CI -0.74, -0.07)
Decrease in pH exposure time (p < 0.0001)	7.51 +/- 0.66 to 1.08 +/- 0.14	9.20 +/- 1.89 to 0.74 +/- 0.15	Group A vs. B: 2.03 (95%CI -1.76, 5.82)

Augmentation in LES (p < 0.0001)	10.8 +/- 0.84 to 19.21 +/- 0.82	5.96 +/- 0.64 to 15.76 +/- 1.10	NS
Reflux score after 6 months (p < 0.0001)	4.87 +/- 0.69	12.41 +/- 1.46	
pH study after 6 months (not reported in on or off meds) (p = 0.0496)	1.08 +/- 0.69	0.74 +/- 0.15	
LES after surgery (p = 0.0065)	19.21 +/- 0.82	15.76 +/- 1.10	

Adverse Events: Morbidly obese patient – acute trans-hiatal herniation of the wrap on POD #1 requiring emergency laparoscopic repair

Quality Assessment:
Description of the biological plausibility for the hypothesis to be tested: yes
Description of inclusion /exclusion criteria and rationale: no
Documentation of how data were collected and analyzed (eg, blinding): yes/ some blinding when selecting matched controls
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): no
Participant drop-out percentage (>20%?): no. Not reported why one person in Group B did not complete the study.
Description of statistical methods in sufficient detail to be replicated: yes
Overall grade: C

Comments: After 6 months, the obese group had a significantly higher reflux score and lower LES pressure when compared to the normal weight group. Overall, both normal weight and obese patients had significant improvement in reflux score, pH exposure time, and LES pressure after anti-reflux surgery.

ND: no data

GERD data extraction form

Author: Anvari	**Yr**: 2006	**UI**: 17227922	**Questions addressed**: 1,3	**Extractor**: SI

Objective/Topic: to compare laparoscopic fundoplication with PPI in pts with well-controlled GERD

Study design: RCT	**Country/Setting**: Canada	**Funding**: government

Interventions(s): laparoscopic fundoplication	**Comparator(s)**: PPI tailored to individual patient

Primary outcome(s): gastroesophageal reflux score (GERSS)	**Other outcome(s)**: pH, endoscopy findings, QoL

Inclusion criteria: 18-70 y/o; PPI ≥1 yr; expected to be on PPI for another ≥2 yrs; symptom score <18 and VAS ≥70 (well-controlled); %acid reflux >4% at baseline; positive Bernstein test	**Exclusion criteria:** aperistaltic esophagus; severe cardiac, lung, hematologic , or other disease leading to unacceptable surgical risk; previous gastric, esophageal or antireflux surgery; malignancy within the past year
Symptoms (describe): VAS 82.2±10.6 in Med; 81.2±12.4 in Surg	**Hiatal hernia (specify whether considered and size used for exclusion)**:
EGD (performed or not and results): 18% esophagitis	**Esophagitis/stricture/Barrett's**: 5 pts Barrett's
pH study (performed or not and results): %time pH <4: 9.46±5.7 (SD) in Med; 10.33±11.51 in surg	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Yes, all responded
Esophageal manometric studies (performed or not and results): LES (mm): 6±4.6 in Med; 5.4±3.5 in Surg	

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B	
Blinding: No	Allocation concealment: Y (?)
Intention-to-treat: Yes	Method of Randomization: computer
Other comments: no adjustment for multiple comparisons, small sample sizes	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 42.9	N enrolled: 104
%Male: 53%	N completed: 96
Race: Not described	
BMI: nd	
Comments:	

GERD data extraction form

Results				
Primary outcome(s):,				
symptoms: VAS at 1 yr: med 73.5±19.7 (SD) vs. surg 89.2±13.5 (SD); diff -15.6 (P<0.0001); GERSS total : med 13.6±9.5 vs. surg 8.3±8.4 ; diff 5.3 (P=0.0020)				
Secondary outcome(s): SF-36 short form: PCS med 43.9±10.3 vs. surg 46.4±10.9, P=0.1308; MCS 51.5±9.1 vs 52.7±10.9, P=0.6114 SF-36 gen health domain med 66.4±23.6 vs. 75.4±23.2; P=0.0048 Data on EQ5D not extracted pH %time <4: less in surg, mean diff btw groups: 3.63 (P=0.0042)				
Comments:				

Compliance:

Adverse Events:
Laparoscopic Nissen Fundoplication • No intraoperative complications 0/52 (0%) • Deaths 0/52 (0%) • Dysphagia 4/52 (7.7%) • Postprandial bloating 7/52 (13.5%) • Dilation of the wrap 2/52 (3.8%) • Fever 2/52 (3.8%) • Delayed oral intake 3/52 (5.8%) • Abdominal pain 2/52 (3.8%) No adverse events with PPI

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Attwood	**Yr**: 2008	**UI**: 18709511	**Questions addressed**: 1, 2	**Extractor**: JC

Objective/Topic: Compare treatment outcome in patients with and without BE submitted to standardized laparoscopic antireflux surgery (LARS) or esomeprazole treatment

Study design: RCT	**Country/Setting**: European/multi-center	**Funding**: AstraZeneca

Interventions(s): maintenance medical treatment with esomeprazole 20 mg od for their disease. Medical treatment was started at 20 mg od but could be dose adjusted, not to exceed 20 mg bid.	**Comparator(s)**: laparoscopic antireflux surgery (LARS)-- performed within 3 months of randomization, but patients could be treated with esomeprazole up to 40 mg od while awaiting surgery

Primary outcome(s): Therapeutic outcomes for symptoms related to GERD as measured by the Gastrointestinal Symptom Rating Scale (GSRS questionnaire) and by investigator assessments after LARS in BE compared to non-BE patients.	**Other outcome(s)**:

Inclusion criteria: adults aged 18–70 years with confirmed GERD, with or without BE. The patients had to have a history of chronic reflux esophagitis (>6 months) or chronic symptomatic GERD (>6 months) with pathological 24-h pH metry, according to local standards, and a requirement for long-term acid suppressive therapy. All patients were required to have had pH monitoring and manometry within 12 months prior to randomization and all had to be considered suitable for both surgical treatment and for long-term management with a PPI (esomeprazole).

Additionally, patients had to be capable of completing quality-of-life questionnaires.

Exclusion criteria: Any patient who had a primary need for surgery (e.g., for paraesophageal hernia or failure of medical therapy to control symptoms adequately) was not eligible to be recruited.

Patients who required PPI treatment for diseases other than GERD were excluded from the study, as were those who had a history of esophageal, gastric, or duodenal surgery or who had other diseases that might have a negative impact on their subsequent treatment within the study.

Symptoms (describe): Symptoms related to GERD as well as other gastrointestinal (GI) symptoms including epigastric pain, flatulence, bloating, diarrhea, ability to vomit, and ability to belch were scored by use of the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire and by investigator assessments (the latter for ability to vomit and ability to belch).

Hiatal hernia (specify whether considered and size used for exclusion): Considered-not used for exclusion

EGD (performed or not and results): Performed and graded according to Los Angeles classification.

	LARS		Esomeprazole	
Grade	Non-BE	BE	Non-BE	BE
None	120	14	109	20
A	72	7	54	1
B	55	9	68	4
C	9	1	7	3
D	0	1	0	0

Esophagitis/stricture/Barrett's: See inclusion criteria: adults aged 18–70 years with confirmed GERD, with or without BE. For the purposes of the trial, BE was defined as intestinal metaplasia on biopsy of endoscopically apparent columnarization.

GERD data extraction form

pH study (performed or not and results): All patients were required to have had pH monitoring within 12 months prior to randomization (see inclusion criteria)

	LARS		Esomeprazole	
	Non-BE	BE	Non-BE	BE
% time pH <4 Median (P10/P90)	7.9 (2.0-21.4)	13.2 (3.6-46.8)	8.8 (2.5-22.8)	7.4 (1.1-38.6)

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Before randomization, the protocol mandated a 12-week run-in period, which allowed baseline recordings to be made and medical treatment with esomeprazole 40 mg od to facilitate healing of the esophagitis.

Esophageal manometric studies (performed or not and results): All patients were required to have had manometry within 12 months prior to randomization (see inclusion criteria). Results not described in this paper.

Other: After 12-week run-in, an investigational week was scheduled without therapy to allow endoscopy, assessment of esophagitis according to the Los Angeles classification, biopsy sampling, laboratory screening, and 24-h pH metry with manometry and symptom association probability (SAP).

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B	
Blinding: Not described	Allocation concealment: Not described
Intention-to-treat: Yes	Method of Randomization: Yes, randomized blocks of four to two parallel study arms
Other comments:	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: Mean-LARS (Non-BE: 45; BE: 47) Esomeprazole (Non-BE: 45; BE: 50)	N enrolled: 554 patients with chronic GERD, 60 patients were found to fulfill the given criteria for BE, of whom 28 were randomized to medical treatment and 32 to antireflux surgery
%Male: LARS (Non-BE: 66.8 ; BE: 87.5) Esomeprazole (Non-BE: 74.8 ; BE: 75.0)	N completed: Not described in this paper
Race: Not described	Dropouts/reasons: Not described in this paper
BMI: Mean-LARS (Non-BE: 27; BE: 28) Esomeprazole (Non-BE: 27; BE: 27)	Follow-up period: 3 years
Comments:	

GERD data extraction form

Results

Primary outcome(s):,

Ambulatory 24-h pH-metry 6-months post-op, Change in total acid exposure time from baseline (p=0.002)
LARS- 13.2%, to a median of 0.4%
Esomeprazole-7.4%, to a median of 4.9%

Therapeutic outcome assessed by GSRS-Mean Scores demonstrate normal values and no significant differences between BE and non-BE patients or between LARS and ESO

	LARS		Esomeprazole	
	Baseline	3 years	Baseline	3 years
Non BE				
Diarrhea	1.8	1.8	1.8	1.7
Indigestion	2.5	2.7	2.4	2.3
Constipation	1.7	1.6	1.6	1.6
Abdom pain	2.1	1.8	2.0	1.8
Reflux	1.9	1.2	1.7	1.7
BE				
Diarrhea	1.5	1.7	1.6	1.3
Indigestion	2.0	2.7	2.5	1.9
Constipation	1.6	1.8	1.6	1.4
Abdom pain	1.6	1.5	1.9	1.5
Reflux	1.5	1.3	1.7	1.3

Mean HRQL scores assessed by QOLRAD

	LARS		Esomeprazole	
	Baseline	3 years	Baseline	3 years
Non BE				
Emotional	6.4	6.9	6.4	6.6
Sleep	6.4	6.9	6.3	6.5
Food/drink	6.1	6.9	6.2	6.4
Physical/social	6.5	6.9	6.5	6.8
Vitality	6.2	6.9	6.2	6.5
BE				
Emotional	6.5	7.0	6.5	6.8
Sleep	6.5	7.0	6.5	6.8
Food/drink	6.5	6.9	6.2	6.5
Physical/social	6.7	6.9	6.5	6.7
Vitality	6.7	6.9	6.2	6.6

Side effects of a total fundoplication compared b/w BE and non-BE patients in the LARS group. BE and non-BE patients expressed similar profiles of obstructive and gas bloat-like complaints—with a trend observed towards less complaints in the BE group.
% without complaints

	Dysphagia		Flatulence	
	Baseline	3 years	Baseline	3 years
Non BE	80	90	51	33
BE	93	88	57	32

Secondary outcome(s):

Comments: #’s for side-effects estimated from graph

Compliance: In the patients with BE, 100% of operations were completed as a 360° Nissen fundoplication, compared to 98% in the patients who did not have BE. No conversions to open surgery—all procedures were completed laparoscopically. When the symptomatic and overall therapeutic outcomes were evaluated at 3 yrs--one treatment failure in BE pts submitted to LARS and three in those treated medically (ns).

Adverse Events: No apparent difference between the groups in postoperative complication rates for LARS (perioperative data described but post op data not described) There were no conversions to open surgery—all procedures were completed laparoscopically. **Postoperative hospital stay** (p=0.11) BE patients- 63% staying 3 days or longer non-BE- 47% staying 3 days or longer

Applicability: (narrow/wide): Wide	Comments: large, multinational, European trial representing a chronic GERD population in which no selection criteria have been made except for those defined in the protocol to regulate the enrollment.

GERD data extraction form

Author: Bardhan	Yr: 2007	UI: 17539986	Questions addressed: 1, 3	Extractor: SI

Objective/Topic: compare esomeprazole with pantoprazole in rates of complete remission

Study design: RCT	Country/Setting: Germany	Funding: ALTANA Pharma AG

Interventions(s): Pantoprazole 40 mg daily for 4, 8, or 12 wk; treated until complete remission (endoscopically proven resolution and symptom relief) or up to 12 wk, whichever comes first	Comparator(s): esomeprazole 40 mg daily for 4, 8, or 12 wk; treated until complete remission or up to 12 wk, whichever comes first

Primary outcome(s): complete remission rates	Other outcome(s): symptom improvement, resolution of esophageal lesions

Inclusion criteria: at least 18 years of age with endoscopically confirmed erosive esophagitis [Los Angeles (LA) classification A-D]	Exclusion criteria: non-erosive reflux, other GI diseases, other concomitant diseases like severe or unstable cardiovascular, pulmonary or endocrine disease, clinically significant renal or hepatic disease or dysfunction and hematologic disorder, marked obesity (BMI >35), malignant disease during the previous 5 y (except for successfully treated skin cancer), tendency to allergic reactions to drugs, alcohol, drug or medication abuse within the past year, abnormal laboratory parameters or vital signs, as well as severe psychiatric or neurological disorders. Pregnant or nursing women as well as women of child-bearing potential not using contraception were also excluded.
Symptoms (describe): baseline not described	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): y Grade A 49% Grade B 36.5% Grade C 10.3% Grade D 4.3%	Esophagitis/stricture/Barrett's: see EGD results
pH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) y

GERD data extraction form

Quality Assessment for RCTs: B/fair	
Blinding: pts were blinded	Allocation concealment: no
Intention-to-treat: yes	Method of Randomization: computer generated
Other comments: power calculation for non-inferiority trial; >20% not completed protocol	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 53.5	N enrolled: 582
%Male: 51	N completed: 418
Race: 98%	Dropouts/reasons: 71% protocol violation
BMI: 27	Follow-up period: up to 12 wk
Comments:	

Results

Primary outcome(s): complete remission rates at 12 wk (endoscopically proven resolution and symptom relief)

ITT	pantoprazole	76%	
	esomeprazole	76%	CI of the difference (-7, +infinity)
Per protocol	pantoprazole	93%	
	esomeprazole	90%	CI of the difference (-2.9, +infinity)

Secondary outcome(s):

endoscopic confirmed healing at 12 wk

ITT	pantoprazole	91%	
	esomeprazole	88%	CI of the difference (-1.75, 8.27)
Per protocol	pantoprazole	98%	
	esomeprazole	94%	CI of the difference (0.02, 7.27)

symptom relief at 12 wk

ITT	pantoprazole	79%	
	esomeprazole	77%	CI of the difference (-4.7, 8.8)
Per protocol	pantoprazole	95%	
	esomeprazole	92%	CI of the difference (-1.8, 7.9)

Comments:

Compliance:
72/582 discontinued study prematurely 10% (28/289) on pantoprazole and 15% (44/293) on esomeprazole

Serious adverse events:
7 patients developed 9 serious adverse events, 2 on pantoprazole (pneumonia and colon cancer) and 7 on esomeprazole (postoperative thrombosis, knee menisectomy, factor V Leiden mutation, nerve paralysis, cholecystitis, renal cell carcinoma and urinary incontinence). None were considered to be related to the study medication.
Adverse Events:
headache (7／582; 1.2%)
gastroenteritis (6／582; 1.0%)
bronchitis (5／582; 0.9%)

nasopharyngitis (4／582; 0.7%) diarrhea (3／582; 0.5%)

Applicability: (narrow/wide): narrow	Comments: no information on the participating centers

Author: Biertho	**Yr: 2006**	**UI: 16823657**	**Questions addressed:1,2**	**Extractor: DM**

Objective/Topic:
Evaluate the long-term effects of LNF on GERD symptoms as well as nonspecific GI symptoms.

Study design:	**Country/Setting:**	**Funding:**
Prospective cohort	Canada / University hospital	nd

Interventions(s):	**Comparator(s):**
laparoscopic Nissen fundoplication (LNF)	None

Primary outcome(s):	**Other outcome(s):**
GERD symptoms Score (for symptoms of heartburn, regurgitation, bloating, dysphagia, epigastric or retrosternal pain). Range:0-60 This questionnaire assessed for 4 GI symptoms: diarrhea, vomiting, constipation, and lack of appetite. Overall GI symptom score was an addition of individual symptom scores. Range: 0-48 A score > 12 for both scores was considered clinically significant. *Symptom Score: Each symptom was scored as a product of severity (0 = none, 3 = severe) and frequency (0 = none, 4 = daily), giving each symptom score a range of 0-12.*	

Inclusion criteria:
documented GERD

Exclusion criteria:
nd

Symptoms (describe):

GERD score	GI score	Vomiting score	Diarrhea score	Constipation score	Lack of appetite score
39.5 ± 15.4 *	7.7 ±8.0 (69.7)	2.2 ± 3.9 (32.6)	1.5 ±3.0 (26.6)	1.9 ± 3.6 (29.9)	2.1 ± 3.7 (31.3)

Hiatal hernia (specify whether considered and size used for exclusion):

Nd

EGD (performed or not and results):
nd

Esophagitis/stricture/Barrett's:
nd

PH study (performed or not and results):
nd

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
nd

Esophageal manometric studies (performed or not and results):
nd

Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: (C)
Comments: No comparators, high loss to follow-up, no reasons for loss of follow-up, eligibility criteria not defined well, statistical adjustments not made

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46 y	**N enrolled: 515**
%Male: 32%	**N completed: 277**
Race: nd	**Dropouts/reasons: nd**
BMI: nd	**Follow-up period: 5 years**
Comments:	

Results

Primary outcome(s):

Time	n	GERD score	GI score	Vomiting score	Diarrhea score	Constipation score	Lack of appetite score
Pre-op	515	39.5 ± 15.4 *	7.7 ± 8.0 *(69.7)	2.2 ± 3.9 *(32.6 #)	1.5 ± 3.0 (26.6#)	1.9 ± 3.6 (29.9)	2.1 ± 3.7 *(31.3)
6months	428	13.9 ± 13.2	4.8 ± 6.3 (56.3)	0.3 ± 1.5 (7.9)	1.5 ± 3.0 (26.6)	1.4 ± 3.0 (26.4)	1.6 ± 3.4 (20.8)
2years	288	16.5 ± 15.1	4.5 ± 6.4 (53.8)	0.3 ± 1.4 (6.6)	1.3 ± 3.0 (22.9)	1.6 ± 3.3 (29.8)	1.2 ± 3.0 (18.4)
5years	277	18.0 ± 16.7 *	5.3 ± 6.7 *(64.6)	0.4 ± 1.6 *(10.1#)	1.6 ± 3.0 (34.3#)	1.9 ± 3.5 (35.0)	1.4 ± 2.9 * (24.9)

Data are reported as mean ± SD (percentage of patients with GI symptoms score >0)

Of the 515 patients, 167 (32.4%) had a nonspecific GI symptoms score above 12 preoperatively (clinical significance) and above 51 (9.9%) at 5 years ($p < 0.05$).

In the group with no preoperative GI symptoms, a small but statistically significant increase in GI symptoms score occurred (0 preoperatively versus 2.9 at 5 years; $p < 0.05$). There was a significant increase in the symptom scores for ‘‘diarrhea,’’ ‘‘constipation,’’ and ‘‘lack of appetite’’ at 5 years ($p < 0.05$; Table 3). Out of 155 patients, 55 had a nonspecific GI symptoms score >0 at 5 years, but only 11 (7.1%) had a GI score >12 (clinically significant).

KQ2:
Patients with preoperative GI symptoms (GI symptoms score>0, n = 360) were defined as group 1 and they were compared to those with no preoperative GI complaints (group II, n = 155).

Treatment/Comparison:	
Potential modifying factor (references)	**Outcomes**

	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
Symptoms – Those with preoperative non-specific GI symptoms (diarrhea, vomiting, constipation, and lack of appetite) versus those without preoperative GI symptoms	Preoperative non-specific GI symptoms: No effect					

Secondary outcome(s):

Comments:

Compliance:

Adverse Events:

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Booth	**Yr: 2008**	**UI: 19248200**	**Questions addressed: 1,2**	**Extractor: DM**

Objective/Topic: Prospective randomized clinical trial of laparoscopic 360° (Nissen) fundoplication versus laparoscopic 270° posterior partial (Toupet) fundoplication in two separate groups of patients, divided according to whether they had normal and ineffective oesophageal motility before surgery.

Study design: RCT	**Country/Setting: United Kingdom / Hospital**	**Funding: nd**

Interventions(s): Laparoscopic Nissen fundoplication with a floppy 360° wrap	**Comparator(s):** Laparoscopic Toupet fundoplication with a posterior 270° wrap

Primary outcome(s): Symptoms as measured by prevalence of Heartburn, regurgitation and dysphagia as well as postoperative symptom severity scores for heartburn, regurgitation; DeMeester symptom scores, epigastric pain and bloating	**Other outcome(s):** Visick scores (modified Visick score ranging from 1 (excellent) to 4(poor)) Manometry pH studies

Inclusion criteria:
All patients aged between 18 and 80 years undergoing surgery for pH-proven symptomatic gastro-oesophageal reflux disease

Exclusion criteria:
1) history of previous oesophagogastric surgery
2) presence of a manometrically proven primary oesophageal motility disorder and pregnancy

Symptoms (describe):
Patient symptom information was obtained using a standardized questionnaire that included a DeMeester symptom score, details of duration of symptoms and medication taken for reflux symptoms. Dysphagia was scored from 0 (no dysphagia) to 3 (severe, with frequent, troublesome dysphagia for solids and liquids). Heartburn and regurgitation were also each scored from 0 (no symptoms) to 3 (severe, with frequent, troublesome symptoms).

Hiatal hernia (specify whether considered and size used for exclusion): no

Variable	Nissen (n=64)	Toupet (n=63)
Hiatal hernia	61%	51%

EGD (performed or not and results): Yes.
Endoscopic oesophagitis grade was scored using the classification of Savary and Miller.

Variable	**Nissen (n=64)**	**Toupet (n=63)**
Erosive oesophagitis	16%	16%
Barrett's oesophagus	5%	10%

Esophagitis/stricture/Barrett's:
See EGD results

PH study (performed or not and results): Yes.

Variable	**Nissen (n=64)**	**Toupet (n=63)**
Preoperative acid exposure time (% total)	6·9 (2·3–28·7)	6·3 (1·3–73·0)

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):

Variable	Nissen (n=64)	Toupet (n=63)
PPI use	92%	90%

Esophageal manometric studies (performed or not

Other:

and results): Yes

Variable	Nissen (n=64)	Toupet (n=63)
Ineffective motility	41%	41%
Lower Oesophageal Sphincter (LOS) pressure (mmHg)	9·9 (0–27)	10·0 (0–23)
LOS length (cm)	3·9 (2–6)	3·9 (2–5)

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B/acceptable	
Blinding: y (Only patients)	**Allocation concealment: Yes**
Intention-to-treat: nd	**Method of Randomization:** sealed envelope technique
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 44.8 yrs	**N enrolled: 127**
%Male: 66.2%	**N completed: 125, 121, 117 (6 weeks, 6 months, 1 year)**
Race: nd	**Dropouts/reasons: nd**
BMI: wt 80.9 kgs (51-120)	**Follow-up period: 1 year**
Comments: The randomization was done after stratifying into normal and ineffective esophageal motility groups, as measured by manometry. It was seen that esophageal motility was not a predictive factor in outcome after surgery, so only the results summarizing overall comparisons are extracted. The paper has data on comparison by esophageal motility groups	

Results

Primary outcome(s):
Symptoms: *All values are represented by n (%)*

Symptom	**pre-op**		**6 months**		**1 year**	
	Nissen (n=64)	**Toupet (n=63)**	**Nissen (n=64)**	**Toupet (n=63)**	**Nissen (n=64)**	**Toupet (n=63)**
Heartburn	60(94)	60(95)	17(28) *	13(22) *	14(24) *	14(24) *
Regurgitation	56(87)	57(90)	13(21) *	8(13) *	10(17) *	7(12) *
Dysphagia	30(47)	22(35)	21(34) *	12(20) *	16(27) *	5(9) * †
Chest pain on eating	14(22)	16(25)	17(28)	14(23)	13(22)	3(5) †
Epigastric pain	45(70)	45(71)	26(43) *	24(40) *	15(25) *	18(31) *
Bloating	46(72)	38(60)	17(28) *	10(17) *	11(19) *	6(10) *

**P < 0·001 versus preoperative values; †P = 0·018 versus Nissen (Fisher's exact test).*
DeMeester symptom scores: nd

Subgroup; KQ2

Preoperative symptoms in effective and ineffective oesophageal motility groups

	Effective (n=75)						Ineffective (n=52)					
	Mild		Moderate		Severe		Mild		Moderate		Severe	
Heartburn	5	(7)	16	(21)	50	(67)	3	(6)	9	(17)	38	(73)
Regurgitation	17	(23)	29	(39)	19	(25)	5	(10)	19	(37)	25	(48)*

Values in parentheses are percentages. *P = 0·014 vs. effective motility

Treatment/Comparison:	**Nissen**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Normal Esophageal motility	Dysphagia rates: no effect					

Treatment/Comparison:	**Toupet**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Normal Esophageal motility	Dysphagia rates: no effect					

Secondary outcome(s):

Visick Scores

Patient satisfaction with the outcome of surgery, expressed by Visick scores, was similar in the Nissen and Toupet groups, with 92 and 91 per cent of patients respectively reporting Visick grade 1 or 2 at 1 year after surgery.

Manometry

Postoperative LOS pressure characteristics were not significantly different from those before surgery in any group (Nissen 12·3 *versus* 9·9 mmHg; Toupet 10·5 *versus* 10·0 mmHg) In the ineffective motility group, the postoperative LOS pressure was significantly higher (10·5 *versus* 7·0 mmHg; $P < 0·001$).

pH studies

- Overall acid exposure times were lower in the Nissen than in the Toupet group (median 0·1 *versus* 0·4 per cent; $P = 0·036$).
- There were 8 surgical failures on pH criteria, 3 in the Nissen group (one with effective and two with ineffective motility before surgery) and 5 in the Toupet group (two with effective and three with ineffective motility before operation). Only 2 patients experienced significant symptoms requiring redo fundoplication.

Comments:

Compliance:

All patients had the assigned procedure. There were no conversions to open surgery.

GERD data extraction form

Adverse Events:
Three patients (two Nissen, one Toupet; 2·4 per cent overall) complained of severe postoperative dysphagia.
These symptoms were only measured at 6 months and 1 year, so I reported them under adverse events.

Symptoms	6 months n (%)		1 year n (%)	
	Nissen (n=61)	Toupet (n=60)	Nissen (n=59)	Toupet (n=58)
Postprandial fullness	54(89)	47(78)	37(63)	37(64)
Restriction in belching	33(54)	25(42)	26(44)	21(36)
Unable to belch	8(13)	3(5)	8(14)	3(5)
Increased flatus	55(90)	48(80)	44(75)	39(67)
Diarrhoea	9(15)	7(12)	4(7)	6(10)
Abdominal pain	11(18)	17(28)	13(22)	15(26)

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Bour	**Yr:** 2005	**UI:** 15801915	**Questions addressed:** 1 (med), 3	**Extractor:** SI

Objective/Topic: continuous vs. on demand therapy, rabeprazole 10 mg daily

Study design: RCT	**Country/Setting:** France	**Funding:** Janssen-Cilag, France

Interventions(s): rabeprazole 10 mg once daily	**Comparator(s):** rabeprazole 10 mg once daily on demand (recurrence of determining symptom at a level the patient judged to be incompatible with his/her well being should lead to start of treatment, continue until symptom has disappeared for 48 h)

Primary outcome(s): rate of symptom relief at 6 mo	**Other outcome(s):**

Inclusion criteria: symptom relief by rabeprazole 10 mg once daily after a 4-week selection phase; at least 18 y; relapse of GERD symptoms (Likert >2); frequent relapse (at least 2 treatments by MD in 12 mo prior to enrollment); non-erosive reflux disease (need positive 24-h pH monitoring); grade 1 or 2 (Savary Miller); endoscopy within past 2 y	**Exclusion criteria:** addicted to PPI or PPI dependent (relapsed in the 15 d following interruption of treatment)
Symptoms (describe): heartburn, acid regurgitation	**Hiatal hernia (specify whether considered and size used for exclusion):** not considered
EGD (performed or not and results): Yes; 62.5% with endoscopy in previous 2 y; no erosion (36%); Gr 1 (53%); Gr 2 (11.2%)	**Esophagitis/stricture/Barrett's:** excluded
PH study (performed or not and results): Yes **(details not provided)**	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** part of inclusion criteria
Esophageal manometric studies (performed or not and results): nd	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) yes

Quality Assessment for RCTs: B/acceptable	
Blinding: no, open-label study	**Allocation concealment: not reported**
Intention-to-treat: yes	**Method of Randomization: not reported**
Other comments:	

GERD data extraction form

Quality Assessment Non-RCTs:
Comments: no power analysis

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 49 y	**N enrolled:** 152
%Male: 54.6	**N completed:** 132 (discrepancy with below)
Race: nd	**Dropouts/reasons:** 23 (adv events, recurrence, lack of efficacy, withdrawal of consent, non-compliance, other)
BMI: 25.8	**Follow-up period:** 6 mo
Comments:	

Results
Primary outcome(s): % of pts with symptoms relief at 6 mo: continuous treatment, 86.4% (70/81) vs. on demand, 74.6% (53/71), P = 0.065 recurrence rate at the end of treatment: continuous treatment, 13.6% (11/81) vs. on demand, 21.1% (15/71), P = 0.065
Secondary outcome(s): QoL (net change between baseline and final, compared between groups): continuous 2.21±10.92 vs. on demand -0.85±12.94, P=0.034)
Comments:

Compliance: average number of tables consumed per day, continuous 0.96 (range 0.64 – 1.03) (67 pts analyzed) vs. on demand 0.31 (range 0.00 – 0.95) (55 pts analyzed), P<0.0001

Adverse Events: actual denominator not reported (all pts who had taken one study tablet) diarrhea (5.9%); bronchitis (5.2%); gastroenteritis (4.6%); cystitis (3.9%), and abdominal pain (3.2%)

Applicability: (wide/narrow): wide	**Comments:**

GERD data extraction form

Author: Brehant	**Yr: 2006**	**UI: 16504893**	**Questions addressed: KQ2; KQ3**	**Extractor: MC**

Objective/Topic:
to compare results and five-year surgical outcome of laparoscopic antireflux surgery (LARS) in patients younger than 65 years and elderly patients aged 65 years or older

Study design:	**Country/Setting:**	**Funding:**
Retrospective cohort study	France	No data

Interventions(s):	**Comparator(s):**
Laparoscopic antireflux surgery (LARS): complete 360-degree fundoplication in 1363 patients (50.8%) including Nissen fundoplication with division of the short gastric vessels in 752 patients (28%) and without division of the short gastric vessels in 611 patients (22.8%); partial posterior fundoplication in 1175 patients (44.8%); and partial anterior fundoplication in 146 patients (5.4%).	Age ≥65 years old (group 1) vs. age <65 years old (group 2)

Primary outcome(s):	**Other outcome(s):**
Outcome of surgery was assessed using Visick classification (grade 1 = no symptoms, grade 2 = minimal symptoms, no lifestyle changes, no need to see a physician; grade 3 = significant symptoms requiring lifestyle changes with a physician's help; grade 4 = symptoms as bad or worse than preoperatively).	

Inclusion criteria:	**Exclusion criteria:**
Patients underwent their first LARS. Indications for surgery were intractable or recurrent symptoms resulting from GERD after an adequate trial (3 months' minimum) of conservative treatment consisting of omeprazole; complications of reflux esophagitis, stricture, and Barrett's esophagus; or complications of large sliding or paraesophageal hiatal hernia	Patients with a second LARS for a relapse of GERD and patients with an initial open laparotomy antireflux surgery
Symptoms (describe): 94.5% heartburn and retrosternal pain	**Hiatal hernia (specify whether considered and size used for exclusion):** Paraesophageal hernia (P<0.0001 between groups)- Group 1 = 29% Group 2 = 9.6%
EGD (performed or not and results): 94.7% Peptic esophagitis, 75.7% peptic stenosis; 15.6% healthy mucosa	**Esophagitis/stricture/Barrett's:** Barrett's esophagus (P<0.0001 between groups)- Group 1 = 15.2% Group 2 = 9.5%
PH study (performed or not and results): 24-hr pH monitoring was performed in 57.6% patients, mostly showing pathologic findings.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No data
Esophageal manometric studies (performed or not and results): Performed in 68.9% patients – 13.2% normal, 47.6% inferior esophagus sphincter hypotony; 7.9% inferior esophagus sphincter	**Other:**

hypertony.	

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Not applicable

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: less than half patients had 5-year results; retrospective design

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
	X	

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: Group 1 = 70.4 (range, 65-94) Group 2 = 45.4 (range, 18-64)	**N enrolled:** Group 1 = 369 Group 2 = 2315
%Male: Group 1 = 39.5% Group 2 = 64.9%	**N completed:** Group 1 = 156 Group 2 = 1184
Race: no data	**Dropouts/reasons:** no 5-year data
BMI: no data	**Follow-up period:** 5 years
Comments: Elderly patients have a significantly higher American Society of Anesthesiologists (ASA) score than the nonelderly patients (2.48 versus 1.98; P<0.001). No significant differences between groups in main GERD symptoms.	

Results						
Treatment/Comparison:	**Laparoscopic antireflux surgery – 5 year results**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Age (≥65 vs. <65)	No effect				No effect	No effect
Primary outcome(s): Symptoms= dysphagia; Satisfaction=Visick grades (which is a functional outcome); Global success/Failure=recurrence						
Secondary outcome(s):						
Comments:						

Compliance:
No data

Adverse Events:

- The global mortality rate was 0.1% (n = 3). There was no mortality in group 1. Two patients had a gas embolism and one patient had an acute coronary syndrome.
- Postoperative complications (adopted from Table 2 of the article):

	Group 1 (n=369)		Group 2 (n=2315)		P value	Total (n=2684)
Pulmonary infection	9	(2.4%)	16	(0.7%)	0.005	25 (0.9%)
Wound infection	2	(0.5%)	12	(0.5%)	NS	14 (0.5%)
Pleural effusion	5	(1.4%)	7	(0.3%)	0.04	12 (0.4%)
Pneumothorax	0		6	(0.2%)	0.05	6 (0.2%)
Esophagus injury	3	(0.8%)	7	(0.3%)	NS	10 (0.4%)
Arterial hypertension	1	(0.3%)	5	(0.2%)	NS	6 (0.2%)
Acute coronary syndrome	1	(0.3%)	4	(0.2%)	NS	5 (0.2%)
Bleeding	2	(0.5%)	8	(0.3%)	NS	10 (0.4%)
Postoperative ileus	0		7	(0.3%)	NS	7 (0.3%)
Acute pancreatitis	0		1	(0.04%)	NS	1 (0.04%)
Subcutaneous emphysema	1	(0.3%)	2	(0.1%)	NS	3 (0.1%)
Pulmonary embolism	1	(0.3%)	6	(0.2%)	NS	7 (0.3%)
Pyrexia	0		7	(0.3%)	NS	7 (0.3%)
Others	3	(0.8%)	8	(0.3%)	NS	11 (0.4%)

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Broeders	Yr: 2009	UI: 19491839	Questions addressed: 2	Extractor: SI

Objective/Topic: to study the impact of preop reflux pattern on long-term outcome after Nissen fundoplication

Study design: retrospective cohort	Country/Setting: Netherlands	Funding: nd

Interventions(s): Nissen fundoplication	Comparator(s):

Primary outcome(s): reflux symptom	Other outcome(s): QoL

Inclusion criteria: had Nissen fundoplication for GERD refractory to acid suppressants; preop pathological reflux via pH study, had follow up subjective and objective outcomes	Exclusion criteria: incomplete 24-h pH study; physiologic acid exposure; incomplete follow up data
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion): y
EGD (performed or not and results): y; 64% esophagitis in bipositional; 45.6% in upright	Esophagitis/stricture/Barrett's: y
pH study (performed or not and results): y	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): did not respond
Esophageal manometric studies (performed or not and results): y	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) y

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: retrospective, no power analysis, no adjustment

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 43	N enrolled: 338
%Male: 62	N completed: 234

GERD data extraction form

Race: nd	Dropouts/reasons: did not meet inclusion criteria
BMI: 26.7	Follow-up period: 5 y
Comments:	

Results

Primary outcome(s): reflux symptom by Visick score	Visick I or II (resolved or improved)
Upright reflux (acid exposure >8.2% upright, normal (<3.5%) in supine)	86%
Supine reflux (normal (<8.2%) acid exposure upright, >3.5% in supine)	98%
Bipositional (upright(>8.2%) and supine (>3.5%))	95%

Secondary outcome(s):	QoL (VAS 0-100 mm) at 5 y
Upright reflux (n=81)	64 (est. from Fig 3 in paper)
Supine reflux (n=55)	60
Bipositional (n=98)	65

Secondary outcome(s):	using acid suppressants at 5 y
Upright reflux (n=81)	21% (est. from Fig 4 in paper)
Supine reflux (n=55)	11%
Bipositional (n=98)	18%

Secondary outcome(s): LES at 5 y: no significant difference compared to 3 mo after surgery in all 3 groups

Secondary outcome(s): acid exposure at 5 y: no significant difference compared to 3 mo after surgery in all 3 groups

Secondary outcome(s): surgical reintervention more common in bipositional reflux patients (20 vs. 8.9% for upright and 4.1% for supine)

Comments:

Treatment/Comparison:	Nissen fundoplication after 5 yr					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
reflux pattern	no effect	no effect	no effect		no effect	

Compliance:

Adverse Events:

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Cadiere	**Yr: 2008/2009**	**UI: 18071818 / 19288158**	**Questions addressed: KQ1**	**Extractor: DM**

Objective/Topic:

Study design:	**Country/Setting:**	**Funding:**
Prospective cohort	Belgium	

Interventions(s):	**Comparator(s):**
Transoral endoluminal fundoplication to restore the Gastroesophageal valve (GEV) using EsophyX device (EndoGastric Solutions, Inc., Redmond, WA, USA)	None

Primary outcome(s):	**Other outcome(s):**
The primary study endpoint was an improvement of ≥ 50% in GERD health-related quality-of-life (GERD-HRQL) score **Heartburn score** *The heartburn score was calculated by summing the responses to the first six questions of Gastroesophageal Reflux Disease HQRL questionnaire. Absent or rare heartburn (scores ≤ 2 to each of the six questions, or total score ≤ 12) was indicative of heartburn elimination.*	Percentage of time at pH < 4 *Abnormal: Acid exposure > 5.3% of time at pH < 4* Use of PPIs Tx success: No PPI use Patient satisfaction *At 12 months: Likert scale: ''very satisfied'', ''satisfied'', ''neutral'', ''unsatisfied'' or ''very unsatisfied''* *At 25 months: Likert scale: "very satisfied,'' ''satisfied,'' ''neutral,'' or ''dissatisfied.''* Global assessment: *"Cured": no more heartburn or regurgitation, eliminated esophagitis and hiatal hernia, and discontinued all usage of PPIs.* *"Improved": Reduced heartburn, esophagitis, or hiatal hernia and required occasional PPI therapy.*

Inclusion criteria:	**Exclusion criteria:**
Chronic symptomatic Gastroesophageal Reflux Disease ≥ 6 months, Esophagitis grade A–C, chronic PPI dependence ≥ 6 months with recurrence of symptoms upon PPI treatment cessation, deteriorated or absent GEV.	Significant esophageal motility disorder, esophageal pathology, dysphagia, with the addition of BMI ≥ 30 kg/m^2, irreducible hiatal hernia ≥ 3 cm, esophageal stricture, Barrett's esophagus, esophageal ulcer, delayed gastric emptying, and previously failed antireflux procedures.
Symptoms (describe): Heartburn: 17 (100%) Regurgitation: 13 (76%) GERD-HRQL score: Median 17 (range12–31)	**Hiatal hernia (specify whether considered and size used for exclusion):** n (%):13 (76%) patients Median size: 2 cm (range 1–3 cm)
EGD (performed or not and results): LA classification Grade A: 13 (76%) Grade B: 2 (12%) Grade C: 2 (12%)	**Esophagitis/stricture/Barrett's:**
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**

GERD data extraction form

Esophageal manometric studies (performed or not and results):	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: small sample, no comparator, >20% dropout at 2 years

Diagnostic Quality: A/rigorous		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: Median 34 years (range 23–58 years)	**N enrolled: 19**
%Male: 41%	**N completed: 17 at year 1, 14 at year 2**
Race: nd	**Dropouts/reasons:** **Year 1:** moderate preexisting esophageal stenosis (1), pre-op 6 cm hiatal hernia (1) **Year 2:** re-treatment (2), loss to follow up (1)
BMI: Median 22 kg/m^2 (18–31 kg/m^2)	**Follow-up period: Cadiere 2008 (12 months), Cadiere 2009 (median 25 months, range 24-27 months)**
Comments:	

Results

Primary outcome(s):

An improvement in the GERD-HRQL score of ≥ 50%:

12 months	25 months
9/17 patients (53%)	9/14 patients (64%)

Heartburn scores:

Baseline	25 months
range: 12-31	range: 0-13

Heartburn Scores ≤ 12 at 25 months (heartburn elimination): 13/14 patients (93%).

Median GERD-HRQL scores

Baseline	12 months	25 months
17	6 (-67%, p=0.02)	7 (-59%, p=0.004)

Secondary outcome(s):
Patient satisfaction:
12 months: 14 (82%) patients were “satisfied” or “very satisfied”
25 months: 12/14 (86%) patients were “satisfied”

Acid exposure
12 months:
1) Normal esophageal acid exposure (percentage time at pH<4 should be ≤ 5.3% of time): 10/16 (63%)
2) Median % of time with pH <4: 4.7%

25 months: no data

PPI use:
No PPI use at 12 months: 14/17 patients (82%)
No PPI use at 25 months: 10/14 patients (71%)

Global assessment:
Cured: 4/14 (29%)
Improved: 7/14 (50%)

Learning curve:
A learning curve was observed along with improvements in device performance. The median number of devices used per patient was one (1–4) and decreased from two for the first seven patients (1–4) to one for the last 10 patients. The median procedure time was 123 min (range 55–254 min) and decreased progressively from 132 min (88–254 min) for the first seven patients to 119 min (55–219 min) for the last 10 patients.

Comments:
The Likert scale for satisfaction changed between 1 year and 2 years. Global assessment was not done at 1 year.

Compliance:

Adverse Events:
No serious immediate adverse events: no bleeding, perforation, death

Other events at Week 2:

Adverse Event	Week 2 n (%)
Bloating	3 (18%)
Difficulty swallowing	2 (12%)
Epigastric	1 (6%)
Eructation	6 (35%)
Flatulence	1 (6%)
Pharynx	3 (18%)
Vomiting	1 (6%)

25 months:

Adverse Event	Month 25 n (%)
Difficulty swallowing without pain	1/14 (7%)
Daily bloating / gassy feelings	7 (50%)

Applicability: (narrow/wide): wide	**Comments:** Cadiere 2008 is the results from the 1 year follow up and Cadiere 2009 reports 2 year follow up

GERD data extraction form

Author: Cadiere	**Yr:** 2008	**UI:** 18443855	**Questions addressed:** 1,3	**Extractor:** JHL

Objective/Topic: To assess the safety and efficacy of Transoral Incisionless Fundoplication Using EsophyX in GERD patients

Study design: Prospective cohort	**Country/Setting:** Belgium, Germany and Italy	**Funding:** EndoGastric Solutions, Inc.

Interventions(s): EsophyX	**Comparator(s): NA**

Primary outcome(s): quality of life	**Other outcome(s):** PPI usage, esophageal acid exposure, hiatal hernia size, reflux esophagitis grade, valve Hill grade, and lower esophageal sphincter (LES) resting pressure

Inclusion criteria: patients 18 to 80 years of age with chronic GERD symptoms (>6 months) responsive to PPI therapy	**Exclusion criteria:** severe reflux esophagitis grade D in the Los Angeles classification; body mass index (BMI) ≥ 35 kg m^2; other esophageal diseases, including biopsy-proven Barrett's esophagus, esophageal motility disorders, esophageal stricture, esophageal ulcer, delayed gastric emptying, irreducible hiatal hernia of >2 cm; or previously failed antireflux surgery
Symptoms (describe): ND	**Hiatal hernia (specify whether considered and size used for exclusion):** Excluded patients with irreducible hiatal hernia of >2 cm
EGD (performed or not and results): performed	**Esophagitis/stricture/Barrett's:** Excluded patients with biopsy-proven Barrett's esophagus, and esophageal stricture Esophagitis n=70 (81%)
PH study (performed or not and results): performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No. Patients on PPIs n=86 (100%)
Esophageal manometric studies (performed or not and results): performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments:

GERD data extraction form

Diagnostic Quality: A/rigorous		
pH-metry		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 44 (19-73y)	**N enrolled:** 86
%Male: 66	**N completed:** 79
Race: ND	**Dropouts/reasons:** N=7 (8%): 2, esophageal injury exited the study immediately and later underwent a laparoscopic Nissen fundoplication (LNF); 2, exited the study before the 3-month follow-up; 1, failed to return at the 6-month follow-up visit but returned for the 12-month visit; and 3, unable to make their 12-month visit.
BMI: 25.2 (17.1-36.1)	**Follow-up period:** 12 months
Comments:	

Results

Primary outcome(s):
GERD health-related quality of life scores and symptoms

	Pre–TIF (n = 82)	12 Months Post-TIF (n = 79)
GERD-HRQL score		
Median (range) off PPIs	24 (11–38)	7 (0–30)
No. reduced by ≥50%		58 (73%)
No. eliminated		59 (75%)
Heartburn score		
No. reduced by ≥50%		59 (75%)
No. eliminated		61 (77%)
Regurgitation		
No. eliminated		34 (59%)

Secondary outcome(s):
Use of proton pump inhibitors (PPIs), histamine receptor antagonists (H2RA), and antacids before and after the EsophyX-TIF procedure

Medication	No.	Daily	Occasional	None
PPIs				
Pre-TIF	86	86 (100%)	0	0
6 Months	81	14 (17%)	11 (14%)	56 (69%)
12 Months	79	12 (15%)	13 (16%)	54 (68%)
H2RA				
Pre-TIF	86	3 (3%)	1 (1%)	82 (95%)
6 Months	81	0	1 (1%)	80 (99%)
12 Months	79	0	5 (6%)	74 (94%)
Antacids				
Pre-TIF	86	0	18 (21%)	68 (79%)
6 Months	81	0	21 (26%)	60 (74%)
12 Months	79	0	23 (29%)	56 (71%)
Any GERD medication				
Pre-TIF	86	86 (100%)	0	0
6 Months	81	14 (17%)	25 (31%)	42 (52%)
12 Months	79	12 (15%)	29 (37%)	38 (48%)

Esophageal pH monitoring

	Pre-TIF (n = 82)	12 Months Post-TIF (n = 71)
Percentage of time pH <4		
Median (range)	10 (3–67)	7 (0–22)
Median % reduction		33

p		0.02
Normalized		26 (37%)
Significantly reduced or normalized		43 (61%)
DeMeester score		
Median (range)	34 (11–222)	28 (1–76)
Median % reduction		24
p		<0.001

Resting pressure of the lower esophageal sphincter(LES): Significant improvement by 53% (p<0.001)

Comments:

Compliance: NA

Adverse Events:
Adverse events after the EsophyX-TIF procedure categorized by the MedDRA classification system and grouped by their duration

Adverse event	≤ Week	1 Week to 1 month	> 1 Month
Musculoskeletal pain	8 (9%)	8 (9%)	
Abdominal pain upper	8 (9%)	4 (5%)	1 (1%)
Pharyngolaryngeal pain	6 (7%)	1 (1%)	
Nausea	6 (7%)		1 (1%)
Epigastric pain	4 (5%)	2 (2%)	
Application site bleeding	5 (6%)		
Pyrexia	3 (4%)		
Dysphagia	3 (4%)		
Diarrhea	2 (2%)		

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Cai (Follow-up of Ludemann R BJS 2005; 92: 240-243 & Watson DI BJS 1999;86:123-130)	**Yr: 2008**	**UI: 18942055**	**Questions addressed: 1,3**	**Extractor: JHL**

Objective/Topic: Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180° partial fundoplication

Study design: RCT	**Country/Setting:** Australia	**Funding:** Gov (NHMRC – Australia)

Interventions(s): Laparoscopic total fundoplication	**Comparator(s):** Laparoscopic anterior 180° fundoplication

Primary outcome(s): • Heartburn • Dysphasia • Adverse events • Reintervention	**Other outcome(s):** • Overall outcome

Inclusion criteria: (Follow-up of Watson DI BJS 1999;86:123-130) All patients with proven GERD	**Exclusion criteria:** Patients had had a severe esophageal motility disorder (adynamic oesophagus or achalasia), required a concurrent abdominal procedure such as cholecystectomy, or had undergone previous antireflux surgery
Symptoms (describe): (Follow-up of Ludemann R BJS 2005; 92: 240-243) Heartburn 94% in both groups; Regurgitation 81% in Nissen and 77% in anterior fundoplication	**Hiatal hernia (specify whether considered and size used for exclusion):** 43% in the Nissen group and 50% of those undergoing anterior fundoplication
EGD (performed or not and results): ND	**Esophagitis/stricture/Barrett's:** 24% of Barretts in the Nissen group and 21% in anterior fundoplication group
PH study (performed or not and results): Acid pH <4 was 12.6 and 12.2% respectively	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): 83% Nissen and 82% anterior had normal peristalsis	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes described on the baseline paper

Quality Assessment for RCTs: B/acceptable	
Blinding: Yes (Follow-up of Ludemann R BJS 2005; 92: 240-243)	**Allocation concealment: NA**
Intention-to-treat: NA	**Method of Randomization: ND**
Other comments: No details of the method (described elsewhere)	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 55.9 y	**N enrolled: 184 (randomized, n=107)**
%Male: 70%	**N completed: 89**
Race: ND	**Dropouts/reasons:**

	Nissen (n=54)	Anterior fundoplication (n=53)
Loss to follow-up	2	2
Dementia	1	2
Died during follow-up	3	8

BMI: ND	**Follow-up period: 10y**
Comments:	

Results

Primary outcome(s):

- Outcomes at 10 years for heartburn

	Total fundoplication (n=48)	Anterior fundoplication (n=41)	*p*
Heartburn (yes/no question)	7 (15)	8 (20)	0·580*
Heartburn analogue score			
Mean	1.7	2.3	0·111†
0	28 (58)	16 (39)	
1–3	14 (29)	13 (32)	
4–6	2 (4)	9 (22)	
7–10	4 (8)	3 (7)	
Taking proton-pump inhibitors	9 (19)	11 (27)	0·448*

Values in parentheses are percentages. *Fisher's exact test;
†Mann–Whitney *U* test.

- Outcomes at 10 years for dysphagia

	Total fundoplication (n=48)	Anterior fundoplication (n=41)	*p*
Dysphagia for solids (yes/no)	25 (52)	14 (34)	0.133*
Dysphagia analogue score for liquids			
Mean	1.4	1.0	0.285†
0	28 (58)	30 (73)	
1–3	12 (25)	5 (12)	
4–6	6 (13)	4 (10)	
7–10	2 (4)	2 (5)	
Dysphagia analogue score for solids			
Mean	2.4	1.7	0·229†
0	20 (42)	22 (54)	
1–3	13 (27)	10 (24)	
4–6	12 (25)	8 (20)	
7–10	3 (6)	1 (2)	
Composite dysphagia score (mean)	12.0	7.8	0.121†

Values in parentheses are percentages. *Fisher's exact test;
†Mann–Whitney *U* test.

- Reintervention: "Ten patients (five in each group; 9.3 per cent of 107) underwent a revisional procedure between 6 months and 10 years after fundoplication."

Secondary outcome(s):

Overall outcome at 10 years

	Total fundoplication (n=48)	Anterior fundoplication (n=41)	*p*
Satisfied with outcome (yes/no)	45 (94)	38 (93)	1.000*
Mean analogue score of satisfaction	8.2	8.3	0.707†
Would choose operation again	43 (90)	40 (98)	0.212*

Values in parentheses are percentages. *Fisher's exact test;
†Mann–Whitney *U* test.

Comments:

Compliance: NA

Adverse Events:

	Total fundoplication (n=48)	Anterior fundoplication (n=41)	*p*

Abdominal bloating	14 (29)	19 (46)	0.124*
Able to relieve bloating	17 (35)	12 (29)	0.651*
Able to belch normally	24 (50)	27 (66)	0.141*

Values in parentheses are percentages. *Fisher's exact test.

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Calleja	Yr: 2005	UI: 15810621	Questions addressed: 2	Extractor: SI

Objective/Topic: H. Pylori as a modifying factor in the medical treatment of GERD

Study design: prospective cohort	Country/Setting: multicenter; Spain	Funding: Recordati Espana

Interventions(s): pantoprazole 40 mg qd for 8 wk; then 20 mg qd for 16 wk in those who responded	Comparator(s):

Primary outcome(s): symptom relief	Other outcome(s):

Inclusion criteria: clinical GERD; grade II or III Savary-Miller esophagitis	Exclusion criteria: indeterminate H. Pylori status; serious concomitant disease; use of antacids or prokinetics 10 days before the inception of treatment; lack of consent; impossible to follow up
Symptoms (describe): heartburn 98.3%; regurgitation 75.8%	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's: all grade II or III Savary-Miller esophagitis
pH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results): nd	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) y

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: no statistical adjustment; 21% drop out at 8 wk; univariate analysis only

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 52.3	N enrolled: 227

GERD data extraction form

%Male: 56.3	N completed: 179 at 8 wk; 144 had endoscopic healing and therefore received maintenance therapy and follow up at 24 wk
Race: nd	Dropouts/reasons: lost to follow up; did not have second endoscopy
BMI: 25.9	Follow-up period: 8 wk, 24 wk
Comments:	

Results

Primary outcome(s): GERD symptom relief assessed by GSRS
at 8 wk in pts

	Baseline	8 wk
H. pylori +	98.4%	40.3%
H. pylori -	98.2%	35.3% (P<0.05 compared to H. pylori +)

no statistical difference in the relief of symptom regarding gender (actual data not presented)

relapse of heartburn at 24 wk (in those who received maintenance treatment)

	24 wk
H. pylori +	6/59 (10.1%)
H. pylori -	24/85 (28%)

Secondary outcome(s): erosive esophagitis at 8 wk

H. pylori +	21.4%
H. pylori -	18.3% (NS)

Comments:

Compliance: good or very good in >95% of pts (not defined)

Adverse Events:
6.8% adverse events; most frequent was diarrhea.
“No drug interactions were reported.”

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Chen	**Yr:** 2005	**UI:**15918199	**Questions addressed:** 1, 3	**Extractor:** SI

Objective/Topic: compare esomeprazole with omeprazole in treatment of erosive esophagitis

Study design: RCT	**Country/Setting:** Taiwan	**Funding:** Research Foundation of Digestive Medicine, Taiwan

Interventions(s): esomeprazole 40 mg q am for 8 wk	**Comparator(s):** omeprazole 20 mg q am for 8 wk

Primary outcome(s): healing rate of erosive esophagitis	**Other outcome(s):**

Inclusion criteria: GERD symptoms ≥1 mo; endoscopy to confirm erosive esophagitis	**Exclusion criteria:** coexistence of healed or active peptic ulcer, GI malignancy, esophago-gastric surgical history, esophagitis from systemic diseases, infections, drugs, burn, radiotherapy or physical deformity, severe esophageal stricture that requires/anticipates dilatation, PPI treatment within 8 d prior to endoscopy, or using PPIs for >5 d in the last 28 d prior to endoscopy, H. Pylori eradication therapy within the last 28 d prior to randomization or any time during the study, using other antisecretory or prokinetic agents between endoscopy and randomization or at any time during the study, or with any investigational (non-approved) drug during the last 30 d prior to randomization.
Symptoms (describe): heartburn, acid regurgitation, epigastric/chest pain, belching, nausea, vomiting, and global well-being assessed based on VAS	**Hiatal hernia (specify whether considered and size used for exclusion):** nd
EGD (performed or not and results): y; LA grade A 54% B 29% C 8% D 8%	**Esophagitis/stricture/Barrett's:** see EGD results
PH study (performed or not and results): not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** nd
Esophageal manometric studies (performed or not and results): not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: C/Poor	
Blinding: y	**Allocation concealment: n**
Intention-to-treat: y	**Method of Randomization:** automated, randomization

	number, ratio in block of 4
Other comments: small sample size, no power calculation	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 54	N enrolled: 48
%Male: 79	N completed: 44
Race: Asians	Dropouts/reasons: 2 lost of follow up, 2 discontinued meds
BMI: wt: 69.6 Kg	Follow-up period: 8 wk; 2 refused repeat endoscopy at 8 wk, excluded from analysis
Comments: mean age 49.2 ± 3.7 in esomeprazole group; 59 ± 3.4 in omeprazole group; difference not statistically significant	

Results
Primary outcome(s): esophagitis healing rate per protocol analysis esomeprazole 16/22 (72.7%; 95%CI 49.8%, 89.3%); omeprazole 10/20 (50%; 95%CI 27.2%, 72.8%) ITT analysis esomeprazole 16/25 (76.4%; 95%CI 44.3%, 83.8%); omeprazole 10/22 (45.5%; 95%CI 22.7%, 68.3%) P=0.2481 OR 2.667 (95%CI 0.739, 9.63) P=0.2040
Secondary outcome(s): change in heartburn (VAS 0 (none) to 100 (most severe) see Table 2 in paper for other symptoms esomeprazole (n=22) -22.3 ± 2.1 omeprazole (n=22) -21.4 ± 2.2 P=0.5453
Comments:

Compliance: nd

Adverse Events: see table below (from paper)

Table 4 AE in studied patients 8 wk after esomeprazole or omeprazole (from paper)
treatment (ITT)

	Esomeprazole (n = 25) n (%)	Omeprazole (n = 23) n (%)	P
Patient with at least one AE	7 (28.0)	6 (26.1)	1.0000
Constipation	2 (8.0)	1 (4.4)	1.0000
Dry skin	1 (4.0)	3 (13.0)	0.3381
Diarrhea	1 (4.0)	1 (4.4)	1.0000
Headache	1 (4.0)	1 (4.4)	1.0000
Somnolence	1 (4.0)	1 (4.4)	1.0000
Cellulitis	0 (0.0)	1 (4.4)	0.4792
Bronchitis	0 (0.0)	1 (4.4)	0.4792

Applicability: (narrow/wide): narrow	**Comments:**

GERD data extraction form

Author: Chisholm	Yr: 2009	UI: 19259752	Questions addressed: 2	Extractor: WY

Objective/Topic:
To determine effect of BMI on post-op clinical outcomes

Study design:	Country/Setting:	Funding:
Cohort study, retrospective	Australia	Not “a commercial entity”

Interventions(s):	Comparator(s):
NA	NA

Primary outcome(s):	Other outcome(s):
See KQ2 table	

Inclusion criteria:	Exclusion criteria:
Had laparoscopic fundoplication in the Departments of Surgery at the University of Adelaide and Flinders University of South Australia, known pre-op height and weight, had been followed for at least 12 months after surgery	none
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): yes	Esophagitis/stricture/Barrett’s: no
PH study (performed or not and results): Yes for pts without typical GERD symptoms	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results): yes	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B
Comments: unclear statistical comparison among BMI groups, retrospective

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 50.3 (range: 16-91)	N enrolled: 481
%Male: 58%	N completed: 481

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Race: ND	Dropouts/reasons: NA
BMI: 103 pts (21%) normal BMI, 208 pts (43%) overweight, 115 pts (24%) obese, 55 pts (12%) morbidly obese	Follow-up period: 7.25 years (range 1-15 years)
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Treatment/Comparison:	Laparoscopic fundoplication					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
BMI/weight In 4 groups: normal weight (BMI<25); overweight (BMI 25–29.9); obese (BMI 30–34.9); and morbidly obese (BMI 35 or greater)	For overall, male only, female only, anterior partial fundoplication only, or nissen fundoplication only: Heartburn score4-10: no effect Abdominal bloating: no effect Ability to relieve bloating: no effect Ability to belch: no effect Solid dysphagia score 4-10: no effect For overall, male only, female only, or nissen fundoplication only: Liquid dysphagia score 4-10: no effect For anterior partial fundoplication only, Liquid dysphagia score 4-10: sig diff between groups, unclear which comparison				For overall, male only, female only, anterior partial fundoplication only, or nissen fundoplication only: Satisfaction score 0-6: no effect For overall, male only, anterior partial fundoplication only: Stated “made correct decision to have operation”: no effect For female only or nissen fundoplication only: Stated “made correct decision to have operation”: sig diff between groups, unclear which comparison	

GERD data extraction form

Compliance: NA

Adverse Events: NA

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Cibor	**Yr: 2006**	**UI: 17357336**	**Questions addressed: 1**	**Extractor: DM**

Objective/Topic:
Comparison of three models of pharmacological management using PPI: "on-demand" therapy, maintenance therapy and intermittent therapy in non-erosive reflux disease with mild complaints

Study design:	**Country/Setting:**	**Funding:**
RCT with 3 arms	Poland, University hospital	nd

Interventions(s):	**Comparator(s):**
Group 1, administered 30 mg lansoprazole as needed ("on-demand" therapy);	**Group 2**, receiving a daily maintenance dose of 15 mg of lansoprazole; **Group 3**, on a four-week course of lansoprazole at the dose of 30 mg, in case of recurrent symptoms (intermittent therapy).

Primary outcome(s):	**Other outcome(s):**
Intensity of symptoms The intensity of symptoms was rated each time using the Visual-Analog Scale (VAS; 0-10 points). Patients marked the intensity of symptoms with a vertical line on a 10-cm segment, with the left end described as "no symptoms at all" and the right end described as "insufferable symptoms". Each evaluation was marked by the patient on a separate evaluation form.	**Overall satisfaction derived from the therapy** By a 4-point Verbal Rating Scale (VRS; 0 – completely dissatisfied from treatment, 1 – rather dissatisfied, 2 – rather satisfied, 3 – completely satisfied).

Inclusion criteria:	**Exclusion criteria:**
Individuals with mild reflux symptoms (baseline intensity of symptoms 4 or less points on VAS) that would not affect daily activities of the patients and persisted for at least three months prior to the visit.	severe systemic diseases, esophagitis, esophageal ulceration, esophagostenosis, peptic ulcers, past surgery involving the upper gastrointestinal tract or reporting complaints, which in the opinion of the investigators might suggest the irritable bowel syndrome or dyspepsia, medication with any drugs that influence either the lower esophageal sphincter motility or gastric secretion and emptying.
Symptoms (describe): All patients were diagnosed based on reported heartburn, belching and regurgitation but data is not presented	**Hiatal hernia (specify whether considered and size used for exclusion):** nd
EGD (performed or not and results): yes	**Esophagitis/stricture/Barrett's:** nd
PH study (performed or not and results): nd	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Out of 65 enrolled patients, 60 showed a successful treatment outcome (*success being defined as no complaints whatsoever, or not more than one day with mild complaints, within 7 days immediately prior to the assessment*) after a four-week therapy with PPI (lansoprazole) administered at the dose of 30 mg once a day
Esophageal manometric studies (performed or	**Other:**

not and results): nd	

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B/rigorous;	
Blinding: no	**Allocation concealment: yes**
Intention-to-treat: Yes	**Method of Randomization:** not reported
Other comments: small sample size, no power calculation	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 48.3 yrs	**N enrolled:** 65
%Male: 50%	**N completed:** 60
Race: nd	**Dropouts/reasons:** no treatment response to initial 4 week therapy with lanzoprazole
BMI: nd	**Follow-up period:** 12 months
Comments:	

Results

Primary outcome(s):

Intensity of symptoms

Time	Group 1: "On-demand" treatment	Group 2: Daily treatment	Group 3: Intermittent treatment
Baseline	2.75±1.0	2.95±1.0	2.85±0.9
After 1 month	0.4±0.5	0.5±0.4	0.3±0.5
After 3 months	0.85±0.6	0.65±0.7	1.1±0.6
After 6 months	1.0±0.8	0.65±0.7	1.55±0.7
After 12 months	1.1±0.9	0.5±0.3	1.65±0.8

Significant differences (F-test, $p<0.05$) were found between

- group 1 vs 3 after 6 and 12 months of therapy
- group 2 vs 3 after 3, 6 and 12 months of maintenance therapy

Secondary outcome(s):

Overall satisfaction derived from the therapy

	Group 1 "On-demand" treatment	Group 2 Daily treatment	Group 3 Intermittent treatment

Time	VRS (mean ± SD)	% patients completely satisfied	VRS (mean ± SD)	% patients completely satisfied	VRS (mean ± SD)	% patients completely satisfied
After 3 months	2.85±0.48	90%	3±0	100%	2.85±0.48	90%
After 6 months	2.9±0.3	0.9	2.95±0.22	0.95	2.8±0.52	0.85
After 12 months	2.9±0.3	90%	2.95±0.22	95%	2.75±0.63	85%

intermittent therapy (Group 3) was significantly less effective as compared to “on-demand” therapy (Group 1) after 6 and 12 months of treatment ($p<0.05$), as well as in comparison to daily therapy (Group 2) after 3, 6 and 12 months ($p<0.05$).

Comments: pilot study;

Compliance:
In Group 1, the patients took the mean number of 0.3±0.3 PPI capsules per day.

Adverse Events:

Applicability: (narrow/wide): wide	**Comments:** pilot study with a small sample size, maybe underpowered to detect a small change in satisfaction scales

GERD data extraction form

Author: Cipolletta	**Yr: 2005**	**UI: 15868272**	**Questions addressed: KQ1**	**Extractor: DM**

Objective/Topic: Efficacy and safety of radiofrequency (RF) energy delivery (Stretta) to Lower esophageal sphincter (LES) in the treatment of selected GERD patients in Italy

Study design:	**Country/Setting:**	**Funding:**
Prospective cohort	Italy	nd

Interventions(s):	**Comparator(s):**
Radiofrequency (RF) energy delivery (Stretta) to Lower esophageal sphincter (LES) - Stretta system (Curon Medical, Sunnyvale, CA, USA)	none

Primary outcome(s):	**Other outcome(s):**
Heartburn - *6-point Likert scale ranging from no symptoms to incapacitating symptoms* **GERD health-related quality of life (HRQL)** - *6-point Likert scale for multiple different symptoms, each ranging from no symptoms to incapacitating symptoms. GERD HRQL improvement was evaluated as a continuous variable and as a dichotomous variable (responder vs nonresponder). A response was a >50% improvement compared with baseline values off medications.* **General quality of life** - *Medical Outcomes 36-item Short-Form Health Survey (SF-36)*	**Medication use** (using a questionnaire) **Esophageal acid exposure times** (using 24-hour pH monitoring) **Presence and grade of esophagitis** on EGD **Lower esophageal sphincter (LES) pressure**. **Adverse events** - patient questionnaires and a dedicated adverse event report form.

Inclusion criteria:	**Exclusion criteria:**
heartburn or acid regurgitation at least partially responsive to and requiring daily medications with PPIs; >18 years; 24-hour pH study (off medications) showing abnormal esophageal acid exposure (‡ 4%) or a DeMeester score of ≥ 14.7; esophageal manometry showing normal esophageal peristalsis and sphincter relaxation; esophagogastroduodenoscopy (EGD; on medications) showing no esophagitis or low-grade esophagitis (Los Angeles grade A–B);	Hiatal hernia ≥ 2 cm long, Barrett's esophagus, coagulation disorders, previous esophagogastric surgery, mechanical prostheses, prominent dysphagia, severe comorbidities, or unstable disorders, and significant ineffective esophageal motility associated with GERD.
Symptoms (describe): Mean heartburn score (off medications): 3.4 ± 0.9 Mean heartburn score (on medications): 2 ± 1.6 Mean HRQL score (off medications): 28 ± 7 Mean HRQL score (on medications): 18 ± 11 *Heartburn and heartburn-related quality of life scores (higher scores for worse symptoms)* Mean SF-36 mental (off medications): 43 ± 9 Mean SF-36 mental (on medications): 48 ± 6 Mean SF-36 physical (off medications): 40 ± 11 Mean SF-36 physical (on medications): 44 ± 11 *SF-36 physical score (higher scores for better function; U.S. general ''healthy group'' population mean = 55.3)*	**Hiatal hernia (specify whether considered and size used for exclusion):** < 2 cm hiatal hernia: 37.5%

GERD data extraction form

EGD (performed or not and results): LA classification Grade A : 7/32 (22%) Grade B: 1/32 (3%)	**Esophagitis/stricture/Barrett's:** See EGD
PH study (performed or not and results): Median 24-h pH: 11.7 (IQR: 7.7–16.6) *Percentage of time esophageal pH was <4 (off antisecretory* medications)	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** PPI use: 100%
Esophageal manometric studies (performed or not and results): Median LES pressure (mmHg) 16 (10–17.5)	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: small sample, no comparator group, LOCF method used for missing data; ITT analysis used but it is not a randomized study

Diagnostic Quality: A/rigorous		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46 ± 19	**N enrolled: 32**
%Male: 62.5%	**N completed: 32**
Race: nd	**Dropouts/reasons:**
BMI: nd	**Follow-up period: 12 months**
Comments:	

Results

Primary outcome(s):

Score	Baseline	Final (12 month)	Absolute change	p value
Mean heartburn score	3.4 ± 0.9	1.6 (1.2, 2.3)	-1.8 (-1.1, -2.3)	0.001
Mean HRQL score	28 ± 7	16 (12, 20)	-12 (-9, -16)	0.003
Mean SF-36 physical	40 ± 11	49 (45, 53)	9 (3, 12)	0.05
Mean SF-36 mental	43 ± 9	56 (52, 60)	13 (2, 16)	0.001

Secondary outcome(s):

Score	Baseline	Final (12 month)	Absolute change	p value
Median 24-h pH (% time pH < 4)	11.7	8.4 (4, 13.3)	-3.3 (-5.8, 4.9)	0.79
Median LES pressure (mmHg)	16	22 (10.5, 27)	6 (-4, 12)	0.72
Esophageal erosions n (%)	8 (25%)	4 (12.5%)	-12.50%	0.9
Daily PPI use n (%)	32 (100)	6 (19%)	-81%	0.9

Comments:

Compliance:

Adverse Events:
Major adverse event: prolonged gastroparesis (1 patient) – spontaneous resolution in 16 weeks.
Other adverse events - n(%):
Chest pain : 6 (19%)
Mild fever (<38°C): 4 (12.5%)
Transient nausea/vomiting: 1 (3%)
Transient dysphagia 1 (3%)

No Perforation , Mucosal lacerations , Bleeding requiring transfusion, or death

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Coron	**Yr**: 2008	**UI**: 18616516	**Questions addressed**: 1,2, 3	**Extractor**: JC

Objective/Topic: Compare radiofrequency (RF) and a PPI strategy in PPI-dependent patients by carrying out a prospective randomized trial

Study design: RCT	**Country/Setting**: Multi-European Country/2 secondary and 6 tertiary referral centers	**Funding**: in part by Societe Nationale Francaise de Gastro-Enterologie, INSERM and CHU of Nantes

Interventions(s): Stretta	**Comparator(s)**: Unspecified PPI therapy (e.g., omeprazole or rabeprazole 10 mg/day)

Primary outcome(s): At 6-month follow up, the possibility or not for the pt to stop or to decrease PPI use to <50% ED during the last 6 weeks	**Other outcome(s)**: Change in symptom scores (acid exposure and endoscopic assessments at 6 months and 1 year), quality of life scores (generic sf36 and REFLUX-QUAL HR-QOL)

Inclusion criteria: (1) age 18 years or older, (2) diagnosis of GERD established by either (i) 24-h oesophageal pH monitoring (performed off medications) showing an abnormal OAE (pH < 4 at least 4% of time) and/or (ii) an upper gastrointestinal (GI) endoscopy showing oesophagitis grade A or B in Los Angeles (LA) classification, (3) presence of typical symptoms of GERD (heartburn and/or regurgitation with at least three episodes of typical symptoms per week in the absence of PPI therapy), (4) adequate sx relief obtained with PPIs, but needing maintenance with at least standard dose	**Exclusion criteria:**. (i) presence of Barrett's oesophagus >3 cm and/or with dysplasia and/or previously treated; (ii) presence of hiatus hernia >3 cm; (iii) presence of oesophagitis grade C or D in LA classification; (iv) presence of oesophageal stricture or achalasia; (v) history of oesophageal or gastric surgery; (vi) presence of gastric or oesophageal varices; (vii) presence of a cardiac pacemaker or any other implanted electro-medical device; (viii) impossibility to stop an anticoagulant therapy or severe coagulopathy; (ix) any contraindication to general anaesthesia; (x) life threatening disorders with a life expectancy of <1 year; (xi) high alcoholic consumption (>60 g/day); (xii) morbid obesity (BMI over 35); (xiii) patients whose symptoms are dequately relieved with half-dose PPI regimen or intermittent acid suppression; and (xiv) inability to understand the study protocol or refusal tog ive informed consent.
Symptoms (describe): acid exposure and endoscopic assessments at 6 months and 1 year. All pts were invited to fill a standardized questionnaire that included questions about the intensity of typical reflux sx (heartburn, regurgitation and epigastric burning)	**Hiatal hernia (specify whether considered and size used for exclusion)**: Considered, pts excluded with presence of hiatus hernia >3 cm—see Exclusion Criteria.
EGD (performed or not and results): Performed Endoscopy PPI RF P-value Oesophagitis (%) 5 (25) 8 (35) 0.49 Oesophagitis A/B 3/2 4/4 – Short Barrett (%) 1 (5) 3 (13) 0.61 Hiatus hernia <=3 cm (%) 9 (45) 7 (30) 0.32	**Esophagitis/stricture/Barrett's**: See exclusion critieria: Excluded pts with presence of oesophagitis grade C or D in LA classification Excluded pts with presence of oesophageal stricture or achalasia Excluded pts with presence of Barrett's oesophagus >3 cm

	and/or with dysplasia and/or previously treated
pH study (performed or not and results): Performed –results not described in this paper 24 h pH-study (off therapy) PPI RF P-value Oesophageal acid exposure abnormal/normal (N) 17/3 23/0 0.09 Total time pH < 4 (%) Mean±SD 12.1±10.7 12.2 ±7.1 0.43	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** See inclusion and exclusion criteria. Run-in phase to determine effective dose (ED): INCLUDED - adequate symptom relief obtained with PPIs, but needing maintenance with at least standard dose EXCLUDED - patients whose symptoms are adequately relieved with half-dose PPI regimen or intermittent acid suppression Also Excluded: -previous tx for Barrett's -history of oesophageal or gastric surgery
Esophageal manometric studies (performed or not and results): Performed Manometry (off therapy) PPI RF P-value LOS pressure (mmHg) Mean±SD 14 ±8 13 ± 8 0.89	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: A	
Blinding: Yes	Allocation concealment: Yes—see Randomization below
Intention-to-treat: Yes	Method of Randomization: Treatment status was assigned using a centrally generated, stratified (by study site) block randomization. Each block consisted of four treatments (i.e., 2 RF and 2 PPI). If eligibility criteria were met, the PI in each centre was allowed to open the appropriate sealed envelope.
Other comments:	

Quality Assessment Non-RCTs: n/a
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: mean ± s.d Control 47+/-14; RF 50+/-10	N enrolled: 43 randomized
%Male: Control 70%; RF 70%	N completed: 34 completed 12 month follow up
Race: n/d	Dropouts/reasons: 4 lost to follow up, 1 tongue carcinoma, 1 grade C esophagitis, 1 withdrew due to car accident, 2 withdrew consent
BMI: mean ± s.d Control 27+/-4; RF 26+/-3	Follow-up period: 12 months
Comments:	

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Results

Primary outcome(s):

Primary endpoint outcome = proton pump inhibitor (PPI) discontinuation or reduction of at least 50% of baseline effective dose in patients on PPI regimen alone (control) and after radiofrequency therapy (RF)

	Intention-to-treat analysis (n = 43)			Per-protocol analysis (n = 36)		
	PPI (n = 20)	RF (n = 23)	p-value	PPI (n = 16)	RF (n = 20)	p-value
Stopped or decreased PPI use						
At 6 months* (%)	8 (40)	18 (78)	0.01	8 (50)	18 (90)	0.01
At 12 months** (%)	7 (35)	13 (56)	0.16	6 (38)	13 (65)	0.10
Completely stopped PPI therapy						
At 6 months* (%)	0 (0)	3 (13)	0.24	0 (0)	3 (15)	0.24
At 12 months** (%)	0 (0)	4 (17)	0.11	0 (0)	4 (20)	0.11

Intention-to-treat analysis.
* At 6 months, no data were available for 3 and 4 patients in the RF and in the control group, respectively.
**At 12 months, no data were available for 3 and 6 patients in the RF and in the control group, respectively.
Missing patients were considered as failures (inability to stop or decrease PPI therapy).

Secondary outcome(s): Per-protocol analysis only

	6 months			12 months		
	PPI (n = 16)	RF (n = 20)	p-value	PPI (n = 14)	RF (n = 20)	p-value
Dose of proton pump inhibitor Required to achieve symptom control* (mg) (mean ± s.d.)	30 ± 19	12 ± 11	0.01	37 ± 30	16 ± 14	0.05
Patients with double dose, N (%)	0 (63)	5 (25)	0.02	8 (57)	2 (10)	0.01
Patients on demand therapy, N (%)	9 (56)	6 (30)	0.11	8 (57)	7 (37)	0.25
Symptom frequency						
<3 per week	6 (40)	16 (80)	0.01	8 (62)	11 (69)	0.71
Symptom intensity						
Mean heartburn score*	2.4 ± 1.4	2.1 ± 1.0	0.47	2.3 ± 1.5	1.7 ± 0.8	0.42
Mean regurgitation score*	2.2 ± 1.3	1.3 ± 0.6	0.01	1.7 ± 1.4	1.2 ± 0.4	0.58
Mean epigastric burning score*	2.5 ± 1.4	1.4 ± 0.9	0.01	2.0 ± 1.4	1.3 ± 0.6	0.08
HR-QOL scores						
SF-36						
Mean standardized physical component*	49 ± 7	48 ± 8	0.81	40 ± 10	53 ± 7	0.50
Mean standardized mental component*	45 ± 12	51 ± 9	0.20	50 ±7	51 ± 9	0.30
REFLUX-QUAL						
Global score*	68 ± 21	75 ± 21	0.43	77 ± 18	84 ± 9	0.24
Oesophageal acid exposure abnormal/normal (N)	9/3	17/1	0.27	–	–	–

Total time pH <4 (%)*	8.8 ± 6.1	11.4 ± 6.3	0.11	–	–	–
Oesophagitis (%)	7 (54%)	10 (53%)	0.97	–	–	–
Oesophagitis A/B	5/1	5/5	–	–	–	–
Oesophagitis C/D	1/0	0/0	–	–	–	–

* Values are expressed as mean ± s.d.

Comments: In 6 month PPI group, Sx Frequency, Intensity and HR-QoL scores had one missing value.
In 6 month group, four pts in PPI arm and two in RF arm declined pH assessment
In 6 month group, three pts in PPI arm and one in RF arm declined endoscopy

Compliance: See Results above

Adverse Events: No severe complication occurred and both treatments were safe and well tolerated at a 1-year horizon.

Applicability: (narrow/wide): narrow	Comments: Small sample size of PPI dependent pts.

First author: Cowgill SM	**Year: : 2006**	**UI: 16986386**

Modifying Factor(s): Age

Study design: prospective cohort, not randomizd Follow up duration: mean follow up time (19 months (older group) vs 16 months (younger)	**Country: :** Florida, usa **Multicenter:** no	**Funding: :** undisclosed

Interventions(s): Nissen fundiplication undertaken in 109 patient s greater than 70 year and compared with 108 concurent patients less than 60 years old to determine outcome

Primary outcome(s): Laproscopuc fundiplication safely ameliorates symptoms of GERD in elderly patients with symptomatic outcomes superior to those seen in younger patients	**Other outcome(s):** At similar durations of follow-ip, reflux and dysphagia scores significantly improved forl older younger patients. 91% of patients 70 y and older versus 85 % of patients less than 60y would undergo Nissen fundiplic. again

Baseline characteristics:
GERD definition for the population included:: Group A: greater or equal to 70, Group B less than 60
Age: e.g., Group A: median 74, mean 75 +-4.7; Group B: median 45 mean 44+-9.2
Gender: Group A80% Male, Group B: 100% male
Race: n/a
BMI: n/a
Severity of symptoms: assessed by DeMeester score; Table 3 gives detailed pre-op symptom scoring
Duration of symptoms: group A 19months vs. group B 16 months
Frequency of symptoms: no reported
Type of medications: not reported
Acid reflux (by pH study): yes, data not reported
Abnormal manometry study: yes, data not reported
Esophagitis by endoscopy: not reported

Significant baseline differences between GroupA (older) vs Group B (younger)

Symptoms (DeMeester score): GroupA median 31 (mean 41+-34.1) vs. Group B median 39 (mean 60+-61.3)
Extensive comparison of preop symptoms made using symptoms scoring (table 3)

EGD: n/a
EMS: done but no data provided
PH study: done but no data provided
Hiatal hernia: e.g., No difference
Meds used in the groups: e.g., No difference in proportion of PPI used

Other: barium study esophagram done as well

N enrolled per group:	GroupA: nd	GroupB: nd
N completed per group:	GroupA: 108	GroupB: 108
Follow-up:	19 mo	16 mo

Outcomes (as reported in the Results)	**Results**		
Likert Scale 0= not bothersome, or never 10= very bothersome. Or always everytime I eat	GroupA: *greater or equal to 70*	GroupB: *younger than 60*	
Symptom improvement			
Dysphagia frequency	2.0	2.0	
Dysphagia severity	0	1.0	
Regurgitation severity Heartburn frequency Heartburn severity Choking frequency Choking severity Chest pain frequency Chest pain severity Good or excellent outcomes Would undergo laproscopic fundoplic again	0 0 0 0 0 0.8 0 82% 91%	1.0 2.0 1.0 0 1.0 2.0 0 81% 85%	

Adverse Events: ND (if reported, please add proportion of patients per adverse event; also separate to minor or major adverse events)

Quality Assessment:
Description of the biological plausibility for the hypothesis to be tested: yes
Description of inclusion /exclusion criteria and rationale: not well explained
Documentation of how data were collected and analyzed (eg, blinding): no
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): no
Participant drop-out percentage (>20%?): n/a
Description of statistical methods in sufficient detail to be replicated: yes
Overall grade: C

Comments: not matched controlled "a group of patients younger than 60 who concurrently underwent lap. Nissen were identified for comparative purposes; unclear how the comparative group was selected

ND: no data

GERD data extraction form

Author: Cowgill	**Yr: 2007**	**UI: 17879678**	**Questions addressed: 1,3**	**Extractor: DM**

Objective/Topic:
Evaluate the long-term (10 year) symptomatic outcomes and results of laparoscopic Nissen fundoplications on GERD

Study design:	**Country/Setting:**	**Funding:**
cohort	USA/Hospital	nd

Interventions(s):	**Comparator(s):**
laparoscopic Nissen fundoplication	None

Primary outcome(s):	**Other outcome(s):**
Subjective scoring of both frequency and severity of 1) dysphagia 2) chest pain 3) regurgitation 4) choking 5) heartburn on a Likert scale (0 = never/not bothersome to 10 = always/very bothersome).	

Inclusion criteria:	**Exclusion criteria:**
Anyone who had an undergone laparoscopic fundoplications and are prospectively followed for at least 10 years	
Symptoms (describe): **Pre-op Symptom score**	**Hiatal hernia (specify whether considered and size used for exclusion):** nd

Symptom	Frequency	Severity
Dysphagia	4.5±4.1	2.4±4
Chest pain	8.6±3.6	2.4±4.2
Regurgitation	6.5±3.8	7.5±4
Choking	4.4±3.8	5.5±3.9
Heartburn	8.7±3.2	10.8±3.1

EGD (performed or not and results): nd	**Esophagitis/stricture/Barrett's:** nd
PH study (performed or not and results): Nd	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** **Nd**
Esophageal manometric studies (performed or not and results): nd	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Y

GERD data extraction form

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C/Poor
Comments: Due to lack of data to assess internal or external validity, erroneous reporting of main outcome, inadequate statistical analysis,

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
		X (No data)

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 53 y (median)	**N enrolled: 829**
%Male: 44%	**N completed: 239**
Race: nd	**Dropouts/reasons: no follow up for 10 years**
BMI: nd	**Follow-up period: 11 years**
Comments:	

Results

Primary outcome(s):
Symptom score

Symptom	Time	Frequency	Severity
Dysphagia	Pre-op	4.5±4.1	2.4±4
	Post-op	1.2±1.5	1.2±2.9
	p-value	0.0071 *	<0.001 *
Chest pain	Pre-op	8.6±3.6	2.4±4.2
	Post-op	1.1±1.3	1.2±2.5
	p-value	<0.0001 *	<0.0001 *
Regurgitation	Pre-op	6.5±3.8	7.5±4
	Post-op	0.1±1.4	0.2±2.8
	p-value	<0.0001 *	<0.0001 *
Choking	Pre-op	4.4±3.8	5.5±3.9
	Post-op	1.1±1.4	1.2±2.9
	p-value	<0.0005 *	<0.0001 *
Heartburn	Pre-op	8.7±3.2	10.8±3.1
	Post-op	1.1±1.4	1.2±2.6
	p-value	<0.0001 *	<0.0001 *

* significantly different using Wilcoxon's matched pair test

Secondary outcome(s):

Comments:
The heartburn score shows a mean of 10.8 while according to the outcome measurement, the Likert scale only ranged from 0-10. This indicates either an erroneous reporting of outcome measurement or poor statistical analysis.

Compliance:

Adverse Events:

Total number of re-operative, or "redo," laparoscopic fundoplications were 28 (12%). 17/28 were operator related, as the initial laparoscopic fundoplications were done outside the authors' institution.

Thirty-five patients (15%) required conversion to open after attempted laparoscopic fundoplication.

No of "significant complications": 30 events (no of participants with these events not reported)

Inadvertent events and/or complications infrequently occurring

Postoperative Complication	Number
Early postoperative gastroesophageal junction edema	4
Dysrhythmia	3
Urinary retention	3
Gastric/esophageal leak	3
CO_2 pneumothorax	3
Gastrotomy/esophagotomy	2
Superficial wound infection	2
Postpneumonic empyema	1
Atelectasis	1
Urinary tract infection	1
Ileus	1
Fascial dehiscence	1
Intraabdominal abscess	1
Splenic laceration	1
Postoperative hemorrhage	1
Perioperative death	2

Applicability: (narrow/wide): wide	**Comments:**

KQ3 result template and instruction: Please use the primary GERD extraction form. Please indicate if adverse events were the primary outcome, and report the data in the adverse events section. Do make an attempt to extract n/N for the adverse event (subjects affected/total population at risk).

Author: Csendes	**Yr: 2005**	**UI: 16137596**	**Questions addressed: 3**	**Extractor: JC**

Objective/Topic: Show laparoscopic Nissen fundoplication performed by different surgical approach and to see clearly all structures of the esophagogastric junction, to keep fatty tissue away from plication, to construct a symmetrical plication, and to preserve intact both vagal trunks outside the wrap.

Study design: Case report	**Country/Setting: Not described**	**Funding: ND**

Interventions(s): Laparoscopic Nissen Fundoplication: The "Right Posterior" Approach	**Comparator(s): None**

Primary outcome(s): Effect of surgery (Visick score)	**Other outcome(s): Conversions and complications**

Inclusion criteria: Pts with severe GERD with incompetent lower esophageal sphincter	**Exclusion criteria: Not described**
Symptoms (describe): Used Visick score. I No symptoms, resolved II Mild occasional symptoms easily controlled, improved III Mild symptoms not controlled, unchanged IV Not improved, worsened	**Hiatal hernia (specify whether considered and size used for exclusion):** Not described for inclusion/exclusion criteria. There were three conversions due to a large fixed intrathoracic hiatal hernia (1.3%).
EGD (performed or not and results):	**Esophagitis/stricture/Barrett's: Not described.**
PH study (performed or not and results): 24-hr pH study performed—used to determine "incompetent lower esophageal sphincter" in inclusion criteria above	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): Not described**
Esophageal manometric studies (performed or not and results): Not described	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) n/a

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding: n/a	**Allocation concealment: n/a**
Intention-to-treat: n/a	**Method of Randomization: n/a**
Other comments:	

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Quality Assessment Non-RCTs: C:
Comments: Case report—limited description of study design methods.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: ND	**N enrolled: 225**
%Male: ND	**N completed: 225**
Race: ND	**Dropouts/reasons: n/a**
BMI: ND	**Follow-up period: 4-5 years**
Comments:	

Results
Primary outcome(s): late evaluation 4–5 years after surgery demonstrated Visick I and II results in 85% of the pts and Visick III and IV results in 15%.
Secondary outcome(s):
Comments:

Compliance: Three conversions due to a large fixed intrathoracic hiatal hernia (1.3%).

Adverse Events:
Three conversions due to large fixed intrathoracic hiatal hernia (3/225 = 1.3%).
No intraoperative complication e.g., esophageal or gastric perforation or splenectomy occurred.
No operative mortality and only one postoperative morbidity (1/225 = 0.4%) due to necrosis of lesser curve of stomach--repaired 6 days after operation via laparoscopic approach, with an uneventful recovery.

Applicability: (narrow/wide): Narrow	**Comments: Case report describing surgical procedure. Limited data on pt. characteristics.**

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Author: Cutler	Yr: 2010	UI: 19557517	Questions addressed: 3	Extractor: DM

Objective/Topic:
Assessment of efficacy and safety in patients with erosive GERD treated with rabeprazole 20 mg through week 8 of treatment

Study design:	Country/Setting:	Funding:
Open label interventional cohort study	USA/Community center	Industry (Eisai Inc, Woodcliff Lake, NJ, and Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ.)

Interventions(s):	Comparator(s):
Rabreprazole 20 mg	none

Primary outcome(s):	Other outcome(s):
Gastroesophageal reflux disease (GERD) symptom severity	Safety (assessed by recording patient- and investigator-reported adverse events) *An adverse event was considered serious if it was life-threatening, resulted in persistent or significant disability or incapacity, required prolonged hospitalization, required medical or surgical intervention, or resulted in a congenital anomaly or death*

Inclusion criteria:
Male and female patients aged ≥ 18 years; endoscopically confirmed erosive esophagitis (Hetzel-Dent Grade 2–4); understood English, had access to telephone for monitoring; able to comply with study protocols; signed informed consent.

Exclusion criteria:
Pregnancy or breastfeeding; known hypersensitivity to rabeprazole, substituted benzimidazoles, or drug product excipients; and use of any PPI within 7 days prior to administration of the study drug.

Symptoms (describe):

Symptom severity	Severe [n (%)]	Moderate [n (%)]	Mild [n (%)]	Absent [n (%)]
Daytime heartburn	479 (19.8)	970 (40.1)	653 (27)	314 (13)
Nighttime heartburn	689 (28.5)	780 (32.3)	475 (19.7)	472 (19.5)
Belching	365 (15.1)	731 (30.3)	708 (29.4)	606 (25.1)
Regurgitation	344 (14.2)	544 (22.5)	617 (25.5)	911 (37.7)
Dysphagia	247 (10.2)	394 (16.3)	447 (18.5)	1327 (54.9)

Hiatal hernia (specify whether considered and size used for exclusion):

EGD (performed or not and results):
Yes

Hetzel-Dent grade (% erosion)	n (%)
Grade 2 (2 – ≤ 10% erosion)	1,562 (62.3)
Grade 3 (10–50% erosion)	720 (28.7)
Grace 4 (>50% erosion)	225 (9.0)

Barrett's esophagus without dysplasia: 208 (8.2%)

Esophagitis/stricture/Barrett's:

See EGD result

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

PH study (performed or not and results): nd	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): nd	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 52.1 ± 14.9	**N enrolled: 2,579 patients (423 sites)**
%Male: 58.3%	**N completed: 2,579 patients (for safety-100%), 2,449 (efficacy-95%), 2,130 (completed study-82.6%)**
Race: n(%) Caucasian: 2,185 (85.5) African American : 146 (5.7) Hispanic: 179 (7.0) Oriental/Asian: 18 (0.7) Others: 28 (1.1)	**Dropouts/reasons: nd**
BMI: nd	**Follow-up period: 8 weeks**
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:
Adverse events: the safety population (N = 2,579) abdominal pain (1.2%), chest pain (0.5%), diarrhea (1.5%), dizziness (0.7%), dyspepsia (0.6%), belching (0.5%), headache (1.6%), nausea (1.0%), rash (0.5%), and upper respiratory tract infection (0.5%)

Compliance:

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Adverse Events:
Safety population N = 2,579

Serious adverse events :
Esophageal spasm - 1 (0.04%)
Death: 3 (0.1%) judged to be unrelated to the study drug)
Hospitalizations: 56 (2.2%). Commonly, serious cardiovascular adverse events, judged to be unrelated to study medication.
Other adverse events:
abdominal pain (1.2%), chest pain (0.5%), diarrhea (1.5%), dizziness (0.7%), dyspepsia (0.6%), belching (0.5%), headache (1.6%), nausea (1.0%), rash (0.5%), and upper respiratory tract infection (0.5%).

14.9% of patients reported ≥ 1 adverse event,
2.4% discontinued due to adverse events,
1.4% reported a serious adverse event.

Applicability: (narrow/wide): wide	**Comments: An acute (short term) adverse event in a large cohort of patients, as the time interval of study –8 weeks- is small.**

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

First author: D'Alessio	**Year:** 2005	**UI: 16137590**

Modifying Factor(s): BMI

Study design: Retrospective **Follow up duration:** 1, 3, and 12 months, then annually **Mean** 25.5 +/- 23.9 months	**Country:** USA **Multicenter:** no	**Funding:** not reported

Interventions(s): laparoscopic Nissen fundoplication

Primary outcome(s): Preoperative and postoperative symptom scores (frequency and severity of heartburn and dysphagia)	**Other outcome(s):** Overall result and willingness to repeat the operation

Baseline characteristics:
GERD definition for the population included:
(A= BMI < 25, B = BMI 25-30, C= BMI > 30)
Age: A: 52.3 +/- 17.5, B: 54.1 +/- 13.7, C: 50.2 +/- 13.5
Gender (% male): A: 42%, B: 48%, C: 44%
Race: not reported
BMI: A= BMI < 25, B = BMI 25-30, C= BMI > 30
Severity of symptoms: Demeester score – A: 43.6 +/- 53.5, B: 51.7 +/- 44, C: 51.0 +/- 35.4
Duration of symptoms: not reported
Frequency of symptoms: not reported
Type of medications: PPI, A: 86%, B: 91%, C: 87%
Acid reflux (by pH study): yes/not defined
Abnormal manometry study: yes/not defined
Esophagitis by endoscopy: yes, A: 37%, B: 33%, C: 42%

Significant baseline differences between GroupA and GroupB and GroupC

Symptoms: The preoperative Demeester score was lower in the normal weight patients; however, the score was highly elevated above normal in all groups.
EGD: No difference
EMS: No difference
PH study: No difference
Hiatal hernia: No difference (A: 58%, B: 67%, C: 63%)
Meds used in the groups: No difference in proportion of PPI used

Other: Only 3 of 62 patients in the obese group had a BMI > 35.

N enrolled per group:	GroupA: 79	GroupB: 116	GroupC: 62
N completed per group:	GroupA: 79	GroupB: 116	GroupC: 62

Outcomes (as reported in the Results)	**Results**		
	GroupA: *BMI < 25*	GroupB: *BMI 25 - 30*	GroupC: BMI > 30
Dysphagia symptom score (pre vs post surgery) (p < 0.001 in all groups)	3.7 to 2.3	4.8 to 2.2	5.2 to 2.2
Heartburn symptom score (pre vs post surgery) (p < 0.001 in all groups)	7.3 to 2.1	7.3 to 1.2	7.3 to 1.9

No significant difference in the mean postoperative dysphagia symptom scores	2.3	2.2	2.2
No significant difference in the mean postoperative heartburn symptom scores	2.1	1.2	1.9
Exacerbation of dysphagia post-op (p not significant)	14%	14%	22%
Patient satisfaction (p not significant)	73%	84%	82%
Willing to repeat the operation (p not significant)	82%	85%	89%

Adverse Events: 8% had complications overall. A: 10%, B: 7%, C: 8%

Minor:

Urinary retention – 5
Uncomplicated CO2 PTX – 4
Atelectasis – 4
UTI -2
Afib – 2
Superficial wound infection – 2
DVT -1
Ileus - 1
Pleural effusion - 1
Pneumonia -1

Major:

BMI 27 – Sm bowel perf requiring celiotomy and repair on POD #5

Quality Assessment: Description of the biological plausibility for the hypothesis to be tested: yes. Obesity is thought to contribute to poor outcomes by multiple factors. Longer OR time, difficulty of the procedure, etc. Description of inclusion /exclusion criteria and rationale: yes, but fair Documentation of how data were collected and analyzed (eg, blinding): yes Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): yes Participant drop-out percentage (>20%?): Not applicable. Description of statistical methods in sufficient detail to be replicated: yes **Overall grade: B**
Comments: One downside is the follow-up time.

ND: no data

GERD data extraction form

Author: Dallemagne	Yr: 2006	UI: 16333553	Questions addressed: 1,3	Extractor: JHL

Objective/Topic: To investigate the results for laparoscopic antireflux surgery after 10 years

Study design: Cohort study	Country/Setting: Belgium	Funding: ND

Interventions(s): Laparoscopic antireflux surgery • Nissen fundoplication	**Comparator(s):** • Toupet procedure

Primary outcome(s): • Symptoms (heartburn, regurgitation, dyspagia, chest pain, nauseam belching, abdominal distension, and flatulence)	**Other outcome(s):** Gastrointestinal Quality of Life (GIQLI)

Inclusion criteria: Patients underwent laparoscopic antireflux surgery by a single surgeon in 1993	**Exclusion criteria:**
Symptoms (describe): Heartburn (100%), Regurgitations (54%), Dysphagia (8%), Atypical symptoms (40%)	**Hiatal hernia (specify whether considered and size used for exclusion):** Hiatal hernia (n=71)
EGD (performed or not and results): Performed for all the patients	**Esophagitis/stricture/Barrett's:** Esophagitis using the Savary-Miller classification; grade 1 esophagitis (n=12), grade 2 (n=67), grade 3 (n=6) Barrett's esophagus (n=15)
PH study (performed or not and results): Performed for 60 patients; Abnormal DeMeester values (n=53), normal scores (n=7)	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): Performed for 99 patients Lower esophageal sphincter (LES) • Residual pressure (> 6 mmHg); 19 patients • Residual pressure (< 6 mmHg); 80 patients Esophageal motility • Normal esophageal peristalsis; 73 patients • Impaired esophageal peristalsis; 26 patients	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

No

"The choice between the two fundoplications was based on the results of esophageal manometry and perioperative anatomic factors such as the size and shape of the gastric fundus. Therefore, a partial wrap was chosen because of severe motility disorders (n = 14) or a normotonic LES (n = 9), or because of a small gastric fundus (n = 8), which was found in one young patient who did not undergo a preoperative manometry."

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B/acceptable
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A/rigorous (gastrointestinal endoscopy, pH monitoring, standard esophageal manometry, upper gastrointestinal		

series)

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 52y	**N enrolled: 100**
%Male: 62%	**N completed: 86**
Race: ND	**Dropouts/reasons:** death (n=7, not related to surgery), revision surgery (n=4), lost to follow-up (n=3)
BMI: ND	**Follow-up period: 10 y**
Comments:	

Results

Primary outcome(s):

- Heartburn relief at 5 years: 98% after Nissen, 86% after Toupet
- Recurrence-free of significant reflux proportions at 10 years: 93.3% after Nissen, 81.8% after Toupet
- Heartburn, regurgitation, and dysphasia scores 5 years after laparoscopic fundoplication

	Toupet (n =28) 5 years n (%)	Nissen (n = 58) 5 years n (%)	
Heartburn (score)			
None (0)	18 (64.2)	44 (75.8)	NS
Occasional (1)	6 (21.4)	13 (22.4)	
Moderate, therapy (2)	4 (14.2)	1 (1.7)	
Severe, constant (3)	0	0	
Regurgitations (score)			
None (0)	20 (71.4)	51 (88)	NS
Occasional (meal) (1)	8 (28.5)	7 (12) 0	
Moderate (supine) (2)	0	0	
Severe, constant (3)	0	0	
Dysphagia (score)			
None (0)	18 (64.2)	36 (62)	NS
Occasional, coarse food (1)	10 (35.7)	19 (32.7)	
Cleared with liquids (2)	0	3 (5.1)	
Severe, solids and liquids (3)	0	0	

- Heartburn scores at 10 years

	Toupet (n =20) 10 years n (%)	Nissen (n = 49) 10 years n (%)
Heartburn (score)		
None (0)	13 (65)	35 (71.4)
Occasional (1)	5 (25)	13 (26.5)
Moderate, therapy (2)	2 (10)	1 (2)
Severe, constant (3)	0	0

- Heartburn score for 65 patients who completed the 5- and 10- year follow-up studies

Nissen (n=45)				Toupet (n=20)			
5 years		10 years		5 years		10 years	
Score	n	Score	n	Score	n	Score	n
0	35	0	28	0	14	0	12
		1	6			1	2
		2	1				
1	9	0	3	1	4	0	1
		1	6			1	3
2	1	1	1	2	2	2	2
3	0	0	0	3	0	0	0

Secondary outcome(s):

- "The GIQLI scores at 10 years were significantly better than the preoperative scores of the patients under medical therapy with proton pump inhibitors….The mean GIQLI score was 115.5 ± 20.75 for the Nissen group and 108.5 ± 27.9 for the Toupet group (nonsignificant difference)….the scores of GERD patients receiving PPI medical therapy (96.4 ± 10.2, p = 0.01 vs Toupet, p = 0.0001 vs Nissen)."

GERD data extraction form

Comments:

Compliance: NA

Adverse Events:

No conversion to open surgery

Deaths

- Nissen fundopl. – 6/68
- Toupet fundopl. – 1/32

Redo

- Nissen fundopl. – 1/68
- Toupet fundopl. – 3/32

	Toupet		Nissen	
	5 years (n=28) n (%)	10 years (n=20) n (%)	5 years (n=58) n (%)	10 years (n=49) n (%)
Dysphagia (score)				
None (0)	18 (64.2)	15 (75)	36 (62)	38 (77.5)
Occasional, coarse food (1)	10 (35.7)	5 (25)	19 (32.7)	10 (20.4)
Cleared with liquids (2)	0	0	3 (5.1)	1 (2)
Severe, solids and liquids (3)	0	0	0	0
Gaz (score)				
None (0)	0	5 (25)	4 (6.8)	17 (34.6)
Occasional (1)	10 (35.7)	9 (45)	19 (32.7)	16 (32.6)
Frequently (2)	14 (50)	2 (10)	27 (46.5)	12 (24.4)
Continuously (3)	4 (14.2)	4 (20)	8 (13.7)	4 (8.1)
Abdominal bloating				
None (0)	6 (21.4)	6 (30)	17 (29.3)	9 (18.3)
Occasional (1)	11 (39.2)	5 (25)	24 (41.3)	16 (32.6)
Frequently (2)	8 (28.5)	4 (20)	9 (15.5)	9 (19.3)
Continuously (3)	3 (10.7)	5 (25)	8 (13.7)	15 (30.6)

Applicability: (narrow/wide): Wide	**Comments:**

Author: Davies	**Yr:** 2008	**UI:** 18366242	**Questions addressed:** 3	**Extractor: DM**

Objective/Topic:
To assess the safety profile of Esomeprazole

Study design:	**Country/Setting:**	**Funding:**
Observational – prescription event monitoring	United Kingdom	Organization conducting the study is a charity receiving donations from pharmaceutical companies

Interventions(s):	**Comparator(s):**
Esomeprazole	none

Primary outcome(s):	**Other outcome(s):**
Incident densities for reported events: first report of an event per 1000 patient months of exposure (PME) ID for events in first month of treatment (ID_1) ID for events in 2-6 month of treatment (ID_2) *Event: Any new diagnosis, any reason for referral to a consultant or admission to a hospital, any unexpected deterioration (or improvement) in a concurrent illness, any suspected adverse drug reaction, any alteration of clinical importance in laboratory values or any other complaint which was considered of sufficient importance to enter in to the patient's notes*	Number of Type A events (Pharmacologically important): N_A *If the difference between the value of ($ID_1 - ID_2$) and lower 99% CI level for that difference is > 0, then the event is Type A event* ID for events over course of treatment (ID_A)

Inclusion criteria:	**Exclusion criteria:**
All patients prescribed esomeprazole between Sep 2000 and Apr 2001	
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):**
EGD (performed or not and results):	**Esophagitis/stricture/Barrett's:**
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results):	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**

Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: median 56 y	**N enrolled: 31886**
%Male: 46.1	**N completed: 11595**
Race:	**Dropouts/reasons:**
BMI:	**Follow-up period:**
Comments:	

Results

Primary outcome(s):

Event	**N_1**	**N_2**	**ID_1**	**ID_2**
Diarrhoea	67	50	7.52	1.99
Nausea/vomiting	64	51	7.19	2.03
Pain abdomen	64	55	7.19	2.19
Dyspepsia	58	89	6.51	3.54
Headache/Migraine	47	43	5.28	1.71
Higher respiratory tract infection	40	92	4.49	3.66
Lower respiratory tract infection	40	71	4.49	2.82
Intolerance	30	24	3.37	0.95
Malaise/lassitude	29	17	3.26	0.68
Pain joint	24	41	2.69	1.63

No of events in first month of treatment (N_1); No of events in 2-6 month of treatment (N_2);
ID for events in first month of treatment (ID_1); ID for events in 2-6 month of treatment (ID_2)

Secondary outcome(s):

Event	**ID_1-ID_2 (99%CI)**	**N_A**	**ID_A**
Diarrhoea	5.53 (3.06,8.01)	153	2.65
Nausea/vomiting	5.16 (2.73,7.58)	132	2.28
Pain abdomen	5 (2.56,7.43)	153	2.65
Dyspepsia	2.97 (0.57,5.38)	218	3.77
Headache/Migraine	3.57 (1.47,5.66)	119	2.06
Higher respiratory tract infection	0.83 (-1.25,2.91)	188	3.25
Lower respiratory tract infection	1.67 (-0.36,3.69)	164	2.84
Intolerance	2.41 (0.75, 4.07)	62	1.07
Malaise/lassitude	2.58 (0.97,4.19)	71	1.23
Pain joint	1.06 (-0.5,2.62)	110	1.9

N_A: Number of Type A events (Pharmacologically important): N_A, ID for events over course of treatment (ID_A)

Comments:

Compliance:

Adverse Events:
119 events reported as suspected adverse drug reactions (ADRs) for 87 patients (0.75%) 223 deaths reported during the total observation period. No deaths were ascribed by the physicians to esomeprazole

Applicability: (narrow/wide): wide	**Comments:**

KQ3 result template and instruction: Please use the primary GERD extraction form. Please indicate if adverse events were the primary outcome, and report the data in the adverse events section. Do make an attempt to extract n/N for the adverse event (subjects affected/total population at risk).

Author: del Genio	**Yr: 2007**	**UI: 17426906**	**Questions addressed: 3**	**Extractor: JC**

Objective/Topic: Addresses technical details of antireflux technique (Laparoscopic Nissen-Rossetti fundoplication) adopted w/o modifications to highlight avoidable complications, and provide physiologic rationale for our preferred procedure.

Study design: Retrospective cohort	**Country/Setting: Italy, multicenter**	**Funding: ND**

Interventions(s): Laparoscopic Nissen-Rossetti fundoplication	**Comparator(s): None**

Primary outcome(s): avoidable complications	**Other outcome(s):**

Inclusion criteria: Pts with GERD undergoing Laparoscopic Nissen-Rossetti fundoplication	**Exclusion criteria: Not described**
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):** Considered, not used for exclusion
EGD (performed or not and results): Performed, results not described	**Esophagitis/stricture/Barrett's: 39.2% esophagitis; 3.9% Barretts**
PH study (performed or not and results): Performed, mean percentage with pH < 4 at 24 h monitoring was 7.8 +/- 4 for total time, 9.2 +/- 5 and 5.0 +/- 3 in the upright and recumbent positions, respectively; mean DeMeester score was 52.1 – 10.2.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): Not described**
Esophageal manometric studies (performed or not and results): Performed, mean pLES 11.0+/-1.2 mmHg	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) N/A

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding: n/a	**Allocation concealment: n/a**
Intention-to-treat: n/a	**Method of Randomization: n/a**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: Lacks full description of inclusion/exclusion criteria

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A		

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: mean age 41.8 +/- 21	**N enrolled: 380**
%Male: 40.3%	**N completed: 380**
Race: ND	**Dropouts/reasons: n/a**
BMI: ND	**Follow-up period:** Side effect data available for 6-month follow up for 368 pts, however overall follow-up had a median of 83 months (range: 1–13 years)
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Compliance: No conversion to open surgery occurred

Adverse Events:

No mortality occurred.

Major avoidable perioperative complications in 4/380 patients (1.1%); in one patient (0.3%) an intraoperative mucosal tear immediately repaired by placing one stitch. In other 3 cases a reintervention necessary to stop postop bleeding (1 at the trocar site, and in 1 at the gastroesophageal junction w/o the exact identification of the source, and 1 at the spleen). In the latter case, splenectomy necessary.

Postoperative side effects at 6 months

Dysphagia	13/368 (3.5%)
Heartburn	14/368 (3.8%)
Hyperflautulence	7/368 (1.9%)
Early satiety	14/368 (3.8%)
Bloating	9/368 (2.4%)
Chest pain	2/368 (0.5%)

Applicability: (narrow/wide): Narrow	Comments: Single-surgeon study

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

GERD data extraction form

Author: Demyttenaere	Yr: 2010	UI: 19730949	Questions addressed: 1,3	Extractor: DM

Objective/Topic:
Efficacy and safety of EsophyX in an unselected patient population

Study design:	Country/Setting:	Funding:
Prospective Cohort	USA	nd

Interventions(s):	Comparator(s):
Esophyx Transoral incisionless fundoplication recreate the gastroesophageal junction valve	**none**

Primary outcome(s):	Other outcome(s):
Self-reported symptom severity *(Anvari scale: range 0-7, lower scores indicate improved symptom scores)* health-related quality of life *(HRQL)* *(Velanovich score: range 0-50; lower scores indicate improvement)*	Medication use overall patient satisfaction

Inclusion criteria:	Exclusion criteria:
18–80 yrs Documented GERD Received PPI treatment for more than 6 months with normal or reduced manometry.	BMI > 40 moderate to large hiatal hernias (>3 cm) Grade D esophagitis Pregnancy
Symptoms (describe): nd	**Hiatal hernia (specify whether considered and size used for exclusion):** small ≤ 3 cms: 11/26 (42%)
EGD (performed or not and results): yes	**Esophagitis/stricture/Barrett's:** esophageal stricture: 1/11 (9%) Barrett's esophagus: 3/11 (27%)
PH study (performed or not and results): yes, no data	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** nd
Esophageal manometric studies (performed or not and results): yes esophageal dysmotility: 5/11 (45%)	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

GERD data extraction form

Quality Assessment Non-RCTs: C
Comments: small sample, selection bias, short follow up

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 45 ± 15 y	**N enrolled: 26**
%Male: 38%	**N completed: 22**
Race: nd	**Dropouts/reasons: no follow up information available for 4**
BMI: 28 ± 5	**Follow-up period: 3 months for primary outcome, 10 months for patient satisfaction**
Comments:	

Results

Primary outcome(s):

Outcome	Pre-operatively	Post-operatively	P value
HRQL (Velanovich scale, 0-50)	22 ± 13	10 ± 7	0.0007
Symptom score (Anvari Scale, 0-72)	34 ± 14	17 ± 15	0.002

Secondary outcome(s):

Outcome	Pre-operatively	Post-operatively
Medication use (%)	100	68

After 10 months of followup (mean followup)
Satisfied with the procedure: 45%
Neutral: 25%
Dissatisfied with the procedure: 30%

Comments:

Compliance:

Adverse Events:
Peri-operative:
1) Sore throat and left shoulder pain on postoperative day 1 seen in many patients – resolved within week 1
2) Sharp chest pain in week 1 – 2/26 (8%)
3) Postop nausea and vomiting – 1/26 (4%)
4) Tachycardia on day of procedure– 2/26 (8%)

Long term:
1 death: drug overdose unrelated to the procedure a few months after the operation
3 Tx failures due to:
1) loss of fasteners: 2/26 (8%); further Tx with Nissen fundoplication
2) Gastric fundus attached to Gastroesophageal junction: : 1/26 (4%); further Tx with Nissen fundoplication
3)

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Dent	**Yr**: 2008	**UI**:18184117	**Questions addressed**: 1, 3	**Extractor**: SI

Objective/Topic: Compare AZD0865 (potassium-competitive acid blocker) with esomeprazole in patients with non-erosive GERD

Study design: RCT	**Country/Setting**: multiple	**Funding**: AstraZeneca

Interventions(s): AZD0865 25, 50, or 75 mg daily	**Comparator(s)**: esomeprazole 20 mg daily

Primary outcome(s): time to sustained absence of patient-reported heartburn (time to the first of 7 consecutive days without a burning feeling behind the breastbone)	**Other outcome(s)**: proportion of patients free from heartburn 1st, 2nd, and 4th wk of treatment

Inclusion criteria: 18–70 y; main symptom of NERD heartburn; history of heartburn for at least 6 months; experienced heartburn episodes of moderate or severe intensity on at least 4 days during the 7 days prior to randomization; no esophageal mucosal breaks at an endoscopy at the screening visit; ability to use an electronic diary.	**Exclusion criteria:** other major GI diseases; current peptic ulcer/erosions; a history of upper GI surgery; pain or burning feeling in the upper center of the stomach of equal or higher intensity as that of heartburn during the 7 days prior to enrollment; cardiovascular disease, cerebrovascular diseases, unstable diabetes mellitus, pulmonary, renal, pancreatic or liver diseases, malignancy, or generalized bleeding disorders; clinically significant abnormal laboratory values or "alarm symptoms"; a history of heartburn not relieved within 2 wk with PPIs or H2RAs; use of any PPIs or continuous H2RA use within 2 wk of endoscopy and between endoscopy and the first treatment; hypersensitivity to PPIs or AZD0865; concomitant therapy with acid suppressive therapy (other than the study treatment); antacids and alginates; prostaglandin analogs or sucralfate; prokinetic drugs; nonsteroidal anti-inflammatory drugs including COX-2 inhibitors with the exception of acetylsalicylic acid at a dose of ≤165 mg/day for cardiovascular prophylaxis; bisphosphonates; antithrombotic drugs; strong inhibitors of CYP3A4 or strong inducers of CYP3A4, and digoxin; use of another investigational drug 28 days prior to randomization
Symptoms (describe): heartburn	**Hiatal hernia (specify whether considered and size used for exclusion)**: nd
EGD (performed or not and results): y (see inclusion criteria)	**Esophagitis/stricture/Barrett's**: none by inclusion criteria
pH study (performed or not and results): 90 pts had pH study	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** patients with a history of heartburn not relieved within 2 wk with PPIs or H2RAs were excluded
Esophageal manometric studies (performed or	Other:

not and results): no	

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) yes

Quality Assessment for RCTs: A/rigorous	
Blinding: y	Allocation concealment: n
Intention-to-treat: n	Method of Randomization: computer generated
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 46	N enrolled: 1470
%Male: 40	N completed: 1329
Race: 82% white; 6% black	Dropouts/reasons: 141 (adverse events, not willing to continue)
BMI: nd	Follow-up period: 4 wk
Comments:	

Results
Primary outcome(s): median time (95%CI) to sustained absence of patient-reported heartburn AZD0865 25 mg 14 d (11-18 d) 50 mg 11 d (9-13 d) 75 mg 12 d (8-18 d) esomeprazole 20 mg 12 d (9-17 d) No statistically significant differences
Secondary outcome(s): percentage of patients reporting freedom from heartburn at 4 wk (estimated from Fig 3 in paper) AZD0865 25 mg 45% 50 mg 52% 75 mg 47% esomeprazole 20 mg 53% no significant differences percentage of time that intragastric pH was >4 at 2 wk (n=62) (estimated from Fig 4 in paper) AZD0865 25 mg 70% 50 mg 68% 75 mg 76% esomeprazole 20 mg 58% significant difference between AZA0865 75 mg and esomeprazole 20 mg (P<0.05)
Comments:

Compliance: A total of 47 patients (3.2%) discontinued treatment due to adverse events.

GERD data extraction form

Rates of discontinuation for the four treatment groups were:
AZD0865 25 mg 13 patients (3.6%)
AZD0865 50 mg 10 patients (2.8%)
AZD0865 75 mg 18 patients (5.0%)
esomeprazole 20 mg 6 patients (1.6%)

Adverse Events:
Serious adverse events not related to treatment (details not provided)
AZD0865 25 mg n=2
50 mg n=3
75 mg n=4
esomeprazole 20 mg n=0

See table 2 from paper for elevation in liver function tests

Applicability: (narrow/wide): wide	Comments:

Table 2. Number of Patients With Maximal Values >3× ULN and >5× ULN in Liver Function Tests During Treatment

		AZD0865 25 mg N (%)	AZD0865 50 mg N (%)	AZD0865 75 mg N (%)	Esomeprazole 20 mg N (%)
ALT	>3× ULN	2 (0.6)	7 (2.1)	12 (3.5)	1 (0.3)
	>5× ULN	1 (0.3)	4 (1.2)	6 (1.8)	0 (0)
AST	>3× ULN	0 (0.0)	4 (1.2)	5 (1.5)	0 (0)
ALP	>3× ULN	0 (0.0)	1 (0.3)	2 (0.6)	0 (0)

GERD data extraction form

Author: DeVault	**Yr: 2006**	**UI: 16682260**	**Questions addressed: 1, 2,3**	**Extractor: WY**

Objective/Topic: compare esomeprazole and lansoprazole in maintenance of healed erosive esophagitis and healing of GERD-related symptoms

Study design: RCT	**Country/Setting:** US, 143 centers, mostly community-based gastroenterology private practices	**Funding:** AstraZeneca

Interventions(s): Esomeprazole 20mg q day for 6 months, in the morning before breakfast	**Comparator(s):** Lansoprazole 15mg q day for 6 months, in the morning before breakfast

Primary outcome(s): Kaplan-Meier estimate of endoscopic and symptomatic remission rate of erosive esophagitis through 6 months after initial healing	**Other outcome(s):** Endoscopic remission rate at month 3, cumulative remission rate through month 6, symptom control, tolerability

Inclusion criteria: 18-70 years old Had erosive esophagitis diagnosed by EGD and heartburn at least 2 days per week, but healed (after using esomeprazole or lansoprazole) based on EGD and no heartburn or acid regurgitation during the 7 days before randomization	**Exclusion criteria:** GI complications or bleeding disorders Other diseases that affect study participation With positive *H pylori*
Symptoms (describe): Heartburn: None/mild: 6.60% Moderate/severe: 88.40% Acid regurgitation: None/mild: 32.35% Moderate/severe: 67.65% Dysphagia: None/mild: 85.90% Moderate/severe: 14.10% Epigastric pain: None/mild: 54.05% Moderate/severe: 45.95%	**Hiatal hernia (specify whether considered and size used for exclusion):** no
EGD (performed or not and results): yes, all pts must be healed to enter this trial. Prior to healing, distribution of LA grade are as follows: Grade A: 37.15% Grade B: 37.65% Grade C: 20.70% Grade D: 4.50%	**Esophagitis/stricture/Barrett's:** no
PH study (performed or not and results): no	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** healed after using esomeprazole or lansoprazole

Esophageal manometric studies (performed or not and results): no	**Other:** History of GERD for 1-5 years: 46.15% History of GERD for >5 years: 45.45% *H pylori* positive: 11.00%

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: B/acceptable	
Blinding: double blinded	**Allocation concealment:** yes,
Intention-to-treat: yes, defined as all pts who took at least 1 dose of treatment (both ITT and per-protocol analyses were presented)	**Method of Randomization:** computerized randomization schedule
Other comments: large dropout	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
x		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 47.70	**N randomized:** 1026
%Male: 58.95	**N analyzed:** 1001 **N completed**: 746
Race: 77.60% white 6.00% black 16.4% other	**Dropouts/reasons:** - lack of response to treatment: 38 in esomeprazole group, 68 in lansoprazole group (more frequent in the lansoprazole group) - lost to follow-up: 25 in esomeprazole group, 21 in lansoprazole group - unwilling to continue: 22 in esomeprazole group, 17 in lansoprazole group - adverse event: 16 in esomeprazole group, 20 in lansoprazole group - other: 10 in esomeprazole group, 7 in lansoprazole group - failed entry criteria: 1 in esomeprazole group, in 1 lansoprazole group
BMI: not reported	**Follow-up period:** up to 6 months
Comments:	

Results

Primary outcome(s):

Estimate endoscopic/symptomatic remission rate through 6 months

	Total # of pts	% (CI)	P value
Esomeprazole	501	84.8 (81.5, 88.1)	0.0007
Lansoprazole	500	75.9 (72.0, 79.8)	

Estimate endoscopic/symptomatic remission rate through 6 months

	Baseline LA grades A or B	Baseline LA grades C or D	P value
Esomeprazole	87.2%	77.6%	Not reported
Lansoprazole	78.7%	68.4%	

Estimate endoscopic remission rate through 6 months

	Total # of pts	% (CI)	P value
Esomeprazole	501	86.9 (83.8, 90.1)	0.0003

Secondary outcome(s):

Observed endoscopic/symptomatic remission rate at 3 months

	Total # of pts	# of pts , %	P value
Esomeprazole	501	465, 92.8%	<0.0001
Lansoprazole	500	434, 86.8%	

Cumulative endoscopic/symptomatic remission rate at 6 months

	Total # of pts	# of pts , %	P value
Esomeprazole	501	432, 86.2%	<0.0001
Lansoprazole	500	388, 77.6%	

Cumulative endoscopic/symptomatic remission rate at 6 months

	Baseline LA grades A or B	Baseline LA grades C or D	P value
Esomeprazole	336/380, 88.4%	96/121, 79.3%	Not reported
Lansoprazole	297/369, 80.5%	91/131, 69.5%	

Rate of relapse during the study

	All relapse (%)	Endoscopic relapse (%)	Both endoscopic and symptomatic relapse, but without heartburn	Both endoscopic and symptomatic relapse, but without acid re
Esomeprazole	13.8%	11.6%	31/370, 8.4%	37/386, 9.6%
Lansoprazole	22.4%	20.2%	50/362, 13.8%	70/392, 17.9%

Number needed to treat with esomeprazole at 3 months: 17 pts (CI: 10-44)
Number needed to treat with esomeprazole at 6 months: 12 pts (CI: 7-26)

Heartburn

	# of pts without symptom	% observed at 6 months	% of ITT
Esomeprazole	383	82.9% (out of 462 pts)	76.4% (out of 501 pts)
Lansoprazole	369	79.2% (out of 466 pts)	73.8% (out of 500 pts)

Acid regurgitation

	# of pts without symptom	% observed at 6 months	% of ITT
Esomeprazole	401	86.8% (out of 462 pts)	80.0% (out of 501 pts)
Lansoprazole	400	85.8% (out of 466 pts)	80.0% (out of 500 pts)

Dysphagia

	# of pts without symptom	% observed at 6 months	% of ITT
Esomeprazole	451	97.6% (out of 462 pts)	90.0% (out of 501 pts)
Lansoprazole	449	96.4% (out of 466 pts)	89.8% (out of 500 pts)

Epigastric pain

	# of pts without symptom	% observed at 6 months	% of ITT
Esomeprazole	423	91.6% (out of 462 pts)	84.4% (out of 501 pts)
Lansoprazole	417	89.5% (out of 466 pts)	83.4% (out of 500 pts)

Comments:

Compliance:
“adequate” in 91% of pts in esomeprazole group and 92.4% of pts in lansoprazole group

Adverse Events:
Any adverse events
Esomeprazole (n=510): 253 (49.6%)
Lansoprazole (n=514): 234 (45.5%)
Serious adverse events
Esomeprazole (n=510): 10 (2.0%)
Lansoprazole (n=514): 5 (1.0%)
Treatment-related adverse events
Esomeprazole (n=510): 41 (8.0%)
Lansoprazole (n=514): 30 (5.8%)

Diarrhea
Esomeprazole (n=510): not related to treatment: 10 (2.0%); related to treatment: 7 (1.4%)
Lansoprazole (n=514): not related to treatment: 19 (3.7%); related to treatment: 7 (1.4%)
Gastritis
Esomeprazole (n=510): not related to treatment: 22 (4.3%); related to treatment: 0 (0%)
Lansoprazole (n=514): not related to treatment: 18 (3.5%); related to treatment: 0 (0%)
Nausea
Esomeprazole (n=510): not related to treatment: 10 (2.0%); related to treatment: 0 (0%)
Lansoprazole (n=514): not related to treatment: 15 (2.9%); related to treatment: 2 (0.4%)
Headache
Esomeprazole (n=510): not related to treatment: 13 (2.5%); related to treatment: 3 (0.6%)
Lansoprazole (n=514): not related to treatment: 6 (1.2%); related to treatment: 3 (0.6%)

There is no significant difference between groups.
Note: “related to treatment” or not was determined by asking the pt “Do you consider that there is a reasonable possibility that the event may have been caused by the drug?”

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: DeVault	Yr: 2007	UI: 17760655	Questions addressed: 2, 3	Extractor: SI

Objective/Topic: to examine if older adults with GERD are more difficult to treat

Study design: post hoc analysis of 2 RCTs	Country/Setting: US	Funding: Wyeth Research

Interventions(s): 1st RCT: pantoprazole 10, 20, 40 mg or placebo once daily up to 8 wk 2nd RCT: pantoprazole 20 or 40 mg once daily, or nizatidine 150 mg twice daily up to 8 wk	Comparator(s):

Primary outcome(s):	Other outcome(s):

Inclusion criteria: endoscopically diagnosed erosive esophagitis (≥grade 2 in the Hetzel-Dent scale)	Exclusion criteria: 2nd RCT: no therapeutic doses of H2RAs within 2 wks of study drug administration
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): yes	Esophagitis/stricture/Barrett's:
pH study (performed or not and results): nd	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): nd
Esophageal manometric studies (performed or not and results): nd	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) no, 2nd RCT: no therapeutic doses of H2RAs within 2 wks of study drug administration

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: post hoc analysis; no statistical adjustment; no power calculation

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects

GERD data extraction form

Age: 49	N enrolled: 847
%Male: 68%`	N analyzed: 418
Race: 87% white; 6% black; 5% Hispanic	Dropouts/reasons:
BMI: nd	Follow-up period: 4 or 8 wk; pts healed at 4 or 8 wk were combined and presented as 8 wk results
Comments: only analyzed those who received pantoprazole 40 mg, nizatidine 150 mg or placebo; trend towards more severe disease (grades 3 and 4) in the older patients (33/68 (48.5%) vs. 111/350 (31.7%))	

Results
Primary outcome(s): healing rates of erosive esophagitis at 8 wk pantoprazole 40 mg once daily ≥65 (n=44) 86% (95%CI, 76%, 97%) <65 (n=210) 83% (95%CI, 78%, 88%) nizatidine 150 mg twice a day ≥65 (n=13) 46% (95%CI, 19%, 73%) <65 (n=69) 35% (95%CI, 24%, 46%) nizatidine 150 mg twice a day ≥65 (n=11) 27% (95%CI, 1%, 54%) <65 (n=71) 34% (95%CI, 23%, 45%)
Secondary outcome(s):
Comments:

Compliance: nd

Adverse Events:
discontinued treatment due to adverse events; 10/48 at least one adverse event pantoprazole 40 mg 127/254 (50%) nizatidine 150 mg twice daily 48/82 (59%) placebo 43/82 (52%) Most common were abdominal pain, diarrhea, nausea and headache for all 3 groups.

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Domagk	Yr: 2006	UI: 16542275	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
To compare the efficiency and safety of endoluminal gastroplasty EndoCinch and Endoscopic polymer injection Enteryx

Study design:	Country/Setting:	Funding:
RCT	Germany, single center	nd

Interventions(s):	Comparator(s):
endoluminal gastroplasty EndoCinch	Endoscopic polymer injection Enteryx

Primary outcome(s):	Other outcome(s):
reduction of PPI dosage of ≥50%	drug consumption, GERD symptoms, quality-of-life, endoscopy, pH monitoring, manometry, and adverse events

Inclusion criteria:	Exclusion criteria:
With GERD symptoms for >1 yr, responsive to PPI treatment	none
Symptoms (describe): See "baseline" in results	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B/acceptable	
Blinding: no	Allocation concealment: yes
Intention-to-treat:no	Method of Randomization: computer generated
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:48±15	N enrolled: 51
%Male:53%	N completed: 49

GERD data extraction form

Race:nd	Dropouts/reasons:2 withdrawal
BMI: 26±4	Follow-up period: 6 months
Comments:	

Results

Primary outcome(s):
Medication use

	Number of pts off medication at baseline	Number of pts off medication at 6 months	Number of pts with reduced PPI dosage by >50%	Pre vs. post	EndoCinch vs. Enteryx
EndoCinch (n=26)	26	20	0	<0.0001	0.365
Enteryx (n=23)	23	14	6	<0.0001	

Secondary outcome(s):
Modified DeMeester symptom score

	Baseline	6 months	P (pre vs post)	EndoCinch vs. Enteryx
EndoCinch (n=26)	4.5±1.9	2.2±2.4	<0.0001	0.315
Enteryx (n=23)	4.4±1.3	2.0±1.6	<0.0001	

Heartburn severity score

	Baseline	6 months	P (pre vs post)	EndoCinch vs. Enteryx
EndoCinch (n=26)	53.7±23.7	20.9±24.2	<0.0001	nd
Enteryx (n=23)	56.1±18.8	19.9±24.4		

Quality of Life GLQI

	Baseline	6 months	P (pre vs post)	EndoCinch vs. Enteryx
EndoCinch (n=26)	74.6±14.6	85.2±14.2	<0.0001	nd
Enteryx (n=23)	77.4±13.5	90.4±16.8	<0.0001	

Quality of Life SF36 physical score

	Baseline	6 months	P (pre vs post)	EndoCinch vs. Enteryx
EndoCinch (n=26)	45.2±6	50.3±8.1	<0.0001	nd
Enteryx (n=23)	45.3±8.1	49.5±7.9	0.003	

Quality of Life SF36 mental score

	Baseline	6 months	P (pre vs post)	EndoCinch vs. Enteryx
EndoCinch (n=26)	43.1±10.1	43.5±8.9	0.708	nd
Enteryx (n=23)	43.4±8.9	43.5±8.9	0.287	

% Time of pH<4

	Baseline	6 months	P (pre vs post)	EndoCinch vs. Enteryx
EndoCinch (n=26)	14.5±14.5	9.6±8.9	0.071	0.147
Enteryx (n=23)	15.5±11.2	13.9±13.2	0.93	

LES pressure (mmHg)

	Baseline	6 months	P (pre vs post)	EndoCinch vs. Enteryx
EndoCinch (n=26)	38.9±14.9	38.4±10.6	NS	NS

Enteryx (n=23)	27.8±9.4	25.4±10.1	NS	

Esophagitis grading

	Baseline	Improvement in grading 6 months	P (pre vs post)	EndoCinch vs. Enteryx
EndoCinch (n=26)	Grade O: 50% Grade I: 35% Grade II: 15%	33%	NA	0.908
Enteryx (n=23)	Grade O: 48% Grade I: 26% Grade II: 26%	35%		

Comments:

Compliance:
NA

Adverse Events:
Enteryx: transient retrosternal pain, Forrest II a-bleeding situation (from an ulceration at the injection site) (n=1), fever (n = 3), and painful singultus (n=1)
EndoCinch-therapy: reinterventions in 7 patients

Applicability: (narrow/wide): narrow	Comments: small size

GERD data extraction form

Author: Draaisma Broeders 2009	Yr: 2006, 2009	UI:16794387 19801931	Questions addressed: 1,3	Extractor: SI

Objective/Topic: compare laparoscopic with conventional Nissen fundoplication

Study design: RCT	Country/Setting: the Netherlands	Funding: nd

Interventions(s): laparoscopic fundoplication	Comparator(s): conventional Nissen

Primary outcome(s): subjective outcomes	Other outcome(s):

Inclusion criteria: refractory GERD	Exclusion criteria: nd
Symptoms (describe): nd	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): nd	Esophagitis/stricture/Barrett's: nd
pH study (performed or not and results): total esophageal acid exposure (%time pH<4) baseline laparoscopy (n=48) 10.5 (1.3) conventional (n=49) 11.1 (1.2)	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): nd
Esophageal manometric studies (performed or not and results): end expiratory LES (kPa) baseline laparoscopy (n=48) 1.1 (0.1) conventional (n=49) 1.1 (0.1)	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) nd

Quality Assessment for RCTs: B/fair	
Blinding: nd	Allocation concealment: no
Intention-to-treat: yes	Method of Randomization: nd
Other comments: objective data only in 20/146 pts	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		x

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 43.5 y	N enrolled: 177 (+64?)
%Male: 59%	N completed 5 y follow up: 148

GERD data extraction form

Race: nd	Dropouts/reasons: 8 lost to follow up, 4 died (not related to reflux), 4 emigrated, 3 refused follow up
BMI: 26.4	Follow-up period: 5 y
Comments:	

	N completed 10 y follow up: 146
	Dropouts/reasons: 2 pts in the conventional group died (1 from pancreatic cancer; 1 from heart failure); 1 pt in the laparoscopy group died from esophageal varices during the analysis of clinical outcome
	Follow-up period: 10 y

Results

1. subjective symptoms (VAS 0-100) general quality of life at 5 y
laparoscopy (n=79) 67.1 (SEM 2.8)
conventional (n=69) 60.5 (SEM 3.2)

no significant differences between groups

subjective symptoms (VAS 0-100) general quality of life at 10 y
laparoscopy (n=79) 65.3 (SEM 2.4)
conventional (n=63) 61.4 (SEM 3.1)

no significant differences between groups

subjective symptoms (VAS 0-100) general quality of life at 5 y
laparoscopy (n=79) 67.1 (SEM 2.8)
conventional (n=69) 60.5 (SEM 3.2)

no significant differences between groups

2. subjective symptoms (Visick I and II; resolved or improved) at 10 y
laparoscopy (n=79) 73/79 (92.4%)
conventional (n=63) 59/65 (90.7%)

no significant differences between groups

Secondary outcome(s):
1. Medication use at 5 y (PPI, H2RA or prokinetics)
laparoscopy (n=79) 11/79 (13.9%)
conventional (n=69) 11/69 (15.9%)

Medication use at 10 y (PPI, H2RA or prokinetics)
laparoscopy (n=79) 21/79 (26.6%)
conventional (n=67) 15/67 (22.4%)

no significant differences between groups

2. total esophageal acid exposure (%time pH<4) at 5 y

	baseline	5 y
laparoscopy (n=48)	10.5 (1.3)	2.2 (0.6)
conventional (n=49)	11.1 (1.2)	1.8 (0.6)

GERD data extraction form

3. total esophageal acid exposure (<5.8% acid exposure for total time) in PPI dependent pts at 10 y

	baseline	10 y
laparoscopy (n=10)		8/10
conventional (n=10)		7/10

4. change in end expiratory LES (kPa)

	baseline	5 y
laparoscopy (n=48)	1.1 (0.1)	1.7 (0.2)
conventional (n=49)	1.1 (0.1)	1.5 (0.2)

no significant differences between groups

3. reintervention

	5 y	10 y	
laparoscopy (n=79)	12/79 (15.2%)	12/79 (15.2%)	P=0.006 btw groups at 10 y
conventional (n=69)	8/69 (11.6%)	24/69 (34.8%)	

Comments:

Compliance:

Adverse Events:
At 5 y, of the 20 who had reinterventions,
2/20 had reinterventions for intrathoracic herniation
1/20 had reintervention for cicatricial hernia

At 10 y, of those who had reinterventions,
in laparoscopy group, 2/12 had reintervention for incisional hernia
in conventional group, 9/24 had reintervention for incisional hernia

in laparoscopy group, 1/12 had reintervention for gastric perforation

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Draaisma	Yr: 2006	UI:16794387	Questions addressed: 1,3	Extractor: SI

Objective/Topic: compare laparoscopic with conventional Nissen fundoplication

Study design: RCT	Country/Setting: the Netherlands	Funding: nd

Interventions(s): laparoscopic fundoplication	Comparator(s): conventional Nissen

Primary outcome(s): subjective outcomes	Other outcome(s):

Inclusion criteria: refractory GERD	Exclusion criteria: nd
Symptoms (describe): nd	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): nd	Esophagitis/stricture/Barrett's: nd
pH study (performed or not and results): total esophageal acid exposure (%time pH<4) baseline laparoscopy (n=48) 10.5 (1.3) conventional (n=49) 11.1 (1.2)	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): nd
Esophageal manometric studies (performed or not and results): end expiratory LES (kPa) baseline laparoscopy (n=48) 1.1 (0.1) conventional (n=49) 1.1 (0.1)	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) nd

Quality Assessment for RCTs: C/Poor	
Blinding: nd	Allocation concealment: no
Intention-to-treat: no	Method of Randomization: nd
Other comments: Patient flow through the study was unclear	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		x

GERD data extraction form

Characteristics of enrolled patients at 5 year follow up	Results: Disposition of Enrolled Subjects
Age: 43.5 y	N enrolled: 177 (+64?)
%Male: 59%	N completed: 148
Race: nd	Dropouts/reasons: 8 lost to follow up, 4 died (not related to reflux), 4 emigrated, 3 refused follow up
BMI: 26.4	Follow-up period: 5 y
Comments:	

Results

Primary outcome(s):
subjective symptoms (VAS 0-100) general quality of life at 5 y
laparoscopy (n=79) 67.1 (SEM 2.8)
conventional (n=69) 60.5 (SEM 3.2)

no significant differences between groups

Secondary outcome(s):
Medication use at 5 y (PPI, H2RA or prokinetics)
laparoscopy (n=79) 11/79 (13.9%)
conventional (n=69) 11/69 (15.9%)

total esophageal acid exposure (%time pH<4)

	baseline	5 y
laparoscopy (n=48)	10.5 (1.3)	2.2 (0.6)
conventional (n=49)	11.1 (1.2)	1.8 (0.6)

change in end expiratory LES (kPa)

	baseline	5 y
laparoscopy (n=48)	1.1 (0.1)	1.7 (0.2)
conventional (n=49)	1.1 (0.1)	1.5 (0.2)

no significant differences between groups

reintervention

	5 y
laparoscopy (n=79)	12/79 (15.2%)
conventional (n=69)	8/69 (11.6%)

Comments:

Compliance:

Adverse Events:
Of the 20 who had reinterventions,
2/20 had reinterventions for intrathoracic herniation
1/20 had reintervention for cicatricial hernia
LNF 12/79 (15.1%)
CNF 8/69 (11.6%)

GERD data extraction form

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Dundon	**Yr**: 2008	**UI**: 18829607	**Questions addressed**: 1, 2	**Extractor**: JC

Objective/Topic: Assess long term effectiveness of Stretta procedure for pts presenting to a surgical practice for the treatment of refractory GERD

Study design: Retrospective cohort	**Country/Setting**: USA/Single Academic Medical Center	**Funding**: n/d

Interventions(s): Stretta	**Comparator(s)**: None

Primary outcome(s): Change in symptom scores, GERD quality of life parameters	**Other outcome(s)**:

Inclusion criteria: Documented reflux by clinical dx, abnormal pH probe study, or endoscopically documented abnormalities were offered Stretta. Pts were counseled and those without significant anatomical derangements were given option to undergo Stretta. Those who completed a 6 month follow up survey and were more than 3 years post Stretta were included.	**Exclusion criteria:**. Large hiatal hernia excluded
Symptoms (describe): Regular symptom assessment with GERD health-related quality of life questionnaire.	**Hiatal hernia (specify whether considered and size used for exclusion)**: See exclusion criteria--large hiatal hernia excluded
EGD (performed or not and results): Performed on some—see inclusion criteria	**Esophagitis/stricture/Barrett's**: Not described
pH study (performed or not and results): Performed on some—see inclusion criteria	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Previous failed surgery were not considered exclusion criteria
Esophageal manometric studies (performed or not and results): Not described.	Other: All pts who did not undergo any other antireflux procedures were determined to be responders and were asked to complete a GERD QoL symptom survey. Also, see Compliance section below. Obesity not considered exclusion criteria

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) n/a—no comparator

Quality Assessment for RCTs: n/a	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

GERD data extraction form

Quality Assessment Non-RCTs: C
Comments: Retrospective analysis – no comparator

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous, though not described fully		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: mean (s.d): 46	N enrolled: 37
%Male: 43.8%	N completed: 32 completed long term follow-up
Race: n/d	Dropouts/reasons: 19 considered treatment failures—SEE COMPLIANCE BELOW
BMI: mean (s.d) n/d	Follow-up period: Average 53 months (range 36-68)
Comments: Weight-kg mean (sd): 77 (10)	

Results

Primary outcome(s):

Patients who did not undergo any other antireflux procedure were determined to be responders. Of 32 patients, 19 were considered treatment failures (or non-responders), with 12 undergoing Nissen fundoplication and 7 undergoing Roux-en-y gastric bypass surgery.

Mean Scores for Heartburn and Quality of Life

Parameter	Baseline	Follow-up (mo)	
Mean heartburn scores	Responders	Non responders	P value
Initial	2.43	3.66	.0401
6 month	1	2.25	.05
Final	1.43	---	---
GERD QoL			
Initial	3.14	3.66	>.05
6 month	1.83	1.92	>.05
Final	1.46	---	---

Mean heartburn score in those not undergoing an antireflux procedure showed no statistically significant decrease in heartburn related sx at long term follow up. There was a significant improvement in satisfaction with GERD condition going from a pre-stretta score of 3.14 to a long term follow up score of 1.46 (p=.0006).

Those undergoing surgery still showed a significant improvement in GERD satisfaction going from 3.66 to 1.92 (p=.0104). Overall heartburn at 6 mo also decreased significantly from 3.66 to 2.25 (p=.0233)

Secondary outcome(s):

Comments: Heartburn score data for Responders seem inconsistent—graphs, text and tables differ.

Compliance: Patients who had persistent symptoms or were dissatisfied with the outcome and subsequently underwent anti-reflux surgery or Roux-en-Y gastric bypass were deemed as failures of the Stretta procedure and thus were considered at an end point of evaluation.

Adverse Events: not described

Applicability: (narrow/wide): narrow	Comments: Case series, non-RCT, no comparator, single site, varying follow-up

GERD data extraction form

Author: Eggleston	Yr: 2009	UI: 19210493	Questions addressed: 1,3	Extractor: JHL

Objective/Topic:
To identify the efficacy of rabeprazole 20mg compared with esomeprazole 20 and 40mg

Study design: RCT	Country/Setting: Australia, primary care	Funding: Janssen-Cilag Pty Ltd funded this study in full. Initial data analyses funded by Dr Richard Parsons of Pretium Pty Ltd and Janssen-Cilag Pty Ltd, Writing support from Greg Blanch of Janssen-Cilag and funded by Janssen-Cilag Pty Ltd

Interventions(s):	Comparator(s):
• rabeprazole 20mg	• esomeprazole 20mg • esomeprazole 40mg

Primary outcome(s): Resolution of heartburn and regurgitation	Other outcome(s): Quality of life

Inclusion criteria:	Exclusion criteria:
"… recruited between November 2006 and May 2008 and were eligible for inclusion if they were ≥ 18 years of age; had episodes of heartburn, with or without regurgitation, for 3 months or longer and for >3 days in the 7 days prior to randomization; could understand and complete questionnaires and have access to a telephone; and could give written consent."	"…excluded if they required endoscopy within 4 weeks of randomization or had gastrointestinal symptoms that, in the opinion of the GP investigator, required further investigation prior to or coincident with initiation of PPI therapy; had significant gastrointestinal disease active in the last 12 months; had Barrett's oesophagus (>3 cm); had Zollinger–Ellison Syndrome; scleroderma; malignancy (other than non-melanoma skin cancers) present within the last 5-years which, in the opinion of the investigator, could interfere with the patient's participation in the study; had hypersensitivity to any PPI; were women patients who were pregnant or breastfeeding, or who, in the opinion of the investigator, could become pregnant throughout the study; had used >3 doses of histamine-2 receptor antagonists or PPI within the week before randomization; had used anticholinergics, cholinergics, spasmolytics, opiates, sucralfate, prokinetics, antibiotics or bismuth compounds within 14 days of randomization; had participated in an investigational drug or investigational device study within 30 days prior to the baseline visit."

Symptoms (describe):

	Rabeprazole 20mg (n=464)	Esomeprazole 40mg (n=469)	Esomeprazole 20mg (n=459)
Mean baseline symptom PAGI-SYM scores (95% CI)			
Heartburn	2.04 (1.92, 2.16)	1.96 (1.83, 2.09)	1.97 (1.85, 2.10)
Regurgitation	1.55 (1.42, 1.68)	1.48 (1.35, 1.60)	1.54 (1.41, 1.67)

Hiatal hernia (specify whether considered and size used for exclusion): ND

EGD (performed or not and results): Not performed	Esophagitis/stricture/Barrett's: Excluded patients with Barrett's oesophagus (>3cm)
PH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B/acceptable	
Blinding: Yes	**Allocation concealment: ND**
Intention-to-treat: Yes	**Method of Randomization: Yes**
Other comments: The results were also reported for per protocol population.	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
		X
C (included "patients presenting their general practitioner with symptoms of GERD")		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46.7 y	**N enrolled: 1406 (randomized, n=1392)**
%Male: 55.5%	**N completed: 1201**
Race: Caucasian 89.6%	**Dropouts/reasons: n=191/1392** • Rabeprazole 20mg – Loss to follow-up (n=29), Discontinued intervention (n=40; AE=20, Investigator decision=1, Subject choice=15, Other=2) • Esomeprazole 40mg – Loss to follow-up (n=19), Discontinued intervention (n=44; AE=27, Investigator decision=1, Subject choice=13, Other=3) *discrepancy with patient flow diagram • Esomeprazole 20mg – Loss to follow-up (n=20), Discontinued intervention (n=39; AE=20, Investigator decision=16, Subject choice=21, Other=2)
BMI: 29.2	**Follow-up period: 4 weeks**
Comments:	

Results

Primary outcome(s):
Complete and satisfactory relief of GERD symptoms

	Rabeprazole 20mg	**Esomeprazole 40mg**	**Esomeprazole 20mg**	**Rabeprazole 20mg**	**Esomeprazole 40mg**	**Esomeprazole 20mg**
	Complete resolution			Satisfactory resolution		
Heartburn						
% patients	58.6	64.4	60.6	87.3	89.1	90.2
	P=0.184			*P*=0.991		
Regurgitation						
% patients	60.6	60.3	60.1	85.6	88.1	87.6
	P=0.363			*P*=0.483		

Secondary outcome(s):
Quality of life: "… as measured by SF-36, improved significantly from baseline for all domains for all treatment groups with no significant differences observed among treatment groups. The greatest improvements were seen in bodily pain, role-physical and role emotional."

Comments:

GERD data extraction form

Compliance: ND

Adverse Events:

	Rabeprazole 20 mg	**Esomeprazole 40 mg**	**Esomeprazole 20 mg**
Subjects having ≥1 AE	151	155	158
Number of AE's	242	264	294
Hospitalizations	4 (1.7%)	1 (0.4%)	8 (2.7%)
Considered drug related*			
Yes	84 (34.7%)	72 (27.3%)	122 (41.5%)
No	157 (64.9%)	191 (72.3%)	171 (58.2%)
Unknown	1 (0.4%)	1 (0.4%)	1 (0.3%)
Specific AEs (n)			
Gastrointestinal signs and symptoms	86	80	77
Gastrointestinal motility and defecation conditions	26	32	40
Headaches	22	30	32
Infections-unspecified pathogen	22	10	29

* Chi square P = 0.002.

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Engstrom (Follow-up of Hagedorn C Ann Surg 2003; 238: 189-196)	**Yr: 2007**	**UI: 17453284**	**Questions addressed: 1,3**	**Extractor: JHL**

Objective/Topic: An anterior or posterior approach to partial fundoplication

Study design: RCT	**Country/Setting: Sweden**	**Funding: ND**

Interventions(s): Anterior fundolplication (AF)	**Comparator(s): Posterior fundoplication (PF)**

Primary outcome(s): • Gastroesophageal reflux symptoms • Postfundoplication complaints	**Other outcome(s):**

Inclusion criteria: Patients with chronic gastroesophageal reflux disease	**Exclusion criteria:** Patients without any major abdominal open surgical procedure
Symptoms (describe): Duration of GERD history in months (range) • PF: 117 (12-480), AF: 111 (24-600) Heartburn score, none/moderate/severe • PF: 7/16/23 • AF: 2/10/31	**Hiatal hernia (specify whether considered and size used for exclusion):** • PF: n=32/48, AF: 32/47
EGD (performed or not and results): Performed	**Esophagitis/stricture/Barrett's:** Esophagitis (any grade) • PF: n=13/48, AF: n=17/47 Stricture • PF: n=3/48, AF: n=2/47
PH study (performed or not and results): Performed 24-hr monitoring	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**

	Anterior (n=23)	Posterior (n=18)
Total	10.1 ± 1.6	9.9 ± 1.3
Upright	12.0 ± 2.0	11.7 ± 1.8
Supine	7.2 ± 1.4	7.2 ± 2.0

Esophageal manometric studies (performed or not and results): Performed	**Other:**

	PF (n=48)	AF (n=47)
Dysphasia score	9.6 ± 1.7	5.54 ± 1.27

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B/acceptable	
Blinding: ND	**Allocation concealment: NA**
Intention-to-treat: Yes	**Method of Randomization: ND**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 49.98 y	**N enrolled: 95**
%Male: 67%	**N completed: 88**
Race: ND	**Dropouts/reasons:** • AF: n=3/47, PF: 4/48 • "Two patients had moved abroad (n = 2 in the AF) and three were lost to follow-up because of a change in address (n = 1 in the AF and n = 2 in the PF). Two patients died during the follow-up period, one in the AF group in the first year of follow up because of cardiac failure and one in the PF group from a malignancy not related to the GI tract."
BMI: ND	**Follow-up period: 5 years** Mean number of months: 64.6 (AF), 65.3 (PF)
Comments:	

Results
Primary outcome(s): Heartburn at 5 years • No symptoms at all of heartburn: PF (75.6%) vs. AF (39.5%), $p < 0.0001$ (ITT) Acid regurgitation at 5 years • No symptoms of acid regurgitation: PF (82.2%) vs. AF (34.9%), $p < 0.0001$ (ITT) Antisecretory drug medication after surgery • Regular use (daily) of antisecretory drugs: PF (7%) vs. AF (23.2%), $p = 0.003$ Faltulence at 5 years • "… insiginificantly fewer AF patients who complained of flatulence after 5 years of follow-up." Ability to belch at 5 years • PF (86.7%) vs. AF (88.4%), n.s Ability to vomit at 5 years • PF (27.3%) vs. AF (63.4%), $p = 0.001$ Overall outcome of the operation • "… the overwhelming majority of those having a posterior repair fully replied in the affirmative (93%), in contrast to only 59% of those having an anterior fundoplication." $p < 0.001$ Dysphagia scores at 5 years • PF (5.5 ± 1.2) vs. AF (7.2 ± 1.6), n.s
Secondary outcome(s):
Comments: "With regard to reflux control, the per protocol analysis basically revealed the same differences between the study groups."

Compliance:

Adverse Events:
• "During the 5 years of follow-up, five AF patients had a reoperation due to relapse of GERD compared to only one of the Toupet operated cases."

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Farup	Yr: 2009	UI:19236727	Questions addressed: 1	Extractor: SI

Objective/Topic: compare on-demand treatment of Aflurax® (Pectin, Raft-forming, anti-reflux agent) with esomeprazole for 6 wk

Study design: RCT	Country/Setting: Norway	Funding: Ferrosan AS

Interventions(s): PRA 1 chewable when experiencing heartburn/regurgitation (up to 8 per day) for 6 wk	Comparator(s): esomeprazole 20 mg one tablet when experiencing heartburn/regurgitation (no more than one per day)

Primary outcome(s): reflux symptom (assessed by GI Symptom Rating Scale) (0-30 score)	Other outcome(s): pt reported overall satisfaction with treatment (y/n)

Inclusion criteria:	Exclusion criteria:
9 outpatient clinics included consecutive patients >18 years of age with mild/moderate heartburn/ regurgitation as main symptom for >3 mo and symptoms at least 2 days per week the last 2 weeks. Mild symptoms were defined as symptoms not interfering with daily activities, and moderate as symptoms interfering with daily activities but not interrupting or avoiding daily activities. Endoscopy was performed and pts with non erosive reflux disease (NERD) and esophagitis Los Angeles grade A and B were included.	Pts in need of continuous treatment; taken acid secretion inhibitors or antacids for 5 or more days the last 2 weeks; pts who preferred continuous treatment; pts with other diseases that could influence the assessment; and those with anticipated poor compliance or significant drug or alcohol abuse; pregnant or breastfeeding women and fertile women not practising a medically approved method of contraception
Symptoms (describe): symptom score (scale ranged from 0-30) 11.3	Hiatal hernia (specify whether considered and size used for exclusion): 65% yes, not used for exclusion
EGD (performed or not and results): NERD 36.4% Grade A 48% Grade B 15.6%	Esophagitis/stricture/Barrett's: nd
pH study (performed or not and results): nd	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): see exclusion criteria
Esophageal manometric studies (performed or not and results): nd	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) yes

Quality Assessment for RCTs: B/acceptable	
Blinding: not blinded	Allocation concealment: no

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Intention-to-treat: y	Method of Randomization: multi-center computer based, variable block size, stratified for centers and NERD vs. esophagitis
Other comments: non-inferiority study, interim analysis with early termination because PRA was less effective than esomeprazole	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 47 y	N enrolled: 82; 77 for ITT analysis
%Male: 56	N completed: 73 (per protocol)
Race: nd	Dropouts/reasons: lost to follow up (n=1); no symptoms (n=2); needed regular treatment (n=2)
BMI: 26	Follow-up period: unclear (?4 wk)
Comments:	

Results
Primary outcome(s): symptom score baseline final PRA 11.3 mean (SD 4.1) 8.0 (SD 4.4) esomeprazole 11.3 mean (SD 3.9) 5.9 (SD 3.4) P for difference between final values = 0.019
Secondary outcome(s): overall satisfaction with treatment as reported by patients (yes or no) satisfied PRA 22/38 (58%) esomeprazole 36/39 (92%) P for difference between groups = 0.001
Comments:

Compliance: mean daily use for esomeprazole was 0.59 tablet (95%CI 0.49-0.68) could not calculate corresponding information for PRA

Adverse Events: PRA esomeprazole diarrhea 6/38 (16%) 1/39 (2.6%)

Applicability: (narrow/wide): wide	Comments:

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Author: Fass	Yr: 2006	UI: 16431305	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
To compare the efficacy and safety of esomeprazole 40mg q day and lansoprazole 30mg bid

Study design:	Country/Setting:	Funding:
RCT	US, 52 sites of various settings (offices, research clinics, academic hospitals	AstraZeneca

Interventions(s):	Comparator(s):
Esomeprazole 40 mg q day for 8 wk, 30min before breakfast Note: pts were allowed to take max of 6 tablets of antacid for heartburn per day.	Lansoprazole 30mg bid for 8 wk, 30min before breakfast and 30min before dinner Note: pts were allowed to take max of 6 tablets of antacid for heartburn per day.

Primary outcome(s):	Other outcome(s):
% of heartburn free days from day 8 to the end of study treatment	• Symptom free days for nighttime heartburn, epigastric pain, and acid regurgitation • Weekly average symptom scores • % of pts with symptom improvements from baseline • Supplemental antacid usage from day 8 to the end of treatment • Average heartburn symptom severity

Inclusion criteria:	Exclusion criteria:
History of heartburn (any severity) for at least 2 days/week in the 30 days before screening Not missed more than 3 days of heartburn severity recording in 14-17 consecutive days of baseline period Had cumulative heartburn score of at least 4 during baseline period using this scale: • None (score 0) • Mild (score 1, easily tolerated, did not last long) • Moderate (score 2, some discomfort, did not interfere with usual activities) • Sever (score 3, much discomfort, interfered with usual activities) At least 18 years old	Esophageal ulcers or strictures, gastric or duodenal ulcers or other clinically significant gastric or esophageal pathology, significant gastric or esophageal pathology, persistent heartburn for more than 1 year while on lansoprazole, serologic evidence of H pylori infection, pregnancy (women), lactation (women), on medically acceptable form of birth control (women), use of the following drugs in the 2 weeks prior to start of study treatments: theophylline, bismuth salts, warfarin, phenytoin, barbiturates, antineoplastic agents, erythromycin, clarithromycin, sucralfate
Symptoms (describe): Heartburn: None: 0.69% Mild: 32.27% Moderate: 48.22% Severe: 14.16% Unknown: 4.61% Acid regurgitation: None: 10.26% Mild: 37.93% Moderate: 35.19% Severe: 12.42% Unknown: 4.61%	Hiatal hernia (specify whether considered and size used for exclusion): no

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Epigastric pain: None: 21.61% Mild: 35.78% Moderate: 28.39% Severe: 9.57% Unknown: 4.61%	
EGD (performed or not and results): no	Esophagitis/stricture/Barrett's: no
pH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other: H pylori negative: 98.96% H pylori positive: 1.04%

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: B/acceptable	
Blinding: double blinded	Allocation concealment: yes
Intention-to-treat: "modified intention-to-treat", defined as pts who took at least 1 dose of treatment, had diary data after day 8, from sites that followed good clinical practice guidelines	Method of Randomization: computer-generated by study sponsor
Other comments: - pts were allowed to take max of 6 tablets of antacid for heartburn per day. - Not sure if the use of 1-tailed test is appropriate	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		x

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 48.64	N enrolled: 328
%Male: 43.26%	N completed: 281 completed [282 analyzed for efficacy (see modified ITT description), 326 that took at least 1 dose of drug and analyzed for safety]
Race: 83.67% white 10.6% black 4.62% Hispanic 1.06% other	Dropouts/reasons: - adverse event: 13 in esomeprazole group, 11 in lansoprazole group - lost to follow-up: 2 in esomeprazole group, 3 in lansoprazole group - consent withdrawn: 2 in esomeprazole group, 2 in lansoprazole group - protocol noncompliant: 4 in esomeprazole group - unwilling to continue: 2 in lansoprazole group - sponsor/investigator decision: 2 in esomeprazole group, 4 in lansoprazole group - failed entry criteria: 1 in esomeprazole group, in 1 lansoprazole group
BMI: not reported Mean Weight: 87.21	Follow-up period: 8 weeks

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Comments:
there is a 2-week run-in period when all pts took 30mg lansoprazole q day.
Not sure what “sponsor/investigator decision” meant among dropout reasons.
Not sure what is the difference between “consent withdrawn” and “unwilling to continue” among dropout reasons.

Results

Primary outcome(s):
Percentage of heartburn free days

	Least square means ± SEM	90% CI of difference between groups	P value
Esomeprazole (n=138)	54.4 ± 3.1	-9.02, 2.87	See comment
Lansoprazole (n=144)	57.5 ± 2.9		

Secondary outcome(s):
Percentage of nighttime heartburn free days

	Least square means ± SEM	90% CI of difference between groups	P value
Esomeprazole (n=138)	76.6 ± 2.5	-1.82, 7.82	0.31
Lansoprazole (n=144)	73.6 ± 2.4		

Percentage of epigastric pain free days

	Least square means ± SEM	90% CI of difference between groups	P value
Esomeprazole (n=138)	65.0 ± 2.8	-7.27, 3.41	0.55
Lansoprazole (n=144)	66.9 ± 2.6		

Percentage of acid regurgitation free days

	Least square means ± SEM	90% CI of difference between groups	P value
Esomeprazole (n=138)	60.3 ± 2.8	-10.41, 10.40	0.13
Lansoprazole (n=144)	65.3 ± 2.6		

Percentage of pts with any improvements in heartburn from baseline to end of study

	%, n	P value
Esomeprazole (n=138)	83.3%, 115	1.00
Lansoprazole (n=144)	83.3%, 120	

Percentage of pts with any improvements in acid regurgitation from baseline to end of study

	%, n	P value
Esomeprazole (n=138)	76.8%, 106	0.58
Lansoprazole (n=144)	72.9%, 105	

Percentage of pts with any improvements in epigastric pain from baseline to end of study

	%, n	P value
Esomeprazole (n=138)	67.4%, 93	0.32
Lansoprazole (n=144)	61.1%, 88	

Symptom free during final week

	%, n	90% CI of difference between groups	P value
Esomeprazole (n=138)	28%, 39	-5.7, 15.8	0.36
Lansoprazole (n=144)	33%		

Weekly heartburn score

	Baseline week	Final week	P value
Esomeprazole (n=138)	1.3	0.6	Not reported
Lansoprazole (n=144)	1.2	0.6	

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Percentage improvements in weekly symptom score

	Esomeprazole	Lansoprazole
Heartburn	54%	50%
Acid regurgitation	50%	50%
Epigastric pain	39%	44%

Antacid use per day

	Mean number of tablets ± SD	P value
Esomeprazole (n=138)	0.4 ± 0.6	Not reported
Lansoprazole (n=144)	0.5 ± 0.7	

The severity of heartburn was similar between groups at both week 4 and week 8.

Comments:
Test for primary analyses were 1-tailed; tests for secondary analyses were 2-tailed. Note that the CIs presented are 90% CIs. Not sure if the use of 1-tailed test is appropriate.
Authors claimed to have determined that esomeprazole was not inferior if the lower limit of the 90%CI was greater than -10, and therefore concluded that this study showed that esomeprazole is at least as effective as lansoprazole.

Compliance:
Study drug noncompliance in 5 pts in esomeprazole group and 4 pts in lansoprazole group (all included in analyses)
85% (136/160) pts in esomeprazole group and 87.5% (147/168) pts in lansoprazole group took study drugs for at least 50 days.

Adverse Events:
4 pts had serious adverse events that are unrelated to treatment: mental disorder, uterine hemorrhage, tongue carcinoma, pneumonia.
1 pt had increased alanine aminotransferase (unrelated to treatment assessed by the investigators).
Any adverse events
    Esomeprazole (n=159): 72 (45.3%)
    Lansoprazole (n=167): 65 (38.9%)
Abdominal pain
    Esomeprazole (n=159): 11 (6.9%)
    Lansoprazole (n=167): 5 (3.0%)
Diarrhea
    Esomeprazole (n=159): 4 (2.5%)
    Lansoprazole (n=167): 12 (7.2%)
Nausea
    Esomeprazole (n=159): 9 (5.7%)
    Lansoprazole (n=167): 7 (4.2%)
Respiratory infection
    Esomeprazole (n=159): 6 (3.8%)
    Lansoprazole (n=167): 8 (4.8%)
Headache
    Esomeprazole (n=159): 5 (3.1%)
    Lansoprazole (n=167): 5 (3.0%)
Flatulence
    Esomeprazole (n=159): 5 (3.1%)
    Lansoprazole (n=167): 3 (1.8%)
Epigastric pain
    Esomeprazole (n=159): 2 (1.3%)
    Lansoprazole (n=167): 5 (3.0%)
Bronchitis
    Esomeprazole (n=159): 2 (1.3%)
    Lansoprazole (n=167): 4 (2.4%)
Vomiting
    Esomeprazole (n=159): 2 (1.3%)
    Lansoprazole (n=167): 4 (2.4%)
Pain
    Esomeprazole (n=159): 4 (2.5%)
    Lansoprazole (n=167): 3 (1.8%)
Gastroenteritis
    Esomeprazole (n=159): 5 (3.1%)
    Lansoprazole (n=167): 0 (0%)
Sinusitis
    Esomeprazole (n=159): 0 (0%)
    Lansoprazole (n=167): 5 (3.0%)

Adverse events that led to withdrawals: abdominal pain (4 in esomeprazole group, 3 in lansoprazole group), nausea (4 in esomeprazole group, 0 in lansoprazole group), exacerbation of GERD (1 in esomeprazole group, 3 in lansoprazole group).

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Fass	**Yr:2009**	**UI: 19392864**	**Questions addressed: 1,3**	**Extractor: DM**

Objective/Topic:
Efficacy and safety of dexlansoprazole MR once daily for 4 weeks for relief of heartburn in patients with non-erosive reflux disease (NERD)

Study design:	**Country/Setting:**	**Funding:**
3 arm RCT	USA / community	Industry (TAP Pharmaceutical Products, Inc., Lake Forest, IL, USA, now part of Takeda Global Research & Development Center, Inc.)

Interventions(s):	**Comparator(s):**
Dexlansoprazole MR 30 mg, Dexlansoprazole MR 60 mg	Placebo

Primary outcome(s):	**Other outcome(s):**
Percentage of 24-h heartburn-free days (days with neither daytime nor nighttime heartburn) - *Assessed by a daily electronic diary*	**Patient-reported symptom severity** *Patients rated the severity of heartburn according to the following five point scale: 0 = none, 1 = mild (occasional heartburn that did not influence the patient's daily routine), 2 = moderate (heartburn that could not be ignored; occasionally influenced the patient's daily routine Investigator-reported symptom severity at week 4), 3 = severe (heartburn was present for most of the day; regularly influenced patient's daily routine) and 4 = very severe (constant heartburn; markedly influenced patient's daily routine).* *The PAGI-Symptom Severity Index (PAGI-SYM) is a brief symptom severity instrument (subscales: nausea/ vomiting, fullness/ early satiety/ bloating, upper and lower abdominal pain and heartburn/ regurgitation).* **Patient-reported QOL** *The Patient Assessment of Upper Gastrointestinal Disorders Quality-of-Life Index (PAGI-QOL) assesses health-related QOL in patients with GERD, dyspepsia and gastroparesis (subscales: daily activities, clothing, diet and food habits, relationship, and psychological well-being and distress).* **Investigators assessed GERD symptoms (heartburn, acid regurgitation, dysphagia, belching and epigastric pain)** *Evaluated as none, mild, moderate, severe or very severe during the 7 days before the patient's study visit and throughout the treatment period.* **Percentage of nights without heartburn** **Percentage of days without daytime heartburn** **Mean severity of heartburn**

	Percentage of patients with 24-h heartburn-free days, nights without heartburn, and days without daytime heartburn during the first 3 days of treatment; **Time to sustained resolution of heartburn** - *Defined as the first occurrence of 7 consecutive 24-h heartburn-free days* **Percentage of days without rescue medication use;**

Inclusion criteria: Men and women ≥ 18 years with heartburn; history of heartburn for ≥ 6 months; experienced heartburn on at least 4 of the 7 days preceding randomization; normal oesophageal mucosa at the screening endoscopy	**Exclusion criteria:** pregnancy or lactation; Barrett's oesophagus; active gastric or duodenal ulcers within 4 weeks of the first dose of study drug; coexisting diseases affecting the oesophagus or erosive esophagitis by endoscopy; history of gastric, duodenal or oesophageal surgery; oesophageal strictures requiring dilatation; use of a PPI, histimine-2 receptor agonist, antacid [except study-supplied Gelusil (aluminum/magnesium hydroxide, simethicone; Pfizer Inc., New York, NY, USA)], anticholinergic, sucralfate or prokinetic agent during screening and throughout the study; known hypersensitivity to PPIs or Gelusil; long-term use (>12 doses/month) of NSAIDs within 30 days before screening and throughout the study (low-dose aspirin ≤ 325 mg/day allowed); clinically significant abnormal laboratory values or uncontrolled systemic disease.
Symptoms (describe): Median mean severity for nighttime heartburn: 1.14 (range: 1.57 to 1.60 for patients with daytime heartburn and range: 1.21 to 1.36 for patients with daytime/nighttime heartburn).	**Hiatal hernia (specify whether considered and size used for exclusion):** nd
EGD (performed or not and results): yes (at screening) 100% Non-erosive reflux disease	**Esophagitis/stricture/Barrett's:** see EGD results
PH study (performed or not and results): nd	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): nd	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: A/rigorous	
Blinding: Yes	**Allocation concealment: Yes**
Intention-to-treat: Yes	**Method of Randomization:** Computer generated - Interactive Voice Response System (IVRS; ClinPhone, Inc., Northbrook, IL, USA)
Other comments:	

Quality Assessment Non-RCTs:
Comments:

GERD data extraction form

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
X		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 47.5 ± 13.9 years	**N enrolled: 947**
%Male: 28.9%	**N completed: 873**
Race: White: 773 (81.6) Black: 130 (13.7) Asian: 16 (1.7) Multiracial: 13 (1.4) Unknown: 6 (0.6) American Indian or Alaskan: 5 (0.5) Native Hawaiian or other Pacific Islander: 4 (0.4)	**Dropouts/reasons:** Dexlansoprazole MR 30 mg (n=21) - Adverse event (6), Protocol Violation (1), Lost to follow-up (4), Withdrew consent (6), Did not meet Inclusion/exclusion criteria (1), Other (3) Dexlansoprazole MR 60 mg (n=26) - Adverse event (8), Protocol Violation (1), Lost to follow-up (2), Withdrew consent (5), Did not meet Inclusion/exclusion criteria (5), Other (5) Placebo (n=27) - Adverse event (9), Lost to follow-up (2), Withdrew consent (8), Did not meet Inclusion/exclusion criteria (3), Other (5)
BMI: 29.2 ± 6.8 kg/m^2	**Follow-up period: 4 weeks**
Comments:	

Results

Primary outcome(s):

Percentage of 24-h heartburn-free days
The median percentage of 24-h heartburn-free days was significantly greater in both the Dexlansoprazole MR 30 mg (54.9%) and 60 mg (50%) treatment groups compared with the placebo group (18.5%; $p < 0.00001$)

Secondary outcome(s):

Patient-reported symptom severity (No data, only text)
"The PAGI-SYM total score, as well as the subscale scores for fullness/early satiety and heartburn/regurgitation, was significantly better for the Dexlansoprazole MR treatment groups compared with the placebo group at all patient visits ($P < 0.005$)."

Patient-reported QOL (No data, only text)
"For the PAGIQOL, the total score and score for the diet and food habits subscale were significantly greater for both Dexlansoprazole MR treatment groups compared with the placebo group at all visits ($P < 0.001$)."

Investigator-assessed GERD symptoms
≥ 1 category improvement in investigator-assessed heartburn severity at week 4:
Dexlansoprazole MR 30 mg (76.9%), Dexlansoprazole MR 60 mg (80.4%), placebo (56.6%), $p < 0.00001$

Improvement from baseline in investigator-assessed acid regurgitation at week 4:
Dexlansoprazole MR 30 mg (67.4%), Dexlansoprazole MR 60 mg (62.6%), placebo (58.4%), NS

Percentage of nights without heartburn
The median percentage of 24-h heartburn-free days was significantly greater in both the Dexlansoprazole MR 30 mg (80.8%) and 60 mg (76.9%) treatment groups compared with the placebo group (51.7%; $p < 0.00001$)

Percentage of days without daytime heartburn
The median percentage of 24-h heartburn-free days was significantly greater in both the Dexlansoprazole MR 30 mg (63%) and 60 mg (63%) treatment groups compared with the placebo group (26.9%; $p < 0.00001$)

Mean severity of heartburn

For daytime/night time heartburn: Dexlansoprazole MR 30 mg (0.66), Dexlansoprazole MR 60 mg (0.69), placebo (1.04), $p < 0.00001$
For night time heartburn: Dexlansoprazole MR 30 mg (0.56), Dexlansoprazole MR 60 mg (0.60), placebo (0.9), $p < 0.00001$
For daytime heartburn: Dexlansoprazole MR 30 mg (0.74), Dexlansoprazole MR 60 mg (0.76), placebo (1.15), $p < 0.00001$

Percentage of patients with 24-h heartburn-free days during the first 3 days of treatment
Dexlansoprazole MR 30 mg (13.9%), Dexlansoprazole MR 60 mg (16.2%), placebo (2.2%), $p < 0.00001$

Percentage of patients with nights without heartburn during the first 3 days of treatment
Dexlansoprazole MR 30 mg (38%), Dexlansoprazole MR 60 mg (39.8%), placebo (17.3%), $p < 0.00001$

Percentage of patients with days without heartburn during the first 3 days of treatment
Dexlansoprazole MR 30 mg (18.5%), Dexlansoprazole MR 60 mg (19.8%), placebo (8.7%), $p < 0.01$

Percentage of patients with sustained resolution of heartburn
Dexlansoprazole MR 30 mg (59%), Dexlansoprazole MR 60 mg (42%), placebo (14%), $p < 0.00001$

Percentage of days without rescue medication use;
Dexlansoprazole MR 30 mg (63%), Dexlansoprazole MR 60 mg (63%), placebo (37.3%), $p < 0.00001$

Comments:

Compliance:

Adverse Events:
The incidence of treatment-emergent AEs: Dexlansoprazole MR 30 mg (35%), Dexlansoprazole MR 60 mg (32%), placebo (32%); Most frequent: Diarrhoea, headache, and nausea and vomiting were the most frequently reported (≥5% of patients in any treatment group)
>1 AE that led to withdrawal: Dexlansoprazole MR 30 mg (6/315 – 1.9%), Dexlansoprazole MR 60 mg (8/315 – 2.5%), placebo (11/317 – 3.5%)
Serious AEs (SAEs) during treatment: Dexlansoprazole MR 30 mg (2/315 – 0.6%), Dexlansoprazole MR 60 mg (1/315 – 0.3%), placebo (1/317 – 0.3%)
Change in serum gastrin values from baseline to week 4: Dexlansoprazole MR 30 mg (103.6 pg/mL), Dexlansoprazole MR 60 mg (97.0 pg/mL), placebo (0.9 pg/mL), $p < 0.001$

Applicability: (narrow/wide): wide	**Comments:**

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Author: Fein	Yr: 2008	UI: 18766417	Questions addressed: KQ1	Extractor: SI

Objective/Topic: analyze 10 y follow up of laparoscopic antireflux surgery

Study design: cohort	Country/Setting: Germany	Funding: nd

Interventions(s): laparoscopic fundoplication (Nissen, anterior, Toupet)	Comparator(s):

Primary outcome(s): symptoms, intake of acid-suppressive drugs	Other outcome(s):

Inclusion criteria: patients who had antireflux surgery	Exclusion criteria: had undergone primary open surgery, redo
Symptoms (describe): 82% heartburn; 56% regurgitation	Hiatal hernia (specify whether considered and size used for exclusion): 58% had hiatal hernia preop
EGD (performed or not and results): 56% had esophagitis preop	Esophagitis/stricture/Barrett's:
pH study (performed or not and results): preop pH score = 43.4 (unclear what scale was this)	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results): LES preop 5.3	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) not applicable

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: retrospective design; patient flow unclear; historical comparison

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		x

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 49±14	N enrolled: 120
%Male: 66	N completed: 99/114 (unclear why 114)
Race: nd	Dropouts/reasons: nd
BMI:	Follow-up period: 5 or more years

GERD data extraction form

Comments:

Results

Primary outcome(s):
GI symptoms at 10 y for 99 pts

heartburn 29%
regurgitation 19%

	Nissen (74)	Anterior fundo (16)	Toupet (9)
Heartburn (%)	29.7	37.5	12.5
Regurgitation (%)	15.1	43.8	10.0 (P=0.035)

taking acid suppressive drugs: 28% (27/99)

Secondary outcome(s):
GI quality of life according to GIQIL 109 (significantly higher than preop values (not reported)).

Nissen (73)	Anterior fundo (14)	Toupet (8)
GI QIL 109.8±24.4	104.1±26.9	115.1±21.0

Comments:

Compliance:

Adverse Events:
Prevalence of Gastrointestinal Symptoms According to OP Procedure (%): Results at 10-Year Follow-up

Symptoms	Nissen N=74	Anterior fundopl. N=16	Toupet N=9
Dysphagia	30.6	31.3	28.6
Epigastric pain	43.8	56.3	50.0
Epigastric fullness	60.3	62.5	57.1
Vomiting	18.8	17.8	50.0
Chest pain	38.4	56.3	37.5
Bloating	84.9	75.0	50.0

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Fock	Yr: 2005	UI: 15918196	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
Compare efficacy and safety of Rabeprazole (10 mg) vs. Esomeprazole (20 mg) among GERD pts

Study design:	Country/Setting:	Funding:
RCT	Singapore	Not reported

Interventions(s):	Comparator(s):
Rabeprazole (10 mg) q day for 4 weeks Pts were allowed to take antacid if needed.	Esomeprazole (20 mg) q day for 4 weeks Pts were allowed to take antacid if needed.

Primary outcome(s):	Other outcome(s):
Time to first 24-hr symptom free interval	Satisfactory relief of daytime and nighttime symptoms Complete relief of daytime and nighttime symptoms Antacid use Overall evaluation by pts Safety

Inclusion criteria:	Exclusion criteria:
21 to 65 years old History of heartburn or regurgitation for at least 3 months in the previous year At least 1 moderate-to-very-severe heartburn or regurgitation in the 7 days before treatment No esophageal mucosal break Ability to read and write in English or Chinese	history of gastroduodenal ulcer; infectious or inflammatory conditions of the intestine (including inflammatory bowel disease); malabsorption syndromes; obstruction; gastrointestinal malignancy; gastric or intestinal surgery including vagotomy; Barrett's esophagus; esophageal stricture or pyloric stenosis; scleroderma; erosive esophagitis; positive HIV status; pregnancy; abnormal laboratory tests at screening (including liver enzymes greater than twice the upper limit of normal); GERD treatment refractory to a 2-mo course of H_2-blocker or PPI therapy; taken a PPI within 14 d of screening or a H_2-blocker or prokinetic agent within 7 d of screening; required daily use of NSAIDS, oral steroids, aspirin (>325 mg/d); or were unable to discontinue the use of anticholinergics, cholinergics, spasmolytics, opiates or sucralfate
Symptoms (describe): no	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): Yes, all grade 0	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other: H pylori negative: 62 pts H pylori positive: 50 pts H pylori information missing: 15 pts Mean duration of GERD: 3.6 yr

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

GERD data extraction form

Quality Assessment for RCTs: B/acceptable	
Blinding: “double-blinding”, pts were blinded.	Allocation concealment: no
Intention-to-treat: yes (defined as those having at least 1 post-baseline assessment)	Method of Randomization: computer-generated randomization scheme
Other comments: - There was no measure of compliance. - Authors reported using ITT, but number of pts in reported data varied from outcome to outcome, indicating that ITT was not performed.	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 38.9	N enrolled: 134
%Male:51.2%	N completed: 127
Race: 79.5% Chinese 7.1% Malay 11.8% Indian 1.6% other	Dropouts/reasons: 5 did not take any treatment, 1 had persistent headache, 1 withdrew consent
BMI: not reported	Follow-up period: 4 weeks
Comments: 1 week screening period prior to treatment period	

Results

Primary outcome(s):

Time to first 24-hr symptom free interval

	Rabeprazole 10mg	Esomeprazole 20mg	p-value
Heartburn	8.5 days	9 days	0.265
Acid regurgitation	6 days	7.5 days	0.405

Percentage of pt with 24-hr symptom free during the 4-week period

	Rabeprazole 10mg	Esomeprazole 20mg	p-value
Heartburn	84.4%	60.9%	NS
Acid regurgitation	90%	67.9%	NS

Secondary outcome(s):

Time to first 48-hr symptom free interval

	Rabeprazole 10mg	Esomeprazole 20mg	p-value
Heartburn	9.5 days	8.5 days	0.373
Acid regurgitation	8.5 days	11 days	0.271

Satisfactory relief of daytime and nighttime symptoms, defined as no episode of having moderate or severe in severity during the week, in 81.4-98% of pts.

Among pts with both heartburn and acid regurgitation, percentage of pts with satisfactory symptom relief:

Rabeprazole 10mg: 92.5% (37 out of 40 pts)
Esomeprazole 20mg: 79.4% (27 out of 34 pts)
p-value: <0.05

Complete relief of daytime and nighttime heartburn

	Rabeprazole 10mg	Esomeprazole 20mg	p-value
Daytime	55.3% (26 out of 47)	41.1% (18 out of 43)	NS

Nighttime	44.4% (20 out of 45)	41% (16 out of 39)	NS

Complete relief of daytime and nighttime acid regurgitation: NS, data not reported

Antacid use

	Rabeprazole 10mg	Esomeprazole 20mg	p-value
Weekly average	0.15	0.16	0.887
% of pts antacid free	85.7%	84.9%	0.848

Overall symptom improved, evaluated by pts
Rabeprazole 10mg: 96.4% (54 out of 56 pts)
Esomeprazole 20mg: 87.9% (51 out of 58 pts)
p-value: 0.823

Comments:
Authors reported using ITT, but number of pts in reported data varied from outcome to outcome, indicating that ITT was not performed.

Compliance:
Not reported

Adverse Events:
Analyzed in 129 pts who took at least 1 dose of medication

	Rabeprazole 10mg	Esomeprazole 20mg	p-value
Any adverse events	22%	18.2%	NS
Withdrew from study due to persistent headache	0 pt	1 pt	NS
Elevated ALT	1 pt	4 pts	NS
Elevated AST	1 pt	2 pts	NS

Applicability: (narrow/wide): narrow	Comments: in Asia, no funding source information reported

GERD data extraction form

Author: Franzen	Yr: 2005	UI: 16334434	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
Compare laparoscopic vs. conventional Nissen fundoplication

Study design:	Country/Setting:	Funding:
RCT	Sweden, single location	Not reported

Interventions(s):	Comparator(s):
Laparoscopic 1-2cm 360º floppy Nissen fundoplication with complete fundic mobilization and crural repair	Conventional, open 1-2cm 360º floppy Nissen fundoplication with complete fundic mobilization and crural repair

Primary outcome(s):	Other outcome(s):

Inclusion criteria:	Exclusion criteria:
6 months PPI tx prior to surgery (with or without sucess)	Mixed or paraesophageal hernia, suspected short esophagus, previous operation on stomach, has upper midline scar, BMI>35, weak esophageal peristalsis (amplitudes ≤30mmHg)
Symptoms (describe): Symptom duration <1 year: 5.38% 1-5 year: 25.91% >5 year: 68.82% Dysphagia: 15 in laparoscopy group, 14 in open surgery group	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): yes No or healed esophagitis: 93.55% Unhealed esophagitis: 2.15%	Esophagitis/stricture/Barrett's: Barrett esophagitis: 4.30%
PH study (performed or not and results): yes	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): 59.14% responded to 6-month PPI therapy
Esophageal manometric studies (performed or not and results): yes mean lower esophageal sphincter pressure: 7.5mmHg	Other: % total reflux time at 24hr: 6.1

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: C/Poor	
Blinding: no	Allocation concealment: no
Intention-to-treat: no	Method of Randomization: not reported "in series of 10"

GERD data extraction form

Other comments: 1 pts randomized to the laparoscopic group ended up having open surgery, and was analyzed as open surgery group.

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 50.01 years	N enrolled: 100
%Male: 53.76%	N completed: 93
Race: not reported	Dropouts/reasons: 4 pt withdraw (2 per group), 3 esophageal shortening (2 in laparoscopic, 1 in open)
BMI: not reported	Follow-up period: 57 months for laparoscopic group, 52 months for open surgery group
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments: not clear which is primary outcome

Compliance:

Adverse Events:

Applicability: (narrow/wide):	Comments:

GERD data extraction form

Author: Fujiwara	**Yr**: 2005	**UI**: 15943841	**Questions addressed**: 1	**Extractor**: JC

Objective/Topic: The aim of the study was to examine and evaluate the effectiveness of a PPI (omeprazole 20 mg) vs. an H_2RA (famotidine 20 mg) in Japanese patients (H. Pylori more common) with non-erosive GERD, by assessment of GERD symptoms and health related QoL.

Study design: RCT	**Country/Setting**: Japan/Multicenter	**Funding**: supported , in part, by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture in Japan

Interventions(s): omeprazole 20mg o.d.	**Comparator(s)**: famotidine 20mg b.d.

Primary outcome(s): Frequency of gastro-oesophageal reflux disease symptoms and health-related quality of life were evaluated at baseline and after 4 weeks of treatment in pts with and without H. pylori infection.	**Other outcome(s)**: Health-related quality of life was evaluated at baseline and after 4 weeks of treatment in pts with and without H. pylori infection.

Inclusion criteria: Patients were eligible if they were out-patients with non-erosive GERD and were ≥20 years of age. A diagnosis of non-erosive GERD was made if the patient's primary symptom was significant heartburn (a burning sensation or discomfort behind the breast bone in the chest) and/or acid regurgitation (a bitter- or sour tasting fluid coming into the throat or mouth) which occurred at least twice weekly and had been present for ≥1 month, and if endoscopic examination revealed no mucosal break of the oesophageal mucosa by Los Angeles classification.	**Exclusion criteria:** Patients were ineligible for enrolment if they were pregnant or nursing mother, or had Barrett's oesophagus or oesophageal stricture. Disease-related exclusion criteria included the following: severe disease of any major body system; malignant disease of any kind; clinically relevant deviations from the normal reference range in laboratory studies assessed by the investigator, active peptic ulcer disease, depression or any other psychiatric disease associated with worsened QoL, past history of upper GI tract surgery and H. pylori eradication. Patients were also ineligible if they had received acid-suppressive drugs continuously during the previous month.
Symptoms (describe): Patients were asked the frequency of GERD symptoms at baseline and after 4 weeks of treatment, and personal memo cards were completed daily by patients during treatment. To assess QoL, patients completed two standardized QoL questionnaires, the Gastrointestinal Symptom Rating Scale (GSRS)--designed to measure the amount of discomfort a patient has experienced (none at all, minor, mild, moderate, moderately severe, severe and very severe) across five symptom clusters: reflux, abdominal pain, indigestion, diarrhea and constipation--and the Medical Outcomes Study Short Form-36 (SF-36) at baseline and after 4 weeks of treatment.	**Hiatal hernia (specify whether considered and size used for exclusion)**: Considered but not used for exclusion.
EGD (performed or not and results): Performed to	**Esophagitis/stricture/Barrett's**: Pts. with Barrett's

assess mucosal break of the oesophageal mucosa by Los Angeles classification. See inclusion criteria above. Endoscopic appearance of nonerosive GERD was classified as normal (N) and minimal change (M). **Endoscopic appearance (N/M)** omeprazole bd: 30/20; famotidine bd: 28/20; p = .867	oesophagus or oesophageal stricture excluded. See exclusion criteria.
pH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Patients with past history of upper GI tract surgery, H. pylori eradication or receipt of acid-suppressive drugs continuously during the previous month were excluded per criteria above.
Esophageal manometric studies (performed or not and results): Not performed	Other: Body mass index (BMI) calculated by height and body weight, smoking habits, drinking habits and H. pylori infection were examined before treatment. Helicobacter pylori infection was considered present when at least two of the following tests were positive; serum anti-H. pylori immunoglobulin G (IgG) antibodies, culture or histological examination of antral and corpus biopsy specimens, or the C-urea breath test. Efficacy of treatment was categorized as follows: complete relief (CR), defined as no GERD symptoms during the 7-day interval in week 4; partial relief (PR), a decrease in frequency but not CR of GERD symptoms during the 7-day interval in week 4 compared with baseline; and no response (NR), characterized as no change or increase in frequency of GERD symptoms between baseline and after treatment.

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: C	
Blinding: Not described	Allocation concealment: Not described
Intention-to-treat: Not described	Method of Randomization: Yes, process not described.
Other comments: small multicenter RCT lacking rigorous description of study methodology with short 4 week follow up.	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
X		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects

GERD data extraction form

Age: omeprazole bd: 55.0 ± 16.7; famotidine bd: 56.6 ± 15.5; p = .624	N enrolled: 106
%Male: omeprazole bd: 40.0%; famotidine bd: 52.1%; p = .430	N completed: 98
Race: All Japanese pts.	Dropouts/reasons: 5 patients in the famotidine group and 3 patients in the omeprazole group did not visit after 4 weeks of treatment.
BMI: omeprazole bd: 22.8 ± 4.2; famotidine bd: 22.2 ± 3.0; p = .408	Follow-up period: 4 weeks
Comments:	

Results

Primary outcome(s): no differences in efficacy between famotidine and omeprazole groups (P = 0.385 by chi-square test).

Omeprazole treatment had a higher CR rate (56.0%) compared with famotidine treatment (47.9%) but statistically no significant differences were observed (P = 0.423 by chi-square test).

In H. pylori-positive patients, CR rate was similar between famotidine and omeprazole (63.6 and 59.1%) while famotidine had a lower CR rate compared with the omeprazole group in H. pylori negative patients (34.5 and 53.6%, P = 0.069 by chi-square test).

In the famotidine group, a **significantly** lower CR rate in H. pylori-negative patients than those in H. pylori-positive patients was observed (P = 0.045 by chi-square test).

There was no significant difference in NR rate between famotidine and omeprazole groups (P = 0.552 by chi-square test).

Efficacy of famotidine and omeprazole on control of GERD symptoms after 4 weeks of treatment

		Efficacy of treatment (%)		
	N	CR	PR	NR
Famotidine				
H.pylori-positive	22	14 (63.6)	3 (13.6)	5 (22.7)
H. pylori-negative	26	9 (34.5)	10 (38.5)	7 (26.9)
Total	48	23 (47.9)	13 (27.1)	12 (25.0)
Omeprazole				
H. pylori-positive	22	13 (59.1)	5 (22.7)	4 (18.2)
H. pylori-negative	28	15 (53.6)	10 (35.7)	3 (10.7)
Total	50	28 (56.0)	15 (30.0)	7 (14.0)

CR, complete relief; PR, partial relief; NR, no response

Secondary outcome(s): There were no significant differences in baseline GSRS scores including total and each dimension between famotidine and omeprazole groups.

Both famotidine and omeprazole significantly decreased GSRS scores in total dimensions and category for reflux, abdominal pain and indigestion. Famotidine also decreased in category score for diarrhea and constipation.

Changes in reflux score were highest among GSRS category, and there were no significant differences in total and each dimensions of GSRS between famotidine and omeprazole groups.

Baseline values of GSRS scores & changes between baseline & after 4 weeks of treatment

	Baseline		**Visit week 4**		
GSRS	Mean	s.d.	Mean	s.d.	P-value
Reflux					
Famotidine	3.18	1.38	2.37	1.29	0.002
Omeprazole	3.33	1.49	2.36	1.42	<0.001
Abdominal pain					
Famotidine	2.61	1.15	2.38	1.22	0.013
Omeprazole	2.65	1.43	2.02	1.21	0.002
Indigestion					
Famotidine	2.60	0.96	2.13	0.85	0.002
Omeprazole	2.33	1.03	2.07	1.05	0.029
Diarrhoea					
Famotidine	2.20	1.16	1.76	0.95	0.002
Omeprazole	1.99	1.02	1.80	1.12	0.115
Constipation					
Famotidine	2.67	1.37	2.19	1.06	0.012
Omeprazole	2.68	1.46	2.29	1.21	0.057
Total dimensions					
Famotidine	2.54	0.81	2.12	0.73	0.001
Omeprazole	2.53	0.93	2.11	0.91	<0.001

Changes in GSRS reflux scores according to the H. pylori infection status demonstrate that both famotidine and omeprazole significantly decreased GSRS reflux scores after 4 weeks of treatment, and this observation was found in H. pylori-positive patients. In H. pylori-negative patients, omeprazole significantly decreased reflux scores, however, no significant change was observed in the famotidine group. (Difficult to interpret actual #'s from Figure 2.)

SF-36

SF-36 domains	**Baseline visit**		**week 4**		**P-value***
	Mean	**s.d.**	**Mean**	**s.d.**	
Physical functioning					
Famotidine	80.7	18.7	78.4	20.9	0.16
Omeprazole	78.8	20.4	80.8	21.7	0.037
Role-physical					
Famotidine	59.6	43.2	69.9	41.6	0.067
Omeprazole	59.2	40.4	69.6	39.4	0.004
Bodily pain					

Famotidine	57.7	22.1	66	22.6	0.044
Omeprazole	55.2	24.1	65.8	23.5	0.012
General health					
Famotidine	46.1	18.2	52.8	17.8	0.004
Omeprazole	48.7	17.8	53	19.6	0.03
Vitality					
Famotidine	50.7	23.6	54.8	22	0.275
Omeprazole	48.9	21.8	57.4	22.3	0.001
Social functioning					
Famotidine	69.4	25.8	78.9	21.8	0.03
Omeprazole	77	26.7	80.7	20.3	0.197
Role-emotional					
Famotidine	57.4	41.7	73.5	39.1	0.028
Omeprazole	69.3	96.5	66.4	43.1	0.084
Mental health					
Famotidine	55.6	22.1	66.5	23.6	0.023
Omeprazole	57.1	25.5	65.2	23.1	0.001

*Analysed by the Wilcoxon matched pairs single ranks test.

Comments: Approximate heartburn symptoms estimated from graph (figure 4).

Compliance: 5 patients in the famotidine group and 3 patients in the omeprazole group did not visit after 4 weeks of treatment.

Adverse Events:
Any significant deterioration in clinical status was considered to be an adverse event and was recorded on the case report form. No serious adverse effects or complications were encountered during the treatment.

Applicability: (narrow/wide): Narrow	Comments: Tx population consists of 98 Japanese pts with non-erosive GERD.

KQ3 result template and instruction: Please use the primary GERD extraction form. Please indicate if adverse events were the primary outcome, and report the data in the adverse events section. Do make an attempt to extract n/N for the adverse event (subjects affected/total population at risk).

Author: Fumagalli	**Yr: 2008**	**UI: 18430108**	**Questions addressed: 3**	**Extractor: JC**

Objective/Topic: Determine frequency of postoperative dysphagia, and assess treatments and outcomes for pts undergoing laparoscopic antireflux surgery for GERD

Study design: Retrospective cohort	**Country/Setting: Italy, multicenter**	**Funding: ND**

Interventions(s): Toupet partial posterior fundoplication (22 cases) 360° Nissen (210 cases) Nissen-Rossetti (43 cases) Collis-Nissen fundoplication (1 case)	**Comparator(s): None**

Primary outcome(s): presence and severity of postoperative dysphagia	**Other outcome(s):**

Inclusion criteria: Pts undergoing fundoplication for GERD. Those with clearly reduced motility received Toupet partial posterior fundoplication (22 cases); those with normal motility received 360° Nissen (210 cases) or Nissen-Rossetti (43 cases) total fundoplication. One patient received Collis-Nissen fundoplication for a short esophagus.	**Exclusion criteria: Not described**
Symptoms (describe): Dysphagia using DeMeester Scores	**Hiatal hernia (specify whether considered and size used for exclusion):** Not described.
EGD (performed or not and results): Not described	**Esophagitis/stricture/Barrett's: Not described.**
PH study (performed or not and results): Not described	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): Not described**
Esophageal manometric studies (performed or not and results): Performed, Those with clearly reduced motility received Toupet partial posterior fundoplication (22 cases); those with normal motility received 360° Nissen (210 cases) or Nissen-Rossetti (43 cases) total fundoplication. One patient received Collis-Nissen fundoplication for a short esophagus.	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) No, see inclusion criteria based on esophageal motility

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding: n/a	**Allocation concealment: n/a**
Intention-to-treat: n/a	**Method of Randomization: n/a**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: Limited description of study design methods; criteria for GERD dx not described; limited inclusion/exclusion criteria.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
C= Diagnosis of GERD not described		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: ND	**N enrolled: 276**
%Male: ND	**N completed: 276**
Race: ND	**Dropouts/reasons: n/a**
BMI: ND	**Follow-up period: 1 month post surgery, then every 6 months (total follow up duration not described)**
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Compliance: Redo surgery needed in 1.4% of cases.

Adverse Events:
25/276 (9.1%) marked post-operative dysphasia (DeMeester grade 2 or 3) during follow-up—10 (3.6%) requiring tx for dysphasia. **Among the 24 patients who had preoperative dysphagia:** 5 had persistence of this symptom postop (20.8%); however, it was clinically significant and persistent in 2 pts (8.3%). No correlation found b/w preop and postop persistent dysphagia (chi-square test; *P* =0.067).

Applicability: (narrow/wide): Narrow	**Comments: Single country Retrospective Cohort study; pt characteristics not described**

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

GERD data extraction form

Author: Zheng	**Yr: 2009**	**UI: 19248200**	**Questions addressed:**	**Extractor: DM**

Objective/Topic:

Study design:	**Country/Setting:**	**Funding:**

Interventions(s):	**Comparator(s):**

Primary outcome(s):	**Other outcome(s):**

Inclusion criteria:	**Exclusion criteria:**
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):**
EGD (performed or not and results):	**Esophagitis/stricture/Barrett's:**
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results):	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age:	**N enrolled:**
%Male:	**N completed:**
Race:	**Dropouts/reasons:**
BMI:	**Follow-up period:**

GERD data extraction form

Comments:

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Compliance:

Adverse Events:

Applicability: (narrow/wide):	**Comments:**

GERD data extraction form

Author: Gee	Yr: 2008	UI: 18490558	Questions addressed: 2,3	Extractor: SI

Objective/Topic: long term results from laparoscopic antireflux surgery by BMI, sex

Study design: retrospective cohort	Country/Setting: US	Funding: nd

Interventions(s): Nissen or Toupet laparoscopic fundoplication	Comparator(s): none

Primary outcome(s): GERD-HRQL	Other outcome(s):

Inclusion criteria: GERD related symptoms; criteria for surgery: abnormal 24-h pH recording; erosive esophagitis; or significant improvement of reflux symptoms with antireflux meds	Exclusion criteria: no valid address
Symptoms (describe): typical symptoms (heartburn, regurgitation) 56%; atypical symptoms (cough, upper respiratory symptoms) 41%; dysphagia 3%	Hiatal hernia (specify whether considered and size used for exclusion): 41/173 had paraesophageal hernia
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
pH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: 54% eligible responded; nonresponders were older; no statistical adjustment

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 52	N enrolled: 405
%Male: 40	N completed: 191 (173 primary, 18 redos)
Race: nd	Dropouts/reasons:
BMI:	Follow-up period:
Comments:	

Results
Primary outcome(s): 5 yr HRQL by BMI <25 6.84 (SD 9.36) 25-29.9 3.48 (SD 5.26) 30-34.9 5.21 (SD 6.27) ≥35 11.36 (SD 11.78), P<0.05 compared to 30-34.9 and 25-29.9
Secondary outcome(s): No sex difference overall within the subsets of BMI: women had higher GERD-HRQL scores as BMI increased (P=0.04), men had lower GERD-HRQL scores as BMI increased (P=0.17)
Comments:

Treatment/Comparison:	laparoscopic fundoplication					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
Sex					overall no effect; women with higher BMI were worse; no trend observed in men	
BMI/weight					high BMI associated with worse outcome	

Compliance:

Adverse Events:
5/173 primary required postop upper endoscopy and dilatation 2/173 required reoperation

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Giannini	Yr: 2008	UI:18289194	Questions addressed: 1	Extractor: SI

Objective/Topic: empirical treatment with esomeprazole vs. endoscopy-based treatment with esomeprazole

Study design: RCT	Country/Setting: Italy	Funding: AstraZeneca

Interventions(s): empirical treatment with esomeprazole 40 mg daily for 4 wk *followed by esomeprazole 20 mg od maintenance treatment in both groups	Comparator(s): endoscopy-based treatment: no esophagitis esomeprazole 20 mg daily for 4 wk; esophagitis esomeprazole 40 mg daily for 4 wk

Primary outcome(s): symptom after 4 wk and 20 wk	Other outcome(s):

Inclusion criteria: 18–70 yr; at least 3 mo GERD symptoms (heartburn with or without acid regurgitation) and without alarm symptoms (unintentional weight loss, recurrent dysphagia, anemia [men, <14 g/dL; women, <12 g/dL], hematemesis, melena); see criteria based on results from run-in period below	Exclusion criteria: current or history of the following diseases: previous esophageal, gastric, or duodenal surgery; Zollinger-Ellison syndrome; achalasia; scleroderma and primary esophageal spasms; esophageal stricture; upper gastrointestinal malignancy including dysplastic changes in the esophagus; active malignant disease except for minor superficial skin disease; unstable diabetes mellitus; cerebral vascular disease; alcohol and/or drug abuse; familial history of esophageal or gastric cancer; or continuous treatment with nonsteroidal anti-inflammatory drugs
Symptoms (describe): At enrollment (visit 1), patients were included in a run-in period of 1 wk, during which they recorded their symptoms in a daily diary. Patients rated the severity of their symptoms of heartburn and regurgitation on a four-point scale: 0 = none, 1 = mild (awareness of symptoms, but easily tolerated), 2 = moderate (discomfort sufficient to cause interference with normal activities), 3 = severe (incapacitating, with inability to perform normal activities). At the end of the 1-wk run-in period (visit 2), only patients whose symptoms of heartburn (with or without regurgitation) with a sum of symptom scores of 5 or more during the last 7 days of the run-in period and a sum of symptom scores of 2 or more during the last 3 days of the run-in period were randomized to empirical treatment with esomeprazole 40 mg once daily for 4 wk (group 1) or basal endoscopy (group 2).	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): yes in group 2	Esophagitis/stricture/Barrett's: group 2 grade A 58 grade B 29 grade C 10 grade D 2 no erosion 204

GERD data extraction form

pH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): nd
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) yes

Quality Assessment for RCTs: B	
Blinding: no	Allocation concealment: no
Intention-to-treat: y	Method of Randomization: nd
Other comments: essentially a comparison between esomeprazole 40 mg qd vs. esomeprazole 20 mg qd (67% of group 2) or esomeprazole 40 mg qd (33% of group 2)	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 44 y	N enrolled: 649; 612 randomized
%Male: 57	N completed: 612 (ITT at 4wk); 551 @ wk 24
Race: 99.5% white	Dropouts/reasons: At 4 wks: Empirical treatment: Drop out N = 11; Lost to follow-up N = 8; Consent withdrawn N = 1; Adverse events N = 2 endoscopy-based treatment: Drop out N = 8; Lost to follow-up N = 5; Consent withdrawn N = 1; Adverse events N = 2 At 24 wks: Empirical treatment: Drop out N = 30; Lost to follow-up N = 28; Adverse events N = 2 endoscopy-based treatment: Drop out N = 33; Lost to follow-up N = 31; Consent withdrawn N = 1; Adverse events N = 1
BMI:	Follow-up period: 24 weeks
Comments:	

Results
Primary outcome(s): responders classified by symptom score (A responder to the 4-wk acute treatment phase was a patient whose sum of symptom scores over the last 7 days before visit 3 was 0 or 1. A responder to the 20-wk maintenance phase was a patient whose sum of symptom scores over the last 7 days before visit 4 was 0 or 1.) wk 4 empirical treatment 267/309 (86.4%) endoscopy-based treatment 265/303 (87.5%) P=0.929 wk 24 empirical treatment 222/309 (71.8%) endoscopy-based treatment 207/303 (68.3%) P=0.389

GERD data extraction form

HRQoL score assessed by QOLRAD (Quality of Life in Reflux and Dyspepsia) @ 4 wk

	empirical treatment	endoscopy-based treatment
emotional	6.4 ± 0.9	6.4 ± 0.9
sleep	6.4 ± 0.9	6.4 ± 0.9
food/drink	6.1 ± 1.0	6.1 ± 1.0
vitality	6.3 ± 0.9	6.3 ± 0.9
physical/social	6.4 ± 0.9	6.5 ± 0.8

HRQoL score assessed by QOLRAD (Quality of Life in Reflux and Dyspepsia) @ 24 wk

	empirical treatment	endoscopy-based treatment
emotional	6.6 ± 0.7	6.4 ± 0.8
sleep	6.6 ± 0.8	6.6 ± 0.7
food/drink	6.5 ± 0.8	6.4 ± 0.8
vitality	6.5 ± 0.9	6.5 ± 0.9
physical/social	6.7 ± 0.7	6.7 ± 0.7

ANCOVA – no statistically significant difference between groups

Secondary outcome(s):

Comments:

Compliance: nd

Adverse Events: nd

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Gill	Yr: 2007	UI: 17436134	Questions addressed: 3, learning curve for LAF	Extractor: SI

Objective/Topic: to examine the learning curve for LAF

Study design: retrospective	Country/Setting: UK	Funding: nd

Interventions(s): laparoscopic fundoplication	Comparator(s):

Primary outcome(s): operative time, conversions	Other outcome(s):

Inclusion criteria: indications for LAF: symptomatic GERD despite medical therapy; intolerance of medical therapy due to side effects; volume regurgitation or patient preference for surgery	Exclusion criteria:
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results): y; nd	Esophagitis/stricture/Barrett's:
pH study (performed or not and results): y; nd	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: operating technique evolved over the years in the study; no statistical adjustment; single surgeon experience

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Mean Age: 36.3 to 45.1	N enrolled: 400 consecutive cases
%Male: ~68%	N completed:

GERD data extraction form

Race: nd	Dropouts/reasons:
BMI: wt 71.1 to 80.4 Kg	Follow-up period: nd
Comments:	

Results
Primary outcome(s): 8 cohorts of 50 pts each stratified by time 1. steady decrease in mean operating time from 143 min in first cohort to 86 min in last cohort 2. mean postop hospital stay reduced from 3.7 d to 1.2 d 3. conversion to open procedure reduced from 14% to 2% 4. need for postop endoscopic balloon dilatation reduced from 16% to 0% 5. pts needed reoperation reduced from 14% to 6% 6. no perioperative deaths
Secondary outcome(s):
Comments:

Compliance:

Adverse Events: Reoperation after Laparoscopic Fundoplication – 24/400 (3, within 3 month; 21, after 3 months)

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Glatzel	Yr: 2007	UI: 17489035	Questions addressed: 1, 3	Extractor: SI

Objective/Topic: compare pantoprazole 40 mg with esomeprazole 40 mg in GERD symptom relief

Study design: RCT (non-inferiority study)	Country/Setting: Germany	Funding: ALTANA Pharma AG

Interventions(s): pantoprazole 40 mg daily for 4 wk	Comparator(s): esomeprazole 40 mg daily for 4 wk

Primary outcome(s): GERD symptom per ReQuest	Other outcome(s):

Inclusion criteria: ≥18 yr; endoscopic confirmed Gr A-D GERD	Exclusion criteria: NERD; hypersecretory conditions; acid lowering surgery, esophageal or gastric surgery, strictures, Schatzki's ring, diverticula, varices, achalasia, Barrett's, ulcer, pyloric stenosis, IBD, pregnant or nursing women, not using contraception; acid blockers 5 days prior to start of study, steroids, anti-inflammatory drugs more than 3 consecutive days before the start of the study
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): y; 11% grade C or D	Esophagitis/stricture/Barrett's: see exclusion criteria
pH study (performed or not and results): nd	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): nd
Esophageal manometric studies (performed or not and results): nd	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) yes

Quality Assessment for RCTs: B/acceptable	
Blinding: participant blinded	Allocation concealment: nd
Intention-to-treat: y	Method of Randomization: y
Other comments: 19% did not complete the study	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 53	N enrolled: 585 (561 ITT)
%Male: 53	N completed: 476
Race: nd	Dropouts/reasons: protocol violation including use of prohibited meds, noncompliance regarding ReQuest entries
BMI: 26.9	Follow-up period: 4 wk
Comments:	

Results
Primary outcome(s): median of the mean ReQuest GI subscale last 3 days of treatment (ITT) pantoprazole 0.24 (non-inferior, 97.5% CI upper bound within non-inferiority margin (Δ1.73) esomeprazole 0.31
Secondary outcome(s): proportion of pts with symptom relapse during the post treatment phase (ITT) pantoprazole 51.1% P=0.0216 esomeprazole 61%
Comments:

Compliance: nd

Adverse Events:

serious adverse events

pantoprazole – T cell lymphoma (1, not related to study med)

esomeprazole – drug hypersensitivity (1, not related to study med); hypertensive crisis (1, unlikely related to study med)

any adverse events

pantoprazole 35/61

esomeprazole 32/55

discontinued trail due to adverse event

pantoprazole 3/284

esomeprazole 4/227

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Goh	**Yr: 2007**	**UI:** 17301646	**Questions addressed: 1,3**	**Extractor: DM**

Objective/Topic: To compare pantoprazole 20 mg once daily with esomeprazole 20 mg once daily for 6 month in terms of efficacy and tolerability

Study design:	**Country/Setting:**	**Funding:**
RCT	16 countries throughout Europe, Asia and South America / Hospital	Grant from ALTANA Pharma AG, Germany

Interventions(s):	**Comparator(s):**
pantoprazole 20 mg once daily	esomeprazole 20 mg once daily

Primary outcome(s):	**Other outcome(s):**
Acute phase: Healing rates *Healing defined as absence of esophagitis, and 'no' or 'mild' heartburn and acid regurgitation in Intention to treat (ITT) and Per protocol (PP) population* Maintenance Phase: Combined endoscopic and symptomatic remission rates after 6 months of maintenance therapy *Combined symptomatic and endoscopic remission was defined as the absence of endoscopic findings (GERD Los Angeles grades A-D) and 'no' or 'mild' heartburn and acid regurgitation. Symptomatic non-relapse was defined as 'no' or 'mild' symptom severity for the variables of heartburn and acid regurgitation.* *ITT population: Received any dose of the study drug during either the acute or maintenance phase.* *PP population: Included all of the ITT population that completed the study without major protocol violations or who terminated the study because of an event related to the intake of the study medication.*	Mean sum scores of GI symptoms from baseline *Heartburn, acid regurgitation, dysphagia, epigastric pain/discomfort, retrosternal tightness, burping/ belching, nausea/vomiting, fullness, lower abdominal pain, and flatulence. The intensity of symptoms was scored as none (0), mild (1), moderate (2), and severe (3) by investigators.*

Inclusion criteria:	**Exclusion criteria:**
Outpatients 18 years or older with endoscopically confirmed GERD (Los Angeles grades A-D)	known history- of Zollinger-Ellison syndrome or other gastric hypersecretory conditions, pyloric stenosis, acute peptic ulcer and ulcer complications, endoscopically negative symptomatic GERD, obstructive esophageal strictures, Barrett's esophagus, severe diseases of other body systems, Pregnant or nursing women and women of child-bearing age not using adequate contraception
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):** nd
EGD (performed or not and results): Grade of | Pantoprazole | Esomeprazole	**Esophagitis/stricture/Barrett's:** See EGD

GERD data extraction form

GERD	20 mg (n=636)	20 mg (n=667)
A n (%)	296 (46.5)	305 (45.7)
B n (%)	271 (42.6)	290 (43.5)
C n (%)	58 (9.1)	59 (8.9)
D n (%)	11 (1.7)	13 (2.0)

PH study (performed or not and results): nd	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): nd	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Y

Quality Assessment for RCTs: A/rigorous	
Blinding: Y	**Allocation concealment: Y**
Intention-to-treat: Y	**Method of Randomization: nd**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 48.9 y	**N enrolled:** *Acute phase (before randomization)*- 1452, *Maintenance phase* – 1316 (pantoprazole 642, esomeprazole 672)
%Male: 59%	**N completed:** *Acute phase*- 1268 *Maintenance phase* ITT- 1303 (pantoprazole 636, esomeprazole 667) Per protocol– 1005 (pantoprazole 497, esomeprazole 508)
Race: European (74.9%), Latin American (19.3%), Asian (5.9%)	**Dropouts/reasons:** pantoprazole - 23 dropouts, esomeprazole - 17 dropouts; 5 pantoprazole and 2 esomeprazole recipients withdrew due to adverse events
BMI: 26.9	**Follow-up period:** 6 months
Comments:	

Results
Primary outcome(s): Acute phase (before randomization): *Healing rates* Pantoprazole 40 mg X 4 weeks: 70.2% (ITT), 75.4% (PP) Pantoprazole 40 mg X 8 weeks: 91% (ITT), 96% (PP)

Maintenance Phase:
Combined endoscopic and symptomatic remission rates after 6 months of maintenance therapy
Pantoprazole 20 mg: 84%, Esomeprazole 20 mg: 85% (ITT)

Kaplan-Meir Analysis
Pantoprazole 20 mg: 93%, Esomeprazole 20 mg: 93% (95% CI of difference: -2, 3.8)

Secondary outcome(s):
Mean sum score of GI symptoms
Acute phase:
Baseline: 0.8
4 weeks: 0.2
8 weeks: 0.1

Maintenance phase:
Pantoprazole 20 mg: 0.1
Esomeprazole 20 mg: 0.1

Comments:

Compliance:

Adverse Events:
Percent of recipients with adverse events:
Pantoprazole 20 mg: 22%
Esomeprazole 20 mg: 23%

Percent of recipients with adverse events considered by investigators to be related to study medication:
Pantoprazole 20 mg n(%): 2 (0.9%)
Esomeprazole 20 mg n(%): 8 (3%)

Percent of recipients with severe adverse events:
Pantoprazole 20 mg: 7%
Esomeprazole 20 mg: 10.4%

Percent of recipients with serious adverse events:
Pantoprazole 20 mg: 1.4%
Esomeprazole 20 mg: 2.5%

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Grant	**Yr**: 2008	**UI**: 19074946	**Questions addressed**: 1	**Extractor**: JC

Objective/Topic: Determine relative benefits and risks of laparoscopic fundoplication surgery vs long term drug tx for chronic GORD.

Study design: RCT	**Country/Setting**: UK/21 hospitals	**Funding**: NIHR Health Technology Assessment Programme

Interventions(s): laparoscopic fundoplication	**Comparator(s)**: Placebo bid for 8 weeks.

Primary outcome(s): REFLUX quality of life score	**Other outcome(s)**: SF 36, EQ 5D, and medication use, measured at time points equivalent to 3 and 12 months post surgery and surgical complications.

Inclusion criteria: More than 12 months' sx requiring maintenance treatment with PPI (or alternative) for reasonable control; endoscopic or 24 hour pH monitoring evidence of GORD, or both; suitable for either policy (including American Society of Anesthesiologists (ASA) grade I or II); recruiting doctor uncertain which management policy to follow.	**Exclusion criteria:** Morbid obesity (BMI >40); Barrett's oesophagus > than 3 cm or with evidence of dysplasia; para-oesophageal hernia; and oesophageal stricture. See exclusion criteria.
Symptoms (describe): REFLUX questionnaire score derived from the weighted average of six questions on quality of life (heartburn; acid reflux; eating and swallowing; bowel movements; sleep; and work, physical, and social activities). Secondary sx score measures (general discomfort; wind and frequency; nausea and vomiting; limitation in activity; constipation and swallowing).	**Hiatal hernia (specify whether considered and size used for exclusion)**: Considered para-oesophageal hernia--used for exclusion.
EGD (performed or not and results): Performed. See inclusion criteria.	**Esophagitis/stricture/Barrett's**: Pts. with Barrett's oesophagus of more than 3cm or evidence of dysplasia or oesophageal stricture excluded. See exclusion criteria.
pH study (performed or not and results): Performed. See inclusion criteria.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** > 12 months' sx requiring maintenance treatment with a proton pump inhibitor (or alternative) for reasonable control. See inclusion criteria
Esophageal manometric studies (performed or not and results): In the absence of erosive oesophagitis on endoscopy, and when necessary to exclude achalasia, manometry or pH studies were performed before surgery.	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B	
Blinding: No. Staff in central trial office participants details on the secure database--notified participants and clinical sites of their allocation. No subsequent	Allocation concealment: No.

blinding.	
Intention-to-treat: Yes	Method of Randomization: Yes, Random allocation organized centrally by secure system, using a computer generated sequence, stratified by clinical site, with balance in respect of age, sex, and BMI secured by minimization.
Other comments:	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: Surgical: ITT-46.7, PP-46.3; Medical: ITT-45.9, PP-45.9	N enrolled: 357
%Male: Surgical: ITT-65, PP-61; Medical: ITT-67, PP-68	N completed: 299
Race: Not described	Dropouts/reasons: 58 (withdrawn, lost to follow up, death) SEE TABLE A at BMJ.com for more description
BMI: Surgical: ITT-28.5, PP-28.7; Medical: ITT-28.4, PP-28.3	Follow-up period: 12 months
Comments: % Current smoker: Surgical: ITT-26, PP-26; Medical: ITT-40, PP-36	

Results

Primary outcome(s):

REFLUX QoL at baseline and 12 months – Mean (SD)

	Surgical		Medical	
	Randomized	Per protocol	Randomized	Per protocol
Baseline	63.6 (24.1)	61.9 (24.5)	66.8 (24.5)	68.2 (24.4)
12 months	84.6 (17.9)	88.3 (15.6)	73.4 (23.3)	73.1 (23.7)

Secondary outcome(s):

EQ-5D at baseline and 12 months – Mean (SD)

	Surgical		Medical	
	Randomized	Per protocol	Randomized	Per protocol
Baseline	.71 (.26)	.72 (.24)	.72 (.25)	.73 (.25)
12 months	.75 (.25)	.78 (.23)	.71 (.27)	71 (.27)

Comments: SF-36 data online at BMJ.com

Compliance:

Adverse Events:

Minimally described—includes both randomized and pt preference groups:

No diff detected b/w trial groups in questionnaire responses at 12 months regarding "difficulty swallowing" and "bloatedness/trapped wind," -- some evidence of more frequent "wind from the lower bowel" after surgery.

Applicability: (narrow/wide): Wide	Comments: non-restrictive inclusion/exclusion criteria

GERD data extraction form

Author: Hafez	**Yr: 2008**	**UI: 18449599**	**Questions addressed: Q1; Q2**	**Extractor: MC**

Objective/Topic:
To assess the long-term efficacy of laparoscopic fundoplication in controlling reflux symptoms and to evaluate risk factors for recurrence of reflux symptoms

Study design:	**Country/Setting:**	**Funding:**
Non-RCT	Austria	No data

Interventions(s):	**Comparator(s):**
Nissen (laparoscopic total fundoplication) or Toupet (partial posterior fundoplication)	Risk factors for analysis of time until Tx failure: age, gender, DeMeester score, presence and length of Barrett's mucosa, fraction of time with a pH lower than 4, grade of esophagitis (Los Angeles classification), LES pressure, contraction amplitudes in the distal third of the esophagus, mode of operation (Nissen vs. Toupet), and propensity score

Primary outcome(s):	**Other outcome(s):**
Recurrence of relux symptoms (or Tx failure): obtained by annual phone calls to the patients asking about heartburn or regurgitation symptoms necessitating pharmacologic treatment. Dysphagia without concomitant heartburn or regurgitation was NOT considered to indicate Tx failure.	

Inclusion criteria:	**Exclusion criteria:**
Patients who underwent laparoscopic fundoplication for GERD from 1996 to 1999 at a single institution (Medical University of Vienna).	Patients were excluded from the analysis because prior gastric surgery (n=17), prior fundoplication (n=10), personal case load of surgeon <30 (n=8), missing manometric data (n=10), lost to follow-up within 60 months (n=15)
Symptoms (describe): No data	**Hiatal hernia (specify whether considered and size used for exclusion):** No data
EGD (performed or not and results): Erosive changed in the esophagus were described according to the Los Angeles classification. Biopsies were taken from the Z-line and from the gastroesophageal border: • No intestinal metaplasia at the Z-line: 79% • Short segment Barrett's: 14% • Long segment barrett's: 7%	**Esophagitis/stricture/Barrett's:** Short segment Barrett's: 14% Long segment Barrett's: 7%
PH study (performed or not and results): 24-h pH-metry: Fraction time of pH <4 (data not shown but used in determining the DeMeester score, along with esophageal manometric results) DeMeester score ranged 0.3 to 168 (median 32) DeMeester score ≥50: 30%	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No data
Esophageal manometric studies (performed or not and results): Lower esophageal sphincter pressure: 0-35 (median 10) mmHg Contraction amplitudes in the distal third: 10-198	**Other:**

(median 61) mmHg	

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Unclear

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: Only p-values were reported for the multivariate analyses. Outcome assessment was based on follow-up phone call only. Small inconsistency in reporting of sample size in the analyses (134/133). Propensity analysis was performed to reduce bias caused by the surgeon's decision making.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 27-78 (median 54) yr	**N enrolled: 194**
%Male: 65	**N completed: 134/133**
Race: no data	**Dropouts/reasons: lost to follow-up within 60 months (n=15) but reasons were not stated**
BMI: no data	**Follow-up period: 60-123 months (median 93 months)**
Comments:	

Results

Primary outcome(s):

Q1: Recurrence of reflux symptoms was diagnosed for 16 patients after 2 to 69 months (median, 30 months).

- Univariate analysis of % Tx failure after 93 months: Nissen (n=89) vs. Toupet (n=45): 14% vs. 9%, p=0.44
- Multivariate analysis of % Tx failure after 93 months: Nissen (n=89) vs. Toupet (n=45): p=0.31

Q2: Multiple hazards regression for predicting time until recurrence of reflux symptoms

Analyzed risk factors	p-Value
Operation method (Nissen vs Toupet)	0.31
Propensity score	0.26
Gender	0.13
Age>54 years	0.39
Mean contraction amplitudes<60 mmHg	0.08
Barrett segment ≥3 cm	0.91
Fraction time (pH>4) >15	0.83
DeMeester score ≥50	0.04*

Secondary outcome(s):

Comments:
Only p-values were reported for the multivariate analyses

Compliance:
No data

Adverse Events:
No data

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Hansen	Yr: 2006	UI:16409423	Questions addressed: 1	Extractor: JHL

Objective/Topic: To compare the effects of esomeprazole continuous and on-demand vs. ranitidine on QoL and patient satisfaction in GERD patients

Study design:	Country/Setting: Norway	Funding: ND
• Prospective, randomized, open, parallel-group study		

Interventions(s):	Comparator(s):
• **Esomeprazole 20mg once daily**	• **Esomeprazole 20mg on demand** • **Ranitidine 150mg twice daily**

Primary outcome(s): Quality of life, patient satisfaction	Other outcome(s): GERD symptoms (heartburn, acid regurgitation, dysphasia and epigastric pain)

Inclusion criteria:	Exclusion criteria:
Study population: patients over 18 years of age, with symptoms suggestive GERD (heartburn as the predominant symptom, with or without acid regurgitation) for ≥3 days in the week preceding the start of the study, recruited by 281 Norwegian General Practitioner clinics	
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):** ND

	Esomeprazole 20mg continuous	Esomeprazole 20mg on demand	Ranitidine 300mg continuous
Severity of heartburn; n (%)			
Mild	72 (10.9)	79 (12.5)	69 (11.3)
Moderate	458 (69.6)	452 (71.3)	442 (72.5)
Severe	128 (19.5)	103 (16.2)	99 (16.2)

EGD (performed or not and results): Not performed	**Esophagitis/stricture/Barrett's:** ND
PH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** ND
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B	
Blinding: No	**Allocation concealment: ND**
Intention-to-treat: Yes	**Method of Randomization: ND**
Other comments: Contamination issues ("Patients could contact the clinic throughout the followup phase if they identified a need for a change in therapy, e.g. a relapse in their symptoms. If this was the case, patients who were receiving either of the esomeprazole regimens were prescribed esomeprazole 40 mg once daily for 4 weeks, and patients receiving ranitidine were prescribed ranitidine 300 mg twice daily for 4 weeks. If patients subsequently became symptom-free, they would resume the long-term therapy they were originally randomized to.") –	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		X

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 51 y	**N enrolled: 2156 (1902 randomized)**
%Male: 55.1 %	**N completed: 1797 (QoL questionnaire data were complete)**
Race: 93.3% Caucasian	**Dropouts/reasons: 5.5% (105/1902*100)**
BMI: ND	**Follow-up period: 6 months**
Smoking history: ND	**Comments:** 4-week symptom-control phase (received esomeprazole 40mg once daily) followed by a 6-month follow-up phase

Results
Primary outcome(s): • Both esomeprazole treatments were more effective than ranitidine in all dimensions (emotional, sleep, food, physical, vitality) of the Quality of Life in Reflux and Dyspepsia (QOLRAD) questionnaire ($p < 0.005$). Esomeprazole one daily continuously maintained four QOLAD dimensions (emotional, sleep, food, vitality) better than esomeprazole except physical activity. • Percentage of patients completely satisfied with study medication   o Final visit: continuous: 82.2%, on-demand: 75.4%, vs. ranitidine 33.5% (*$p < 0.01$ for esomeprazole 20mg continuous vs. esomeprazole 20mg on-demand; **$p<0.0001$ for esomeprazole 20mg continuous and on-demand vs. ranitidine)
Secondary outcome(s): Esomeprazole continuous and on-demand led to a significant improvement in symptoms (Overall Treatment Evaluation questionnaire) compared with ranitidine (continuous: 80.2%, on-demand: 77.8%, vs. ranitidine 47%; $p < 0.001$).
Comments:

Compliance: ND

Adverse Events: ND

Applicability: (narrow/wide): Wide	**Comments:** Patients with GERD symptoms were recruited by 281 Norwegian General Practitioner clinics.

GERD data extraction form

Author: Howden	**Yr:2009**	**UI: 19681809**	**Questions addressed: 1,3**	**Extractor: DM**

Objective/Topic:
Evaluate the efficacy and safety of dexlansoprazole MR 60 and 90 mg qd. compared with placebo, as a maintenance therapy, in patients with erosive esophagitis healed by Dexlansoprazole MR or Lansoprazole

Study design:	**Country/Setting:**	**Funding:**
3 arm RCT	USA/Community	Industry (TAP Pharmaceutical Products, Inc., Lake Forest, IL, USA, now part of Takeda Global Research & Development Center, Inc.)

Interventions(s):	**Comparator(s):**	**Interventions(s**
Dexlansoprazole MR 60 mg, Dexlansoprazole MR 90 mg	Placebo	

Primary outcome(s):	**Other outcome(s):**
Percentage of patients who maintained healed EO for 6 months	**Patient-reported symptom severity** *Patients rated the severity of heartburn according to the following five point scale: 0 = none, 1 = mild (occasional heartburn that did not influence the patient's daily routine), 2 = moderate (heartburn that could not be ignored; occasionally influenced the patient's daily routine Investigator-reported symptom severity at week 4), 3 = severe (heartburn was present for most of the day; regularly influenced patient's daily routine) and 4 = very severe (constant heartburn; markedly influenced patient's daily routine).* *The PAGI-Symptom Severity Index (PAGI-SYM) is a brief symptom severity instrument (subscales: nausea/vomiting, fullness/early satiety/bloating, upper and lower abdominal pain and heartburn/regurgitation).* **Patient-reported QOL** The Patient Assessment of Upper Gastrointestinal Disorders Quality-of-Life Index (PAGI-QOL) assesses health-related QOL in patients with GERD, dyspepsia and gastroparesis (subscales: daily activities, clothing, diet and food habits, relationship, and psychological well-being and distress). Scoring is based on a scale of 0 to 5, with higher scores indicating better QOL. A total score is calculated based on the average of all subscale scores. **Investigators assessed GERD symptoms (heartburn, acid regurgitation, dysphagia, belching and epigastric pain)** *Evaluated as none, mild, moderate, severe or very severe during the 7 days before the patient's study visit and throughout the treatment period.*

GERD data extraction form

	Percentage of nights without heartburn **Mean severity of heartburn** **Percentage of patients with 24-h heartburn-free days,** **Percentage of days without rescue medication use;**

Inclusion criteria: Men and women aged ≥ 18 years with endoscopically proven healed erosive esophagitis after 4 or 8 weeks therapy with Dexlansoprazole MR 60 and 90 mg or Lansoprazole 30 mg For women: Required to be surgically sterile, postmenopausal or using a double-barrier method of birth control.	**Exclusion criteria:** Positive for Helicobacter pylori (H. pylori) by serological assay; had any surgery planned; evidence of uncontrolled systemic disease, need for continuous anticoagulant therapy, use of prescription or nonprescription PPIs, histamine 2-receptor antagonists, sucralfate, misoprostol, prokinetics, or non-approved antacids, use of drugs with significant anticholinergic effects (e.g. tricyclic antidepressants) for which a stable dose could not be maintained throughout the trial; chronic use (>12 doses per month) of nonsteroidal anti-inflammatory drugs, including selective cyclo-oxygenase 2 inhibitors (Aspirin up to 325 mg/day permitted)
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):**

Symptom	Placebo	Dexlanzoprazole 60 mg	Dexlanzoprazole 90 mg
24-h days with heartburn per week at baseline (before treatment in the healing study), median	7	7	7
Nights with heartburn per week at baseline (before treatment in the healing study), median	6	5	6
Severity of 24-h heartburn at baseline – (before treatment in the healing study)	1.5 (0.8)	1.5 (0.8)	1.5 (0.8)
Severity of nighttime heartburn at baseline – (before treatment in the healing study)	1.5 (0.9)	1.4 (0.9)	1.5 (0.9)

EGD (performed or not and results): yes	**Esophagitis/stricture/Barrett's:** see EDG results

EO severity (LA classification grade at baseline) n (%)	placebo	Dexlanzoprazole 60 mg	Dexlanzoprazole 90 mg
A	58 (41.4)	60	54 (35.5)

		(37.7)	
B	48 (34.3)	61 (38.4)	58 (38.2)
C	28 (20.0)	33 (20.8)	32 (21.1)
D	6 (4.3)	5 (3.1)	8 (5.3)

PH study (performed or not and results): nd	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): nd	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) yes

Quality Assessment for RCTs: C/poor;	
Blinding: Yes	**Allocation concealment: Yes**
Intention-to-treat: Yes (modified ITT)	**Method of Randomization:** Interactive Voice Response Services (ClinPhone, Inc., Northbrook, IL, USA)
Other comments: 88% loss to follow up in the placebo group	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 48.9 years	**N enrolled: 451**
%Male: 52%	**N completed: 230**
Race: **Race** / **n (%)** White: 395 (87.6) Black: 39 (8.6) Multiracial: 7 (1.6) American Indian or Alaskan Native: 5 (1.1) Asian: 5 (1.1)	**Dropouts/reasons:** Placebo: 123 [EO recurrence (86), Adverse events (7), Lost to follow-up (4), Withdrew consent (15), Others (11)] Dexlanzoprazole 60 mg qd.: 33 [EO recurrence (16), Adverse events (6), Lost to follow-up (3), Withdrew consent (1), Others (7)] Dexlanzoprazole 60 mg qd.: 49 [EO recurrence (13), Adverse events (9), Lost to follow-up (4), Withdrew consent (8), Others (15)]
BMI: 31.2 kg/m^2	**Follow-up period: 6 months**
Comments:	

Results
Primary outcome(s):

Percentage of patients who maintained healed EO over 6 months
Dexlansoprazole MR 60 mg (86.6%) and 90 mg (82.1%) treatment groups compared with the placebo group (25.7%; p < 0.00001)

Secondary outcome(s):

Patient-reported symptom severity (No data, only text)
"For PAGI-SYM questionnaire assessments, both Dexlansoprazole MR treatment groups were also significantly superior to the placebo group in the mean changes during treatment (for total score and all subscale scores). The dexlansoprazole MR 60 and 90 mg groups maintained symptom relief, whereas the placebo group showed increases in symptom severity across all domains"

Patient-reported QOL (No data, only text)
"For PAGI-QOL questionnaire assessments, both dexlansoprazole MR treatment groups were significantly superior to the placebo group in the mean changes during treatment (from Day)1 to final visit) for all subscale scores and total score (with the exception of the relationship subscale). The dexlansoprazole MR 60 and 90 mg groups maintained their QOL on all domains and total QOL, whereas the placebo group reported deterioration in QOL"

Investigator-assessed GERD symptoms (No data, only text)
"Investigator assessments of GERD symptoms indicated overall that symptoms were significantly less severe (as assessed by maximum severity) for patients treated with dexlansoprazole MR 60 and 90 mg vs. placebo at the final visit (p < 0.00001) when adjusted by symptom severity on Day)1. Mean changes in severity of heartburn and acid regurgitation during treatment were small (<0.1 unit change in score) and similar in both dexlansoprazole MR groups, indicating that patients maintained the symptom relief they had attained at the end of the healing trial. Severity of heartburn and acid regurgitation increased in patients receiving placebo (mean changes in total score of 1.25 and 0.94, respectively)."

Mean severity of heartburn
For daytime/night time heartburn: Dexlansoprazole MR 60 mg (0.03), Dexlansoprazole MR 90 mg (0.04), placebo (1.0), p < 0.00001
For night time heartburn: Dexlansoprazole MR 60 mg (0.02), Dexlansoprazole MR 90 mg (0.04), placebo (0.83), p < 0.00001

Percentage of patients with 24-h heartburn-free days during treatment
Dexlansoprazole MR 60 mg (95.8%), Dexlansoprazole MR 90 mg (94.4%), placebo (19.2%), p < 0.00001

Percentage of patients with nights without heartburn during treatment
Dexlansoprazole MR 60 mg (98.3%), Dexlansoprazole MR 90 mg (97.1%), placebo (50%), p < 0.00001

Percentage of days without rescue medication use;
Dexlansoprazole MR 60 mg (94.9%), Dexlansoprazole MR 90 mg (93.6%), placebo (27.5%), p < 0.00001

Comments:

Compliance:

Adverse Events:
Safety population: n= 451
≥ *1 treatment-emergent AE:* Dexlansoprazole MR 60 mg group - 79 (50%), Dexlansoprazole MR 90 mg group - 66 (43%), Placebo group - 37 (26%)

The most frequently reported (≥ 5% of patients) treatment-emergent AEs:

Adverse events	Dexlanzoprazole 60 mg (n=159)	Dexlanzoprazole 90 mg (n=152)	Placebo (n=140)
Diarrhoea	6%,	7%	<1%,
Gastritis	6%,	4%	<1%,
Gastrointestinal and abdominal pains	6%,	4%	1%,
Flatulence, bloating, and distension	5%,	2%	0%,
Upper respiratory tract infections	3%,	7%	4%,

Adjusted for exposure to the drug (due to differential exposure in the three groups because of high dropouts in the placebo group):

Adverse events	N per 100 patient month of exposure (%)
Nausea and vomiting symptoms (Nausea, regurgitation, retching, vomiting)	9 (0.62)
Upper respiratory tract infections (Acute sinusitis, laryngitis, Nasopharyngitis, pharyngitis, sinusitis, upper respiratory tract infection)	11 (0.76)
Gastric ulcers and perforation (Gastric ulcer, erosive gastritis)	3 (0.21)
Headaches (Headache, sinus headache)	9 (0.62)
Diarrhoea (excluding infective) (Diarrhoea)	20 (1.39)
Gastrointestinal atonic and hypomotility disorders (Constipation, gastro-oesophageal reflux disease, impaired gastric emptying)	11 (0.76)
Oesophageal ulcers and perforation (Erosive oesophagitis)	2 (0.14)
Viral infections (Viral gastroenteritis, viral infection, viral pharyngitis)	6 (0.42)
Gastritis (excluding infective) (Gastritis)	16 (1.11)
Gastrointestinal and abdominal pains (excluding oral and throat) (Abdominal pain, upper abdominal pain, lower abdominal pain, abdominal tenderness)	16 (1.11)
Flatulence, bloating, and distension (Abdominal distention, flatulence)	11 (0.76)

No deaths were reported during the trial.

"Serious adverse events" not related to study medications: Dexlansoprazole 60 mg: 2/159 (1.3%); Dexlansoprazole 90 mg: 5/152 (3.3%)

The increases in fasting serum gastrin levels with dexlansoprazole MR 60 and 90 mg (median increases from before the EO healing trial to month 6 of 68 pg/mL and 77 pg/mL respectively) were within the range expected with PPI treatment. The mean serum gastrin for the placebo group returned to baseline at 1 month.

The most commonly reported abnormalities in any tissue biopsy:

Adverse events	Dexlanzoprazole	Dexlanzoprazole	Placebo

GERD data extraction form

	60 mg (n=159)	90 mg (n=152)	(n=140)	
Chronic gastritis	36.3%	34.3%	29.5%	
Reactive gastropathy	6.2%	8.6%	1.6%	
Intestinal metaplasia	2.7%	3.8%	3.3%	

Applicability: (narrow/wide): wide	**Comments: Maintenance therapy with Dexlanzoprazole**

GERD data extraction form

Author: Huttle	**Yr: 2005**	**UI: 16211438**	**Questions addressed: KQ3**	**Extractor: MC**

Objective/Topic: to evaluate the development and outcomes of laparoscopic antireflux surgery in Germany using a nationwide representative survey

Study design:	**Country/Setting:**	**Funding:**
Cross-sectional study	Germany	No funding (part of thesis)

Interventions(s):	**Comparator(s):**
antireflux procedures, including laparoscopic (2053/2540), open (485/2540), and thoracoscopic (2/2540)	Relationship between complication rates and the average experience of the hospital, expressed by the number of surgical procedures performed per year

Primary outcome(s):	**Other outcome(s):**
Complications; technique-dependent outcome	

Inclusion criteria:	**Exclusion criteria:**
Randomly selection of every third German surgical departments, including private practitioners, to answer survey questions. A total of 34 detailed questions required answers concerning 288 structured items. The questions asked for the actual use of diagnostic and therapeutic procedures and the exact number of procedures, as well as treatment-related early morbidity, hospital mortality, and 1-year follow-up data.	Departments and private practitioners obviously not trained in the treatment of GERD (e.g., orthopedic surgeons and vascular surgeons)
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):**
EGD (performed or not and results):	**Esophagitis/stricture/Barrett's:**
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results):	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

GERD data extraction form

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:	**N enrolled:**
%Male:	**N completed:**
Race:	**Dropouts/reasons:**
BMI:	**Follow-up period:**
Comments: no patient level data.	

Results

Primary outcome(s):
Relationship between complication rates and the average experience of the hospital, expressed by the number of surgical procedures performed per year (based on total 1614 cases):

- Significant experience-related differences were found for hospitals performing up to 10 fundoplications per year (14%), as compared with hospitals performing more than 10 procedures per year (5.1%; $p < 0.001$).
- No further significant differences were found between hospitals performing more than 20, 30, or 40 fundoplications per year.
- Lesions of the pleura occurred most often in more experienced departments, with 27 of the 31 reported lesions occurring in hospitals performing more than 25 fundoplications per year ($p < 0.01$).

Secondary outcome(s):

Comments:
In 1999, 92% of the university hospitals (23/25) and 75% of the academic hospitals (60/80) were performing antireflux surgery, but only 34% (81/237) of the community and private nonacademic hospitals and none of the private practitioners were doing so.

Surgery was performed laparoscopically in 2,053 cases (80.8%) in 113 hospitals (mean, 18.5 procedures per center and year; median, 7; range, 0–320), and using the open approach in 485 cases (19.1%) in 124 hospitals (mean, 3 procedures per center annually; median: 7; range: 0–20). One hospital performed two thoracoscopic antireflux procedures.

These procedures included 1,289 total fundoplications (65%) (49% using modified Nissen-Rosetti, 9% using Nissen–Rosetti, 35% using floppy Nissen, 3% using Nissen, and 4% using other modifications), 620 partial fundoplications (31%) (83% using posterior partial Toupet fundoplications, 13% using anterior hemifundoplications [AHFP], 0.8% using posterior partial Guarner fundoplications, 0.2% using Hill procedures, and 2.4% using other modifications), 81 other techniques (4%) (e.g., Lig. teres plasty, Vicrylmesh, Lortat-Jacob procedure).

Compliance:

Adverse Events:

	Nissen (n=1062) %	Toupet (n=470) %
Surgical complications	6.2	3.2
Bleeding (without spleen)	0.5	0.2
Injuries of the spleen	0.4	0.85
Esophageal perforation	0.6	0.4
Injuries of the stomach wall	0.6	0.2
Wound infections	0.85	0.0
Intraabdominal infections	0.2	0.0
Injuries of the pleura		
With thoracic drain	0.5	0.4
Without drain	1.8	0.6
Others (i.e., visceral, trocar injuries)	0.9	0.4
General, nonsurgical complications	2.5	1.1
Total	8.8	4.3

Hospital mortality was reported to be 0.1%, which resulted from a pulmonary embolism after floppy Nissen fundoplication in one case and a nonspecified surgical complication after Toupet fundoplication in another case. Both lethal complications occurred in experienced university hospitals that performed more than 35 fundoplications per year.

Applicability: (narrow/wide): Wide	**Comments:**

First author: Iqbal	**Year:** 2006	**UI: 16368486**

Modifying Factor(s): Diaphragm stressors (gagging, vomiting, lifting weights, coughing, hiccupping, BMI, etc)

Study design: retrospective case-control **Follow up duration:** Study group: 3.12 years (0.4 to 6.2) Controls: 2.87 years (1.7 to 4)	**Country:** USA **Multicenter:** no	**Funding:** not reported

Interventions(s): Laparoscopic Nissen Fundoplication

Primary outcome(s): To the influence of diaphragm stressors on antireflux surgery failure	**Other outcome(s):** none reported

Baseline characteristics:
Group A: reoperation for a failed NF **Group B:** no clinical or symptomatic evidence of surgical failure at least 18 months after NF
GERD definition for the population included: Group A: recurrent hiatal hernia, EGD, manometry, +/- esophagogram and 24-hr pH monitoring
Age: Group A: 50 (29-75), Group B: 52 (16-78)
Gender: Group A: 39%, Group B: 38%
Race: not reported
BMI: Group A: 31, Group B: 30
Severity of symptoms: not reported
Duration of symptoms: not reported
Frequency of symptoms (period of time after primary procedure and redo):
Gagging: Group A: never 71%, >1/wk 29%; Group B: never 92%, >1/wk 8%
Coughing: Group A: 39%; Group B: 28%
Weight lifting (>100#): Group A: 30%; Group B: 20%
Vomiting: Group A: never 71%, >1/wk 29%; Group B: never 92%, >1/wk 8%
Induced vomiting: Group A: 5%; Group B: 2%
Hiccups: Group A: 13%, Group B: 20%
Retching: A: 32%; B: 18%
Belching: A: 20%; B: 40%
Motion sickness: A: 10%; B: 16%
Antidepressant use: A: 29%, B: 23%
Type of medications: PPI
Response to PPI preoperatively (not all patients had a response): Group A: 24% good, 42% poor, 10% never taken; Group B: 42% good, 28% poor, 12% never taken
Acid reflux (by pH study): yes /not defined
Abnormal manometry study: yes in 33 patients/not defined, but LES pressure similar in the 2 groups. A: 5.1; B: 5.5
Esophagitis by endoscopy: yes
Hiatal hernia: A: 78%; B: 82%
Hiatal hernia size: <3cm: A: 50%; B: 75%
>3cm: A: 50%; B: 25%
Duration between primary and redo: 3.12 years
Duration of control follow-up: 2.87 years

Significant baseline differences between GroupA and GroupB

Symptoms: Not reported.
EGD: Not reported, but no difference in grade of esophagitis noted in baseline characteristics chart
EMS: No difference in LES pressures
PH study: Not reported.
Hiatal hernia: Group A (LNF failure requiring redo) was more likely to have a hiatal hernia > 3cm than Group B (LNF successful): 50% vs. 25% p=0.032
Meds used in the groups: No difference in proportion of PPI used

Other:
Vomiting: Group B was more likely to have never vomited after the initial LNF than Group A. 92% vs. 71% p=0.01
Gagging: Group B was more likely to have never vomited after the initial LNF than Group A. 92% vs. 71% p=0.01

N enrolled per group:	Group A: 41	Group B: 50	
N completed per group:	41	50	

Outcomes	Results	
	GroupA: *Case (failure after LNF)*	GroupB: *Control (success after LNF)*
Gagging (post-operative) P=0.03 OR for risk of failure 10.4 (p=0.005)	29%	8%
Vomiting >5/wk (significant only with univariate analysis) P=0.01	12%	4%
Belching P=0.06 OR for risk of failure 0.22 (p=0.02)	20%	40%
Depression P=0.6	29%	23%
Hernia size > 3cm P=0.04 OR for risk of failure 3.17 (p=0.04)	50%	25%
Good response to PPI OR for risk of failure with improving response to PPIs 0.69 (95%CI 0.48-1.00) (p=0.05)	27%	46%
Of the potential stressors investigated, preoperative hernia size greater than 3 cm, postoperative gagging, and decreased belching were found to be associated with failure of reflux surgery after adjusting for other variables through multivariate analysis.		

Adverse Events: none reported

Quality Assessment: Description of the biological plausibility for the hypothesis to be tested: yes Description of inclusion /exclusion criteria and rationale: yes Documentation of how data were collected and analyzed (eg, blinding): yes Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): no, range of followup in failed cases ranged from 0.4 to 6.2 years; range of followup in control cases ranged from 1.7 to 4 years (i.e., the control should have followup range at least as long as the failed cases) Participant drop-out percentage (>20%?): not reported, but some data missing for certain questions. The missing data was most noticeable in regards to PPI data. Description of statistical methods in sufficient detail to be replicated: yes **Overall grade: C**
Comments: accepted only for preoperative characteristics.

ND: no data

GERD data extraction form

Author: Jeansonne	**Yr: 2009**	**UI: 19153320**	**Questions addressed: 1**	**Extractor: JHL**

Objective/Topic: Endoluminal Full-Thickness Plication and Radiofrequency Treatments for GERD

Study design:	**Country/Setting: US**	**Funding: ND**
Prospective two-arm study • Endoscopic full-thickness plication (FTP) • Endoscopic radiofrequency (RF) *But, data was not extracted for FTP group.		

Interventions(s):	**Comparator(s):**
• Endoscopic radiofrequency (RF)	

Primary outcome(s):	**Other outcome(s):**
Medication use, symptom scores, and pH values	

Inclusion criteria:	**Exclusion criteria:**
• Symptomatic GERD patients • Endoluminal therapy based on the following indications: obesity, borderline manometric or impedance study (e.g., low to normal peristalsis, amplitudes, or bolus transit), inability to tolerate general anesthesia, or desire to avoid surgery	Large paraesophageal hernia, esophagitis, and stricture
Symptoms (describe): ND	**Hiatal hernia (specify whether considered and size used for exclusion):** Patients with large paraesophageal hernia were excluded.
EGD (performed or not and results): Not performed	**Esophagitis/stricture/Barrett's:** Patients with esophagitis, and stricture were excluded.
PH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** ND
Esophageal manometric studies (performed or not and results): Performed, ND	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: • High drop-out rates, 40% • Criteria for symptomatic GERD were not provided.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
C (Symptomatic GERD patients were selected.)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 48.8 y	**N enrolled:** 68
%Male: 37.0	**N completed:** 41
Race: ND	**Dropouts/reasons:** 40%

GERD data extraction form

BMI: 27.8	**Follow-up period:** 5.1 months
Comments: Patients with a history of previous fundoplication, 14.7% of patients (RF)	

Results
Primary outcome(s): RF group (preoperative vs. postoperative) • PPI use was reduced from 84% to 50% (*P*=.01) • Patients with moderate to severe heartburn decreased from 55% to 22% (*P*<.01) • Percentage of time the pH was less than 4 was statistically unchanged from 10.8% to 9.1% (*P*>.9) • Decreases in moderate to severe scores were also seen for dysphagia (17.4% to 14.6%, *P*=.04), voice symptoms (29.8% to 14.6%, *P*=.04), and cough (32.6% to 12.2%, *P*=.01). • Three patients (4.4%) underwent laparoscopic Nissen fundoplication for refractory symptoms an average of 11.4 months after RF.
Secondary outcome(s):
Comments:

Compliance: NA

Adverse Events: ND

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Jensen	Yr: 2009	UI: 18855057	Questions addressed:3	Extractor: WY

Objective/Topic:
to evaluate the safety and efficacy of performing laparoscopic Nissen fundoplication as a planned day-case with same-day discharge procedure

Study design:	Country/Setting:	Funding:
Retrospective cohort	UK	nd

Interventions(s):	Comparator(s):
Day-case laparoscopic Nissen fundoplication	NA

Primary outcome(s):	Other outcome(s):

Inclusion criteria:	Exclusion criteria:
Had laparoscopic Nissen fundoplication between January 2003 and December 2007 with minimal comorbidity (ASA 1 + 2) with a responsible cohabiting adult within an hour's drive of the hospital preoperative endoscopy and pH and manometry testing	
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B
Comments: clear reporting of adverse events. There is little description on how patients were selected/recruited, or if it's a convenience sample.

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:42	N enrolled:113
%Male:65	N completed: nd
Race:	Dropouts/reasons:
BMI:	Follow-up period:
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Compliance:

Adverse Events:
perioperative complication: port-site bleeding (n=1) No conversions to open surgery postoperative complications that required readmission to hospital (n=4; 1 due to nausea and 3 due to dysphagia) wound infection (n = 2) persistent regurgitation requiring laparoscopic division of a gastric band adhesion (n = 1) dysphagia (n = 5 with 2 patients requiring redo partial fundoplication and one patient requiring endoscopic dilatation)

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Johnson	**Yr**: 2005	**UI**: 16128933	**Questions addressed**: 1, 3 (2???-GERD assoc sleep disturbance population?)	**Extractor**: JC

Objective/Topic: Examine effects of esomeprazole on nighttime heartburn, GERD-related sleep disturbances, sleep quality, work productivity and regular activities.

Study design: RCT	**Country/Setting**: U.S./Multicenter	**Funding**: supported by AstraZeneca LP, Wilmington, DE

Interventions(s): Esomeprazole 20mg or 40mg od for 4 weeks	**Comparator(s)**: Placebo od for 4 weeks.

Primary outcome(s): Relief of nighttime heartburn during last 7 days of the trial -- recorded by pt on a diary card.	**Other outcome(s)**: Change from baseline to week 4 in the global Pittsburgh Sleep Quality Index (PSQI) score (10), percentage of patients with complete resolution of sleep disturbances, relief of sleep disturbances, percentage of days without GERD-associated sleep disturbances. Percentage of patients with complete resolution of daytime, nighttime, and 24-h heartburn symptoms, and the percentage of patients with relief of daytime and 24-h heartburn symptoms. The Work Productivity and Activity Impairment Questionnaire: Sleep Disturbance-GERD (WPAI-SLEEP-GERD) used to assess work productivity.

Inclusion criteria: men and women aged 18–85 yr with a history of heartburn or acid regurgitation for ≥3 months or with any history of erosive esophagitis. Patients eligible for the screening period had to have an average of ≥2 episodes of nighttime heartburn symptoms per week. Patients also had a ≥1-month history of GERD-associated sleep disturbances. Patients with both GERD-associated sleep disturbances on ≥3 of the last 7 days of the screening period, and nighttime heartburn graded as moderate or severe on ≥3 of the last 7 nights of the screening period were eligible for randomization. GERD-associated sleep disturbances included, but were not limited to, trouble falling asleep, unwanted awakenings, or overall poor sleep quality caused by nocturnal heartburn, reflux, or any other GERD symptom. Patients were eligible for trial participation while taking a stable regimen of any sleep medication,	**Exclusion criteria:** Patients were excluded if they had any conditions other than GERD that could be the primary cause of or a significant contributor to the patient's sleep disturbance. These conditions included, but were not limited to, severe anxiety, severe depression, panic attacks, sleep apnea, obstructed airways, chronic obstructive pulmonary disease requiring oxygen therapy or that was known to have disrupted the patient's sleep, Pickwickian syndrome, restless leg syndrome, excessive need for nighttime urination, chronic insomnia of unknown cause, Buerger's disease, and excessive caffeine use. Nighttime shift workers and patients planning to travel beyond three time zones during the study also were excluded. Exclusion criteria also included the following: use of a PPI within 1 wk before screening; active GI bleeding; any severe, unresolved, or unstable acute illness; any preexisting chronic illness likely to compromise assessment of efficacy or safety; need for continuous concur rent therapy with phenytoin, mephenytoin, warfarin, or antineoplastic agents for active cancer; known hypersensitivity to esomeprazole or antacid tablets (Gelusil 200 mg, aluminum hydroxide,

antihistamine, benzodiazepine, or anti-anxiety medication when use had been consistent for ≥3 months before trial entry and was expected to remain stable throughout the trial.	200 mg magnesium hydroxide, 25 mg simethicone; Warner-Lambert Consumer Healthcare [Parke-Davis], Morris Plains, NJ); and a history of drug addiction or alcohol abuse within the previous year. Women were required to be non-pregnant, non-lactating, and maintain effective contraception if of child- bearing potential.
Symptoms (describe): Pts recorded on diary cards the severity of heartburn symptoms and whether or not they had GERD-associated sleep disturbances by answering a "yes" or "no" question. HEARTBURN SYMPTOMS. Patients assessed their symptoms on a diary card each morning during the screening period and before that morning's study medication dose during the treatment period. Severity of the most severe heartburn episodes experienced in the previous 24 h during daytime and nighttime were rated on a 4-point scale as: none (no heartburn); mild (awareness of heartburn, but easily tolerated); moderate (discomforting heartburn sufficient to cause interference with normal activities [including sleep]); severe (incapacitating heartburn with inability to perform normal activities [including sleep]). Nighttime was defined as the time between when the patient went to bed to try and go to sleep and when the patient got up in the morning to start daily activities. Heartburn was defined as a burning feeling, rising from the stomach or lower part of the chest toward the neck. Twenty-four-hour heartburn severity was derived from the worst response recorded by the patient for daytime or nighttime heartburn. Relief of heartburn was defined as a daily diary card response of "none" on at least 6 of 7 days, allowing for one "mild" response. Complete resolution of heartburn was defined as a response of "none" on 7 consecutive days. Symptom improvement was defined as any decrease in weekly symptom score from baseline compared with the last 7 days in the study.	**Hiatal hernia (specify whether considered and size used for exclusion)**: Not considered
EGD (performed or not and results): Endoscopy was intentionally not performed so that the population would include patients with either symptomatic (nonerosive) or erosive GERD.	**Esophagitis/stricture/Barrett's**: Pts. with Barrett's oesophagus or oesophageal stricture excluded. See exclusion criteria.
pH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** See inclusion criteria: Patients were eligible for trial participation while taking a stable regimen of any sleep medication, antihistamine, benzodiazepine, or anti-anxiety medication when use had been consistent for ≥3 months before trial entry and was expected to remain stable throughout the trial.
Esophageal manometric studies (performed or not and results): Not performed	Other:

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B	
Blinding: Double-blind	Allocation concealment: All medications were provided as capsules of identical appearance to be ingested whole with water once daily in the morning, 30 min before breakfast, for 4 wk. Capsules were supplied in bottles with blinded and coded labels. The treatment code was not to be broken by the investigator except in medical emergencies.
Intention-to-treat: Not described	Method of Randomization: Yes, after the screening period, all eligible patients were randomized sequentially in a 1:1:1 ratio to receive esomeprazole 40 mg, esomeprazole 20 mg, or placebo. The study sponsor provided a separate predetermined, computer-generated randomization schedule to each study center.
Other comments: large randomized double blind multicenter trial, however ITT not described, poor diagnostic quality and short 4-week follow up.	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		X

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: Esom 40mg: 46.3; Esom 20mg: 46.8; Placebo: 46.5	N enrolled: 675
%Male: Esom 40mg: 40.2; Esom 20mg: 40.0; Placebo: 40.7	N completed: 642
Race: Esom 40mg: 46.3; Esom 20mg: 46.8; Placebo: 46.5	Dropouts/reasons: 33 (adverse events, lost to follow up, lack of therapeutic response, non compliance, consent withdrawn, misplaced meds, study specific discontinuation, investigator descision, adverse event)
BMI: Not done	Follow-up period: 4 weeks
Comments:	

Results
Primary outcome(s): A significantly ($p < 0.0001$) higher proportion of patients had relief of nighttime heartburn symptoms during the last 7 days of the trial (the primary trial outcome) in the esomeprazole 40- and 20-mg groups (53.1% and 50.5%, respectively) versus the placebo group (12.7%) (Fig. 2). The esomeprazole results were not significantly different from each other. The mean difference (95% confidence interval [CI] of the difference) between the esomeprazole 40-mg group and placebo was 40.4% (32.4%, 48.5%) and between the esomeprazole 20-mg group and placebo was 37.8% (29.9%, 45.7%). Complete resolution and relief of GERD-associated sleep disturbances were similar in the esomeprazole 40- and 20-mg groups, and significantly higher ($p < 0.0001$) in both groups than in the placebo group (Fig. 3). The percentages of patients who had complete resolution and relief of heartburn symptoms were also significantly higher ($p < 0.0001$) in both esomeprazole groups than in the placebo group (Fig. 2). Significantly more patients in both esomeprazole groups than in the placebo group ($p < 0.001$) had improvement (from baseline) during the last 7 days

of treatment in nighttime heartburn symptoms: 175 of 209 (83.7%), 188 of 220 (85.5%), and 154 of 221 (69.7%) for the esomeprazole 40- and 20-mg and placebo groups, respectively. Similar numbers of patients, 174 of 209, 184 of 220, and 152 of 221, in the esomeprazole and placebo groups, respectively, (both $p < 0.001$ vs placebo) had improvements in daytime symptoms.

Secondary outcome(s):
At baseline, 527 of 632 (83%) of patients had poor sleep quality (global PSQI score, >5). By week 4, 111 of 204 (54%) patients treated with esomeprazole 40 mg and 91 of 214 (43%) patients treated with esomeprazole 20 mg had poor sleep quality compared with 137 of 214 (64%) patients receiving placebo ($p < 0.001$ for both treatments versus placebo). The least square mean (LSM) changes from baseline to week 4 in global PSQI score were similar between the esomeprazole 40-mg and 20-mg groups (−3.64 and −4.00, respectively, p= not significant), and both improvements were significantly greater than in the placebo group (−2.19; $p < 0.0001$ for both comparisons).

At the week-4 assessment, the mean (SD) number of rescue antacid tablets used daily by all randomized patients was similar between the esomeprazole 40-mg and 20-mg groups (1.0 [1.45] and 0.9 [1.41], respectively) but was significantly greater ($p < 0.0001$) in the placebo group (1.7 [1.61]).

Comments:

Compliance:
Compliance with study medications and use of rescue medication were measured by counting returned tablets. Patients were considered compliant with study treatments if they took between 75% and 125% of their study medication. Compliance was similar among groups (93.3% [195/209] in the esomeprazole 40-mg group, 94.5% [208/220] in the esomeprazole 20-mg group, and 94.1% [208/221] in the placebo group).

Adverse Events:
Number (%) of Patients with Adverse Events

	Esomeprazole 40 mg (n = 220)	Esomeprazole 20 mg (n = 226)	Placebo (n = 229)
Any AE	74 (33.6)	59 (26.1)	58 (25.3)
Treatment-related AE	15 (6.8)	15 (6.6)	7 (3.1)
Serious AE	2 (0.9)	1 (0.4)	1 (0.4)
Discontinuation due to AE	1 (0.5)	3 (1.3)	1 (0.4)
Most common AE□			
Diarrhea	5 (2.3)	11 (4.9)	7 (3.1)
Headache	11 (5.0)	4 (1.8)	5 (2.2)
Nausea	6 (2.7)	3 (1.3)	4 (1.7)
Flatulence	5 (2.3)	4 (1.8)	1 (0.4)
Abdominal pain	4 (1.8)	4 (1.8)	3 (1.3)

□ Experienced by ≥4 patients in any treatment group.

Applicability: (narrow/wide): Narrow	Comments: Tx population consists of pts. with GERD-related sleep disturbance

GERD data extraction form

Author: Kahrilas	**Yr: 2007**	**UI:** 17950677	**Questions addressed: 1, 3**	**Extractor: WY**

Objective/Topic: To compare 3 doses of AZD0865 and esomeprazole on the proportion of reflux esophagitis healing and symptom control at 2, 4, and 8 weeks To assess safety and tolerability of AZD0865

Study design: RCT	**Country/Setting:** 188 centers in the US, Canada, France, Germany, Norway, United Kingdom, Finland, Italy, Sweden, and Denmark	**Funding:** AstraZeneca

Interventions(s): AZD0865 25, 50, or 75 mg q day, 30min before breakfast	**Comparator(s):** esomeprazole 40 mg q day, 30min before breakfast

Primary outcome(s): esophagitis healing at 4 weeks	**Other outcome(s):** Esophagitis healing at 8 weeks Symptom control

Inclusion criteria: 18-70 years old With Los Angeles grade A-D reflux esophagitis, assessed by endoscopy At least 6 months of heartburn (burning feeling behind the breastbone) as main GERD symptom Within the 7 days before randomization, experience episodes of heartburn at moderate intensity or more in at least 4 days	**Exclusion criteria:** Within 3 months prior to beginning of study, experienced: esophageal stricture, esophageal motility disorder, systematic sclerosis, irritable bowel syndrome, inflammatory bowel disease, Zollinger-Ellison syndrome, gastric ulcer, duodenal ulcer, duodenal erosion. Abnormal serum chemistry or blood count, significant "alarm symptoms", history of drug or alcohol abuse, heartburn that was not relieved within 2 weeks of treatment with PPIs or histamine2 receptor antagonists, concurrent use of other acid-suppressive therapy, gastroprotective agents, drugs that could alter AZD0865 pharmacokinetics, NSAIDs, bisphosphonates, or antineoplastic drugs. Pts who used a PPI or had continuous histamine2 receptor antagonists within the last 14 days of endoscopy and/or between endoscopy and the first dose of study treatment
Symptoms (describe): 4-grade scale (none, mild, moderate, severe), results not reported	**Hiatal hernia (specify whether considered and size used for exclusion): no**
EGD (performed or not and results): yes Grade A: 35.26% Grade B: 40.96% Grade C: 18.50% Grade D: 5.30%	**Esophagitis/stricture/Barrett's:** Barrett's: 8.26%
PH study (performed or not and results): no	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no**
Esophageal manometric studies (performed or not and results): no	**Other:** Hx of GERD for 6-12months: 4.79% Hx of GERD for >12 months: 95.21%

	H pylori negative: 84.97% H pylori positive: 13.76% H pylori missing: 1.27%

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous	
Blinding: double blinded	**Allocation concealment:** yes
Intention-to-treat: yes (Authors defined intention-to-treat as pts who received treatment. 7 pts were randomized but did not receive treatment, and were not analyzed.)	**Method of Randomization:** computer generated randomization list
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
x		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46.75 years	**N enrolled:** 1521 (number of randomized subjects)
%Male: 63.20%	**N completed:** 1406 completed (analyzed 1514 subjects who started treatment)
Race: 88.23% white 3.32% black 0.47% asian 8.00% other	**Dropouts/reasons:** GI disorders (1.1-1.3%) Nervous system disorders (0.3-1%)
BMI: not reported	**Follow-up period:** some subjects were followed for 4 weeks (767 subjects), and some subjects were followed for 8 weeks (747 subjects)
Comments:	

Results
Primary outcome(s): Rate of esophagitis healing at 4 weeks AZD0865 25 mg (n=386): 76.9% (CI: 72.4, 81.1) (p>0.05) AZD0865 50 mg (n=377): 78.2% (CI: 73.7, 82.3) (p>0.05) AZD0865 75 mg (n=375): 81.1% (CI: 76.7, 84.9) (p>0.05) Esomeprazole 40 mg (n=376): 81.9% (CI: 77.6, 85.7) Rate of esophagitis healing at 4 weeks, stratified by baseline LA grade Grade A AZD0865 25 mg (n=132): 84.1% (CI: 76.7, 89.9) (p= 0.599) AZD0865 50 mg (n=127): 85.0% (CI: 77.6, 90.7) (p= 0.721) AZD0865 75 mg (n=144): 83.3% (CI: 76.2, 89.0) (p= 0.403) Esomeprazole 40 mg (n=131): 87.0% (CI: 80.0, 92.3) Grade B AZD0865 25 mg (n=166): 76.5% (CI: 69.3, 82.7) (p= 0.022) AZD0865 50 mg (n=153): 77.8% (CI: 70.4, 84.1) (p= 0.053) AZD0865 75 mg (n=145): 82.8% (CI: 75.6, 88.5) (p= 0.424) Esomeprazole 40 mg (n=156): 86.5% (CI: 80.2, 91.5) Grade C

AZD0865 25 mg (n=69): 73.9% (CI: 61.9, 83.7) (p= 0.579)
AZD0865 50 mg (n=73): 72.6% (CI: 60.9, 82.4) (p= 0.717)
AZD0865 75 mg (n=65): 83.1% (CI: 71.7, 91.2) (p= 0.051)
Esomeprazole 40 mg (n=73): 68.5% (CI: 56.6, 78.9)

Grade D

AZD0865 25 mg (n=19): 42.1% (CI: 20.3, 66.5) (p= 0.505)
AZD0865 50 mg (n=24): 62.5% (CI: 40.6, 81.2) (p= 0.750)
AZD0865 75 mg (n=21): 47.6% (CI: 25.7, 70.2) (p= 0.743)
Esomeprazole 40 mg (n=16): 43.8% (CI: 19.8, 70.1)

Note: p value compares AZD0865 vs esomeprazole

Secondary outcome(s):

Esophagitis healing at 8 weeks: no significant differences, data not reported

Percentage of patients free from heartburn
AZD0865 25 mg (n=165): 52.7% (CI: 45.1, 60.4)
AZD0865 50 mg (n=155) : 57.4% (CI: 49.6, 65.2)
AZD0865 75 mg (n=159) : 63.5% (CI: 56.0, 71.0)
Esomeprazole 40 mg (n=157) : 54.1% (CI: 46.4, 61.9)
Significant difference between AZD0865 25 mg and AZD0865 75 mg (p=0.4)

Time to sustained absence or the proportion of patients free of other patient-reported symptoms : no significant differences, data not reported

Pattern of heartburn control: no significant differences, data not reported

Comments:

Compliance: by pill count, >75% in 94% of all subjects. No group-specific information reported.

Adverse Events:
Any adverse event (about 30%, not different between groups)
Headache (4.1-7.4%)
Diarrhea (2.4-4.1%)
Nausea (1.9-3.9%)
Gastrointestinal disorders (1.1-1.3%)
Nervous system disorder (0.3-1%)
4 pts had serious adverse effects that were not caused by the treatments (determined by investigators)
Rate of discontinuation of treatment due to adverse effects not different between groups (2.1-3.2%).

Liver transaminases were increase in some pts, almost all in AZD0865 groups.
ALT>3x ULN:
- AZD0865 25 mg: 3 subjects, 0.8%
- AZD0865 50 mg : 6 subjects, 1.7%
- AZD0865 75 mg : 8 subjects, 2.2%
- Esomeprazole 40 mg : 1 subjects, 0.3%

ALT>5x ULN:
- AZD0865 25 mg : 2 subjects, 0.5%
- AZD0865 50 mg : 4 subjects, 1.1%
- AZD0865 75 mg : 5 subjects, 1.4%
- Esomeprazole 40 mg : 0 subjects, 0%

AST>3xULN:
- AZD0865 25 mg : 4 subjects, 1.1%
- AZD0865 50 mg : 5 subjects, 1.4%
- AZD0865 75 mg : 5 subjects, 1.4%
- Esomeprazole 40 mg : 0 subjects, 0%

ALP>3xULN:
- AZD0865 25 mg : 1 subject, 0.3%
- AZD0865 50 mg : 0 subjects, 0%
- AZD0865 75 mg : 0 subjects, 0%
- Esomeprazole 40 mg : 0 subjects, 0%

Note: there is no specific data on the percentage of adverse events (except liver transaminases increases) per group, nor the number of pts that experience these adverse events.

Applicability: (narrow/wide): wide	**Comments:**

Note: At 2 weeks after starting treatment, a subgroup of subjects from some centers was selected to undergo 24-hr ambulatory intraesophageal pH monitoring (85 subjects) and intragastric pH monitoring (77 subjects).

First author: Kalinowska	**Year:** 2006	**UI: 17427490**

Modifying Factor(s): conversion disorder classified by Minnesota Multiphasic Personality Inventory (MMPI); sex

Study design: prospective cohort **Follow up duration:** 3 mo	**Country: Poland** **Multicenter:** no	**Funding:** nd

Interventions(s): laparoscopic Nissen or Toupet fundoplication

Primary outcome(s): Quality of life	**Other outcome(s):** (if reported)

Baseline characteristics:
GERD definition for the population included: "proven" GERD by gastroscopy or Barium study
Age: mean 50 (range 21-74 y)
Gender: 44% male
Race: (if available)
Severity of symptoms:
Duration of symptoms:
Frequency of symptoms:
Type of medications:
Acid reflux (by pH study): done only if previous tests not conclusive
Abnormal manometry study: no
Esophagitis by endoscopy: yes (implied)

Significant baseline differences between GroupA and GroupB (and GroupC… etc)

Symptoms: conversion disorder vs. no conversion disorder: heartburn (95.6% vs. 88%)
EGD: nd
EMS: nd
PH study: nd
Hiatal hernia: all had hiatal hernia; no data on baseline differences between groups
Meds used in the groups: nd

Other:

N enrolled per group:	Conversion Disorder: 28	No conversion disorder: 22	GroupC: (if any)
N completed per group:	28 (?)	22 (?)	GroupC: (if any)

Outcomes (as reported in the Results)	**Results**		
	Conversion	No conversion	Difference between groups
Symptom improvement (metric: e.g., number of patients, mean number of reflux episodes, etc) (p between groups)			
QOL per Polish GI QOL index	84.3±16.3 (preop) to 100.6±21.2 (postop)	93.0±19.4 (preop) to 106.7±18.1 (postop)	NS

Outcomes (as reported in the Results)	Results		
	Conversion	No conversion	
QOL per Polish GI QOL index (women)	N=14; 78.2±15.7 (preop) to 105.1±15.0 (postop) (P=0.004)	N=14; 93.8±17.9 (preop) to 111.1±17.6 (postop) (P=0.02)	
QOL per Polish GI QOL index (men)	N=8; 94.3±12.2 (preop) to 99.9±23.0 (postop) (P=0.55)	N=14; 92.3±21.4 (preop) to 102.6±18.1 (postop) (P=0.23)	

Adverse Events: ND (if reported, please add proportion of patients per adverse event; also separate to minor or major adverse events)

Quality Assessment:
Description of the biological plausibility for the hypothesis to be tested: yes
Description of inclusion /exclusion criteria and rationale: no
Documentation of how data were collected and analyzed (eg, blinding): no
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): no
Participant drop-out percentage (<20%?): yes
Description of statistical methods in sufficient detail to be replicated: yes
Overall grade: C

Comments: relatively small number of subjects; unclear how patients were enrolled

ND: no data

First author: Kamolz	**Year: 2005**	**UI: 15959712**

Modifying Factor(s): endoscopy negative esophagitis patients

Study design: prospective cohort **Follow up duration:** 5 yr (3mo; 1yr; 3yr)	**Country:** Austria **Multicenter:** no	**Funding:** None reported

Interventions(s): laparoscopic ‘‘floppy’’ Nissen fundoplication

Primary outcome(s): German version of the gastrointestinal Quality of Life Index (GIQLI)	**Other outcome(s):** 1) (after surgery) esophageal manometry 2) (after surgery) 24-h pH monitoring 3) (after surgery) standard list of 17 symptoms and **side effects** 4) (5 years after surgery) query for patients’ satisfaction and if they would undergo laparoscopic antireflux surgery (LARS) again, if necessary

Baseline characteristics:
GERD definition for the population included: persistent reflux-related symptoms
Age: 53 y (mean)
Gender: 61% male
Race: ND
BMI: ND
Severity of symptoms: Mean subscore for GI symptoms (GIQLI)=47.1
Duration of symptoms: 7.1 yr (mean)
Frequency of symptoms: ND
Type of medications: PPIs (partly in combination with H2 blockers) at different dosages (20–80mg of different types of medication) (mean duration 17.5 mo)
Acid reflux (by pH study): yes /Describe definition of abnormal: pathological (ND) DeMeester score at presurgical evaluation using 24-h pH monitoring for all participants
Abnormal manometry study: yes /Describe definition of abnormal: ND
Esophagitis by endoscopy: yes

Significant baseline differences between GroupA and GroupB (and GroupC… etc)

Symptoms: No difference (mean subscore for GI symptoms [GIQLI])
EGD: Group A: negative for esophagitis vs. Group B: positive for esophagitis
EMS: No difference (mean LES pressure)
PH study: Group A: mean DeMeester score 41.4 vs. Group B: 59.7 ($P<0.05$)
Hiatal hernia: Group A: 49 vs. Group B: 82 ($P<0.05$)
Meds used in the groups: No difference in mean period of PPI

Other:

N enrolled per group:	GroupA: 89	GroupB: 89	GroupC: NA
N completed per group:	GroupA: 89	GroupB: 89	GroupC: NA

Outcomes (as reported in the Results)	**Results**	
	GroupA: *esophagitis negative*	GroupB: *esophagitis positive*
Mean (SD) DeMeester score (NS)	6.3 (3.1)	5.9 (3.5)
Mean (SD) LES pressure, mmHg (NS)	13.3 (7.0)	13.9 (5.6)
Mean improvement (baseline-5yr) (SD) at GIQLI ($P<0.05$)	81.7 (11.6) – 121.2 (8.5)	93.8 (10.3) – 120.9 (8.5)
Number of patients with “very good/ good” satisfaction (NS)	88	87

Number of patients who would undergo surgery again, if needed (NS)	88	87
Number of patients with laparoscopic redo-surgery (NS)	1	1
Number of patients with recurrent reflux symptoms/ pathological DeMeester score/ restart medication (PPI) (NS)	1	1

Adverse Events:

Postoperative dysphagia (3 mo): Patients in the group A showed a higher grading of present and impairing swallowing problems (29.2 vs 12.4%)
Early satiety (6.1%) (1st yr)
Hiccups (6.7%) (1st yr)
Bloating (7.9%) (1st yr)
Severe flatulence (5.3%) (first weeks)
Severe diarrhea (3.6%) (first weeks)
Severe weight loss (>5Kg) (6.7%) (1st yr)

Quality Assessment: Description of the biological plausibility for the hypothesis to be tested: yes Description of inclusion /exclusion criteria and rationale: yes Documentation of how data were collected and analyzed (eg, blinding): yes Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): no Participant drop-out percentage (>20%?): yes Description of statistical methods in sufficient detail to be replicated: yes **Overall grade: C**
Comments: retrospective database analysis. Baseline patient characteristics were well balanced but not sure if surgical procedures were similar between groups.

ND: no data; NA: non-applicable; NS: non-significant

GERD data extraction form

Author: Katz	Yr: 2007	UI: 17305763	Questions addressed: 1,3	Extractor: SI

Objective/Topic: to assess the relationship between % time intragastric pH >4.0 and healing of erosive esophagitis (EE) (we will only be extracting outcome data at 4 wk)

Study design: RCT	Country/Setting: US	Funding: AstraZeneca

Interventions(s): esomeprazole 10 mg once daily for 4 wk	Comparator(s): esomeprazole 40 mg once daily for 4 wk

Primary outcome(s): esophagitis healing	Other outcome(s):

Inclusion criteria: Men and women (aged 18–75 years) who had EE classified as LA grade C or grade D as diagnosed by EGD within 7 days before study entry	Exclusion criteria: clinically significant GI bleeding, non-acid-related esophagitis as judged by investigator, a history of gastric or esophageal surgery (except simple closure of a perforated ulcer), bleeding disorders, abnormal laboratory values or presence within the past 3 mo of any chronic or unstable acute illness likely to compromise the assessment of efficacy or safety in this study; severe dysphagia, Zollinger–Ellison syndrome, esophageal motility disorders, clinically significant esophageal stricture, esophageal varices, duodenal or gastric ulcer, upper gastrointestinal malignancy or Barrett's esophagus (>3 cm) or dysplastic changes in the esophagus; pregnant or lactating women; women who did not maintain effective contraception in those with child-bearing potential; alcohol or drug addiction (≤12 mo before screening) or intolerance to an ingredient of any PPI or if they had used >7 doses of a PPI or daily H_2RA in excess of approved prescription-strength doses within 28 days of the screening (visit 1), any PPI within 7 days of the screening EGD or any other investigational compound within 28 days of starting study medication; treated concurrently with warfarin or other anticoagulants, prostaglandin analogues, antineoplastic agents, salicylates, steroids, pro-motility drugs, anticholinergics, high-dose narcotics, sucralfate, NSAIDs (>3 times/week) or any medication dependent on gastric acid for optimal absorption
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results): y 92% C; 8% D	Esophagitis/stricture/Barrett's:
pH study (performed or not and results): y	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):

GERD data extraction form

Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
y

Quality Assessment for RCTs: C/Poor	
Blinding: y	Allocation concealment: n
Intention-to-treat: n	Method of Randomization: nd
Other comments: ~39% of randomized participants not in per protocol analysis	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 48.7 (SD12.1)	N enrolled: 169
%Male: 67	N completed: 131; 103 (per protocol analysis)
Race: 94% white; 7% black	Dropouts/reasons: <2 EGDs; no grade C or D EE; drug non-compliance, and others
BMI: 30 (SD6)	Follow-up period: 7 d and 4 wk
Comments:	

Results
Primary outcome(s): esophagitis healing at 4 wk esomeprazole 10 mg 29/53 (54.7%) esomeprazole 40 mg 43/50 (86%)
Secondary outcome(s): % time pH >4 at 5 d esomeprazole 10 mg 41% (SD 21.6) esomeprazole 40 mg 72% (SD 17.3)
Comments:

Compliance:
mean drug compliance rate was 99.7% for the per protocol population

Adverse Events:
no death or serious adverse events; 3 discontinued med due to adverse events, judged not related to med; doses of esomeprazole combined erosive gastritis 4/165 (2%)

increased alanine aminotransferase 3/165 (2%) vomiting 3/165 (2%) nasopharyngitis 4/165 (2%)

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Kiljander	Yr: 2006	UI: 16357331	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
Compare the effect of esomeprazole 40mg bid with placebo in pulmonary functions

Study design:	Country/Setting: US? Finland?	Funding:
RCT	Multi-center	AstraZeneca

Interventions(s):	Comparator(s):
esomeprazole 40mg bid (30 min before breakfast and 30 min before dinner) for 16 weeks	placebo bid (30 min before breakfast and 30 min before dinner) for 16 weeks

Primary outcome(s):	Other outcome(s):
Mean change of the morning PEF (baseline was defined as the last 7 days of run-in, and final was defined as the last 28 days of the study)	Change in evening PEF Asthma symptoms Antacid use Adverse events

Inclusion criteria:	Exclusion criteria:
aged 18 to 70 yr stable asthma outpatients treated with inhaled glucocorticosteroids and/or leukotriene pathway modifiers for at least 3 months prior to the study no change in asthma medication change in the last 30 days FEV1 of 50 to 80% predicted with 12% or greater (and ≥ 0.20 L) reversibility mean morning peak expiratory flow <80% predicted	current smoking or hx of 10 pack-years or more; use of oral, rectal, or parenteral glucocorticosteroids <30 days before study; previous esophageal or gastric surgery; erosive esophagitis in the 16 wk or fewer before enrollment; PPI use in the 14 d before enrollment; recurrent moderate or severe GERD symptoms in the previous year in subjects older than 40 yr
Symptoms (describe): No	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): no	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: C/Poor	
Blinding: no (but used placebo?)	Allocation concealment: no
Intention-to-treat: no	Method of Randomization: not reported
Other comments: randomized within strata (3) based on nocturnal respiratory symptoms and presence of GERD a bit strange to find subjects that did not meet eligibility criteria after randomization	

GERD data extraction form

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		x

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 44.7	N enrolled: 770
%Male: 30.5%	N completed: 624
Race: 80% white	Dropouts/reasons: not treated (1 in esomeprazole, 2 in placebo), did not meet eligibility criteria (22 in esomeprazole, 24 in placebo), adverse events (24 in esomeprazole, 31 in placebo), withdrew consent (8 in esomeprazole, 4 in placebo), lost to f/u (5 in esomeprazole, 5 in placebo), other (5 in esomeprazole, 15 in placebo)
BMI: 28 (median)	Follow-up period: 16 weeks
Comments:	

Results

Primary outcome(s):
Adjusted mean improvement in the change in morning PEF

	Number of subjects	Mean, last 28 days of the treatment period (L/min)
Esomeprazole	386	22.3
placebo	374	16

Change in morning PEF

Pt strata	Based on information from:	Mean difference (L/min) (esomeprazole - placeo)	95% CI	P value
All pts	Last 28 days of the treatment period	6.3		0.061
	Whole treatment period	5.6		0.042
Without GERD With nocturnal respiratory symptoms	Last 28 days of the treatment period	3.6	-8.7, 16.1	0.57
	Whole treatment period	2.6	-7.6, 12.8	0.62
With GERD Without nocturnal respiratory symptoms	Last 28 days of the treatment period	8.3	-3.7, 20.3	0.17
	Whole treatment period	5.6	-4.3, 15.4	0.27
With GERD With nocturnal respiratory symptoms	Last 28 days of the treatment period	7.0	-2.5, 16.5	0.15
	Whole treatment period	8.7	0.8, 16.5	0.03

Secondary outcome(s):
Change in evening PEF

Pt strata	Based on information from:	Mean difference (L/min) (esomeprazole - placeo)	95% CI	P value
All pts	Last 28 days of the treatment period	5.9		0.078

Without GERD With nocturnal respiratory symptoms	Last 28 days of the treatment period	-0.3	-12.7, 12.0	0.96
	Whole treatment period	1.3	-9.0, 11.6	0.81
With GERD Without nocturnal respiratory symptoms	Last 28 days of the treatment period	6.7	-5.1, 18.6	0.27
	Whole treatment period	4.7	-5.2, 14.6	0.35
With GERD With nocturnal respiratory symptoms	Last 28 days of the treatment period	11.2	1.8, 20.6	0.02
	Whole treatment period	10.2	2.3, 18.0	0.012

Asthma symptoms

	Number of asthma exacerbations throughout the study	Median times to exacerbation	P value
Esomeprazole	22	42 days	0.70
placebo	24	67 days	

Use of antacid (daily mean number of tablets)
Esomeprazole (n=387): 0.47
Placebo (n=383): 0.58

Comments:
Analysis on the change in morning and evening PEF in pts who took long acting beta2-agonists only is also available. Briefly, esomeprazole significantly improved both morning and evening PEF among pts with both GERD and nocturnal respiratory symptoms (see table 3 for detailed data).
There was no difference in asthma symptoms and quality of life between the 2 groups. Among pts with both GERD and nocturnal respiratory symptoms, there was a significantly smaller reduction in proportion of days with PEF variability (p=0.016) (see supplemental material).

Compliance:
Not reported

GERD data extraction form

Adverse Events:
Any
Esomeprazole (n=386): 306 events in166 pts
Placebo (n=381): 288 events in 171 pts

Asthma
Esomeprazole (n=386): 23 (6%)
Placebo (n=381): 24 (6%)
All (n=767): 47 (6%)

Nasopharyngitis
Esomeprazole (n=386): 23 (6%)
Placebo (n=381): 22 (6%)
All (n=767): 45 (6%)

Headache
Esomeprazole (n=386): 25 (6%)
Placebo (n=381): 17 (4%)
All (n=767): 42 (5%)

Nausea
Esomeprazole (n=386): 9 (2%)
Placebo (n=381): 7 (2%)
All (n=767): 16 (2%)

Back pain
Esomeprazole (n=386): 6 (2%)
Placebo (n=381): 8 (2%)
All (n=767): 14 (2%)

Rhinitis
Esomeprazole (n=386): 6 (2%)
Placebo (n=381): 8 (2%)
All (n=767): 14 (2%)

Influenza
Esomeprazole (n=386): 9 (2%)
Placebo (n=381): 4 (1%)
All (n=767): 13 (2%)

Applicability: (narrow/wide): narrow	Comments: Applicability may be wide, but there is no information on the centers

GERD data extraction form

Author: Kovacs	**Yr: 2009**	**UI: 19267194**	**Questions addressed: Q2;Q3**	**Extractor: MC**

Objective/Topic: to assess the efficacy of lansoprazole in the prevention of erosive esophagitis relapse in recently healed patients and to evaluate the effectiveness of symptom-based dose titration in management of erosive esophagitis and its symptoms.

Study design: This article focused on the titrated open-label period of a RCT. Therefore, it is a cohort study.	**Country/Setting:** 19 sites in US	**Funding:** industry

Interventions(s): • Acute Tx period (8 weeks) –Lansoprazole 30 QD (n=241) • RCT period (1 year) – Lansoprazole 15 QD (n=100) vs. Ranitidine 150 mg BID (n=106) • Titrated open-label period (up to 82 months) – lansoprazole titrated dose (n=195)	**Comparator(s):** healing status (healed vs. unhealed) at open-label baseline Healed (n=93, 48%): erosive reflux esophagitis grade at entry into open-labeled phase was Grade 0 (n=74) or Grade 1 (n=19) Unhealed (n=102, 52%): Grade 2 (n=82), Grade 3 (n=16) or Grade 4 (n=4)

Primary outcome(s): Recurrence of erosive reflux esophagitis.	**Other outcome(s):** changes in the severity of primary and secondary symptoms

Inclusion criteria: Study population: adult men and women (≥18 yr) with endoscopically proven erosive reflux esophagitis (≥Grade 2) and without coexisting duodenal and/or gastric ulcer of ≥3 mm in diameter (within 7 days before initiating Tx). Subject with Barrett's esophagus (but without dysplastic changes) were eligible. Subjects requiring continuous Tx with digoxin or theophylline-containing drugs were permitted to enroll. Subjects were from a randomized, parallel, multicenter, phase III trial consisting of an 8-week open-label acute Tx periods, a double-blind Tx period lasting up to 12 months, and a titrated open-label Tx period of up to 82 months. The titrated open-label period began when the subject had a recurrence of erosive reflux esophagitis or when they completed the double-blind Tx phase. After completing the acute Tx period, subjects with healed erosive reflux esophagitis were eligible to participate in the RCT period. Subjects who completed the RCT period (regardless of relapse or not) were eligible for inclusion in the titrated open-label Tx period.	**Exclusion criteria:** Evidence of active comorbid illnesses, laboratory results outside normal limits; receipt of other investigational drugs(s) within 12 weeks or Tx with a PPI within 4 weeks before initiating study medication; requirement for more than occasional use (≤10 days per month) of nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids equivalent to >10 mg/day prednisone.
Symptoms (describe): all symptoms were described in 3 scales of severity – mild, moderate, or severe Primary symptoms: daytime heartburn (none=69/194; any severity=125/194); night-time heartburn (none=84/194; any severity=110/194) Secondary symptoms (gastroesophageal regurgitation, dysphagia, painful swallowing, nausea and vomiting, day and night abdominal pain, belching, fullness/gloating/early satiety, abdominal distension, anorexia, flatulence/abdominal rumbling): overall signs	**Hiatal hernia (specify whether considered and size used for exclusion):** No data

and symptoms (non=27/193; any severity=199/193)	
EGD (performed or not and results): Diagnosis included an upper endoscopy using a modified Hetzel-Dent grading scale (Grade 0-4); 38% Grade 0, 10% Grade 1, 42% Grade 2, 8% Grade 3; 2% Grade 4	**Esophagitis/stricture/Barrett's:** All had erosive reflux esophagitis
PH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** • After completing the acute Tx period (Lansoprazole 30 QD), subjects with healed erosive reflux esophagitis were eligible to participate in the RCT period. • Subjects who completed the RCT period (regardless of relapse or not) were eligible for inclusion in the titrated open-label Tx period. RCT compared Lansoprazole 15 QD with. Ranitidine 150 mg BID. • At baseline of the titrated open-label period (the focus of this paper), 93/195 (48%) of patients had healed erosive reflux (by either of the RCT Tx) and 102/195 (52%) had unhealed healed erosive reflux (by either of the RCT Tx)
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C (KQ2)
Comments: Q2: the titrated open-label period only included a highly selected subset of original patients enrolled in the RCT and 105/195 (54%) patients discontinued the Tx prematurely. Logistic regression was used to predict relapse which cannot account for different times for censoring. In statistical methods, the authors stated that 5 subjects who entered the titrated open-label Tx period unhealed and subsequently had no documented healing were excluded from the analysis. Q3: Safety data were available for all patients and well documented

Diagnostic Quality: A/rigorous		
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 50.8	**N enrolled: 195**
%Male: 67	**N completed: 105**
Race: 90% White; 7% Black; 3% Hispanic	**Dropouts/reasons:** 105/195 (54%) patients discontinued the Tx prematurely due to adverse events (9%), personal issues (7%), poor compliance (5%), Tx with another drug that would interfere with evaluation of study drug (4%), pregnancy (1%), therapeutic failure (1%), and other reasons (28%) including closure of study site or lost to follow-up. Two patients discontinued because they required fundoplication.

BMI: 29 (4.6 SD)	Follow-up period: up to 82 months
Comments:	

Results
Primary outcome(s): 39 subjects experienced a total of 50 recurrences of erosive reflux esophagitis (up to 82 months of follow-up). OR of recurrence of erosive reflux esophagitis comparing baseline healing status (healed vs. unhealed) = 0.46, 95% CI 0.22, 0.97 "No other demographic or baseline factors were found to be predictive of recurrence of erosive reflux esophagitis." Factors evaluated were age, BMI (>30 or ≤30), gender, race, tobacco use, alcohol use, erosive reflux esophagitis grade at enrollment into the acute phase, as well as healing status, H. pylori status, and symptom status at entry into the open-label Tx period.
Secondary outcome(s): "Although not statistically significant, a higher proportion of subjects who were asymptomatic at open-label baseline remained relapse-free (72/142; 55%) throughout the open-label period compared with subjects who were symptomatic at baseline (64/142; 45%)"
Comments: It is unlikely the predictive model analysis was done correctly. Unclear if number of recurrences or number of subjects were used in the analyses.

Compliance: assessed by pill counting.
5% of the 195 patients discontinued the Tx prematurely due to poor compliance.

Adverse Events:

- Overall, 69/195 (35%) patients experienced an adverse event that was considered to be at least possibly related to the study drug: Diarrhea (19/195, 10%), headache (16/195, 8%), and abdominal pain (12/195, 6%).
- One patient died during open-label Tx (accidental injury), and 2 subjects died during the follow-up period (1 subject died 432 days after discontinuing Tx due to complications of amyotrophic lateral sclerosis and 1 subject died approximately 10 months after discontinuing Tx due to cardiogenic shock secondary to an acute MI. All deaths were considered by the investigator to be unrelated to the study drug.

Applicability: (narrow/wide): narrow	**Comments:** erosive reflux esophagitis only

GERD data extraction form

Author: Labenz	**Yr**: 2009	**UI**: 19222417 / 19298581	**Questions addressed**: 1,2	**Extractor**: JC

Objective/Topic: To identify factors associated with successful treatment (heartburn resolution after 4 weeks and after maintenance treatment with esomeprazole or pantoprazole) of symptoms in patients with reflux esophagitis.

Study design: RCT	**Country/Setting**: 14 countries / Multicenter	**Funding**: In full by AstraZeneca

Interventions(s): esomeprazole 40 mg once daily. Maintenance: esomeprazole 20 mg once daily	**Comparator(s)**: pantoprazole 40 mg once daily. Maintenance: pantoprazole 20 mg once daily

Primary outcome(s): Resolution of heartburn--defined as an absence of moderate or severe symptoms of heartburn in the last 7 days before the week-4 visit. Relapse rates after maintenance phase.	**Other outcome(s)**:

Inclusion criteria: Healing phase-Men or women aged ≥18 years who had RO [Los Angeles (LA) grade A–D , with a history of GERD symptoms for at least 6 months and heartburn for at least 4 days out of the 7 days prior to enrollment. Maintenance phase included subset of participants above with resolved heartburn (no symptoms or only mild heartburn) and healed RO (absence of mucosal breaks in the oesophageal mucosa according to LA classification system) at week 4 or 8 of the healing phase.	**Exclusion criteria:** previous surgery of the oesophagus, stomach or duodenum (apart from simple closure of an ulcer or cholecystectomy), history or symptoms suggestive of Zollinger–Ellison syndrome, primary oesophageal motility disorder, malabsorption, malignancy (except superficial skin disorders), gastric ulcer, duodenal ulcer or duodenal erosions within the previous 3 months, oesophageal stricture, history of dysplasia in Barrett's oesophagus, use of a PPI within 14 days prior to baseline endoscopy or between baseline endoscopy and first dose of study drug, intake of medication likely to affect the outcome of study [including non-selective nonsteroidal anti-inflammatory drugs and selective cyclo-oxygenase (COX)-2 inhibitors] and alarm symptoms. Data acquired after 4 weeks, for patients with unhealed breaks or persistent symptoms who continued the EXPO study protocol, were not included in the present analysis
Symptoms (describe): Heartburn severity was recorded by the investigator at baseline and week 4 according to a validated 4-point scale: 'none', 'mild' (aware of symptom, but easily tolerated), 'moderate' (discomfort sufficient to cause interference with normal activities) or 'severe' (incapacitating, with inability to perform normal activities). Healing was defined as absence of breaks in the oesophageal mucosa.	**Hiatal hernia (specify whether considered and size used for exclusion)**: The presence of hiatal hernia was determined during the baseline endoscopy, not used for exclusion.
EGD (performed or not and results): Performed and graded according to Los Angeles classification at baseline and 4 weeks. See inclusion criteria above.	**Esophagitis/stricture/Barrett's**: History of dysplasia in Barrett's esophagus used for exclusion.

GERD data extraction form

pH study (performed or not and results): Not described.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): Not described.	Other: Helicobacter pylori status was determined at baseline by means of a C urea breath test

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B	
Blinding: Double blind	Allocation concealment: Not described
Intention-to-treat: Yes	Method of Randomization: Yes
Other comments: analyses for predictors of freedom from heartburn relapse are were multivariate analyses (treatment type was in the model)	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
X		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: mean (s.d) 50.6 (13.9)	N enrolled: 3151
%Male: 62.9%/63.1% Maintenance Ph	N completed: Healing phase-3151; Maintenance phase-2766
Race: Not described	Dropouts/reasons: n/a
BMI: mean (s.d) 27.8 (4.3)	Follow-up period: 4 weeks
Comments: Data acquired after 4 weeks, for patients with unhealed breaks or persistent symptoms who continued the EXPO study protocol, were not included in the present analysis	

GERD data extraction form

Results

Primary outcome(s): Heartburn resolution % at 4 weeks with esomeprazole and pantoprazole

	Esomeprazole (n=1562)	Pantoprazole (n=1589)	Absolute difference b/w group difference
Gender			
M	74.0	69.6	4.4
F	70.0	62.2	7.8
Age			
<65 years	71.3	65.6	5.7
≤65 years	77.9	73.2	4.7
BMI			
<30	71.8	66.4	5.4
≤30	74.4	68.4	6.0
History of GERD symptoms at baseline			
≤5 years	72.0	65.3	6.7
>5 year	73.4	69.7	3.6
Severity of heartburn at baseline			
At most moderate	72.1	65.7	6.4
Severe	73.0	68.3	4.7
LA grade at baseline			
A or B	71.4	66.6	4.8
C or D	75.9	67.8	8.1
Barrett's esophagus at any visit			
Absent	71.5	66.7	4.8
Present	79.0	68.4	10.6
H.pylori status at baseline			
Neg	71.3	64.8	6.6
Pos	76.0	73.5	2.4
Unknown	67.3	60.9	6.3
Hiatal hernia at baseline			
Absent	71.0	67.5	3.5
Present	73.8	66.4	7.4
Acid regurg at baseline			
Absent	76.5	74.7	1.8
Present	71.8	65.5	6.3
Epigastric pain at baseline			
Absent	78.9	73.6	5.3
Present	69.4	63.9	5.5
Dysphagia at baseline			
Absent	73.1	68.5	4.6
Present	70.7	62.9	7.8

Heartburn relapse rates during 6 months' maintenance Tx with esomeprazole and pantoprazole

	Esomeprazole (n=1377)	Pantoprazole (n=1389)
Gender		
M	8.3	17.9
F	12.5	16.5
Age		
<65 years	10.4	18.1

≤65 years	7.1	13.6
BMI		
<30	9.5	15.9
≤30	10.6	21.1
History of GERD symptoms		
≤5 years	9.5	15.6
>5 year	10.3	20.5
Severity of heartburn at baseline		
At most moderate	8.4	15.0
Severe	11.4	20.5
LA grade at baseline		
A or B	9.8	16.4
C or D	9.9	20.5
Barrett's esophagus at any visit		
Absent	9.9	17.3
Present	9.1	17.6
H.pylori status at baseline		
Neg	10.3	19.0
Pos	7.5	13.0
Unknown	19.6	17.6
Hiatal hernia at baseline		
Absent	10.1	16.8
Present	9.5	17.8
Acid regurg at baseline		
Absent	11.0	16.2
Present	9.6	17.6
Epigastric pain at baseline		
Absent	8.1	14.5
Present	10.6	18.7
Dysphagia at baseline		
Absent	9.0	16.6
Present	12.1	19.4

Factor favoring treatment success	Heartburn resolution	Freedom from heartburn relapse
More potent acid inhibition	Yes	Yes
H Pylori infection	Yes	Yes
Greater age	Yes	Yes
Male gender	Yes	
BMI <30		Yes
GERD symptoms ≤ 5 years		Yes
No epigastric pain at baseline	Yes	Yes
No acid regurg at baseline	Yes	
Non-severe heartburn at baseline		Yes

Secondary outcome(s):
Comments:

GERD data extraction form

Compliance: nd Patient's taking 75-110% of prescribed doses were deemed to have been compliant with dosing protocol

Adverse Events: N/A

Applicability: (narrow/wide): Wide	Comments:

GERD data extraction form

Author: Lee	Yr: 2009	UI: 19259354	Questions addressed: 2,3	Extractor: JHL

Objective/Topic: Laparoscopic Nissen Fundoplication in Korean Patients with Gastroesophageal Reflux Disease

Study design: Cohort study	Country/Setting: Korea	Funding: ND

Interventions(s): Laparoscopic Nissen Fundoplication	Comparator(s):

Primary outcome(s): Symptom control	Other outcome(s):

Inclusion criteria:	Exclusion criteria:
• "From Sep. 2003 to Mar. 2008, 31 adult Korean patients diagnosed with GERD underwent laparoscopic Nissen fundoplication at our institution; patients with failed medical therapy, frequent recurrences in spite of medication, particularly if dose escalation was required, laryngopharyngeal and/or respiratory symptoms, complications of GERD, such as esophageal stricture, erosive esophagitis, esophageal ulcer, and/or Barrett's esophagus; patients referred from gastroenterologists, otorhinolaryngologists, or came directly for consultation to our Department; patients taking antireflux medications, including proton pump inhibitors."	
Symptoms (describe): • "Typical symptoms were present in 15 (48%) of patients, and atypical symptoms in 16 (51.6%). Both typical and atypical symptoms were present in 4 of patients (12.9%)."	**Hiatal hernia (specify whether considered and size used for exclusion):** Type I in 13 patients (41.9%)
EGD (performed or not and results): performed, but no results	**Esophagitis/stricture/Barrett's:** Reflux esophagitis in 18 (58.1%) Barrett's esophagus in 10 (32.3%)
PH study (performed or not and results): performed, but no results	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): performed, but no results	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: No specific information on definition and measurement of "symptom control"

GERD data extraction form

Diagnostic Quality: C/Poor		
No specific information on diagnosis of GERD		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46.8 y	**N enrolled: 31**
%Male: 61.3%	**N completed: 31**
Race: ND	**Dropouts/reasons: 0**
BMI: ND	**Follow-up period: 13.3 ± 16.7 months, ranging 4 to 30 months**
Comments:	

Results

Primary outcome(s):

Treatment/Comparison:	**Laparoscopic Nissen Fundoplication**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Symptoms	No effect					
Esophagitis (yes vs. no)	No effect					
Hiatal hernia	No effect					

Secondary outcome(s):

Comments:

Compliance: NA

Adverse Events:

Perioperative complications, 5/31 patients (16.1%)

- 1 major complication: gastric perforation due to forceful insertion of bougie, 1/31 (3.2%)
- 2 moderate complications: atelectasis and prolonged ileus, 2/31 (6.5%)
- 2 minor complications: subcutaneous emphysemas, 2/31 (6.5%)

No conversion to open surgery & no mortality

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Liao	**Yr: 2008**	**UI: 18318824**	**Questions addressed: KQ 1; KQ3**	**Extractor: MC**

Objective/Topic:
To evaluate the long-term benefits of ELGP in Asian patients with GERD

Study design:	**Country/Setting:**	**Funding:**
Prospective single-arm trial	Taiwan	No data

Interventions(s):	**Comparator(s):**
Endoluminal gastroplication (ELGP) using EndoCinch (Bard International Products, Billerica, MA, USA). A regular diet was recommended and patient's actual diet was recorded in a diary for confirmation	Post ELGP vs. baseline off meds or baseline on meds

Primary outcome(s):	**Other outcome(s):**
• GERD-specific HRQL • Chinese version of the SF-36 • Treatment failure: returned to dependence on antisecretory medications of more than 4 doses/month or who was treated with surgical fundoplication after ELGP	Medication use

Inclusion criteria:	**Exclusion criteria:**
• >=3 episodes of GERD symptoms per week while off PPI or H2RAs • dependency and responsiveness on daily antisecretory medications for at least 6 months • confirmation of acid reflux by 24-h esophageal pH study, as evidenced by percentage time of pH < 4 for more than 4% and a DeMeester score >14.7 after discontinuing all GERD medications for at least 10 days willingness to receive the procedure as an alternative treatment for GERD • agreement to attend follow up for 2 years	age <18 years; dysphagia; hiatal hernia >3 cm (length from gastroesophageal junction to diaphragmatic hiatus); grade C or D esophagitis while taking medications; esophageal varices; bleeding disorder; BMI >40 kg/m2; and previous gastroesophageal surgery
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):** <=2 cm: 90.5%
EGD (performed or not and results): LA classification – No esophagitis; 33.3%, Grade A: 52.4%; Grade B: 14.3%	**Esophagitis/stricture/Barrett's:** No data
PH study (performed or not and results): Performed at baseline and 3 months after the procedure	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): Performed at baseline and 3 months after the procedure.	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)

GERD data extraction form

Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: single arm trial; N<30

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46.4 (range 28-66)	**N enrolled: 21**
%Male: 86	**N completed: 20**
Race: Asian	**Dropouts/reasons:**
BMI: 24.8	**Follow-up period: 2 years**
Comments:	

Results

Primary outcome(s): 60% of patients had at least a 50% reduction in GERD-HRQL

	Baseline off med (n=21) Mean ±SD	Baseline on med (n=21) Mean ±SD	24 months (n=20) Mean ±SD	P-value, compared to baseline off med	P-value, compared to baseline on med
heartburn frequency	2.7 ± 0.6	1.2 ± 1.1	1.3 ± 0.9	<0.001	NS
heartburn severity	22.8 ± 6.8	11.0 ± 10.2	10.9 ± 8.6	<0.001	NS
heartburn symptom score	64.0 ± 25.9	22.8 ± 30.8	21.1 ± 26.4	<0.001	NS
regurgitation frequency score	2.4 ± 0.7	1.3 ± 1.0	1.3 ± 1.0	<0.001	NS
General health, SF-36	31.2 ± 14.5	45.1 ± 14.9	38.3 ± 15.3	0.032	NS
Mental health, SF-36	49.7 ± 19.5	51.6 ± 18.3	57.0 ± 16.4	0.030	NS

Note on the GERD-HRQL, a lower value indicates a better quality of life and on the SF-36, a lower value represents a worse result.

Secondary outcome(s):

Comments:

Compliance:
No data

Adverse Events:

- Mild and transient complaints occurred, including sore throat in 13 patients, abdominal pain in five, bloating in four, and vomiting in two.
- Three patients had minor dysphasia but this resolved spontaneously within 3 days.
- One patient experienced delayed bleeding with hematemesis after the procedure and needed a transfusion of one unit of blood.
- There were no serious complications associated with the procedure

Applicability: (narrow/wide): narrow	**Comments: Asian only. Small sample size**

GERD data extraction form

Author: Lightdale	**Yr: 2006**	**UI:** 16773434	**Questions addressed:** **Q1; Q2; Q3**	**Extractor: MC**

Objective/Topic: to compare the efficacy of esomeprazole, 20 mg, with that of omeprazole, 20 mg, in patients with erosive esophagitis (EE).

Study design:	**Country/Setting:**	**Funding:**
Multicenter RCT, double-blind, parallel	US	No data

Interventions(s):	**Comparator(s):**
Esomeprazole 20 mg once daily	omeprazole 20 mg once daily

Primary outcome(s):	**Other outcome(s):**
% healing of esophageal erosions (according to LA classification) after 8 weeks of treatment	% healing of esophageal erosions after 4 week % resolution of heartburn (investigator-assessed rating of "none") at week 4, and patients' diary-recorded assessment of daytime (a 24-hr period) and nighttime heartburn.

Inclusion criteria:	**Exclusion criteria:**
aged 18 to 75 years; EE confirmed by EGD, and men or non-pregnant, non-lactating women who were postmenopausal, surgically sterilized, or using an acceptable form of birth control before and throughout the study	a positive *H. pylori* serology test at screening; any bleeding disorder or signs of gastrointestinal (GI) bleeding at the time of the screening EGD or within 3 days before randomization; a history of gastric or esophageal surgery, except for simple closure of perforated ulcer; current or historical evidence (within 3 months) of Zollinger-Ellison syndrome; primary esophageal motility disorders; esophageal stricture; or any serious medical condition including Barrett's esophagus (>3 cm) or known dysplasia in the esophagus; used a PPI within 28 days before the baseline visit or an H_2-receptor antagonist daily during the 2 weeks before the baseline EGD (occasional use less than daily was permitted) or required an H_2-receptor antagonist for the duration of the study. A known hypersensitivity to any component of esomeprazole (Nexium), omeprazole (Prilosec), or antacid (Gelusil) tablets; use of any other investigational compound within 28 days of starting study medication; and previous participation in this study or another clinical study of esomeprazole.
Symptoms (describe): Heartburn 98%	**Hiatal hernia (specify whether considered and size used for exclusion):** No data
EGD (performed or not and results): 100% EGD confirmed erosive esophagitis (EE) LA classification: Grade A 27%, Grade B 36% Grade C 18.5%; Grade D 7.5%	**Esophagitis/stricture/Barrett's:** Excluded Barrett's esophagus (>3 cm)
PH study (performed or not and results): No data	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** no data
Esophageal manometric studies (performed or not and results): No data	**Other:**

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A	
Blinding: double blinding	**Allocation concealment: yes**
Intention-to-treat: yes	**Method of Randomization: blinded blocks of four allocation numbers at a 1:1 ratio**
Other comments: power calculation was done	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 45	**N enrolled: 1176**
%Male: 63	**N completed: 1106**
Race: White 91.5%, Black 4.8%; Other 3.5%	**Dropouts/reasons: 6%** AE (n = 18), loss to follow-up (n = 23),withdrawn consent (n = 17), and sponsor or investigator decision (n = 12).
BMI: no data	**Follow-up period: 8 weeks**
Comments:	

Results
Primary outcome(s): Life-table estimated healing rate (95% CI): Esomeprazole 20 mg once daily 90.6% (88.1%, 93.0%) Omeprazole 20 mg once daily 88.3% (85.5, 91.0%) P=0.621 between groups (log-rank test)
Secondary outcome(s): • The life-table estimates of healing were 68.7% and 69.5% by week 4 for 20 mg esomeprazole and 20 mg omeprazole, respectively. • There were also no significant between-treatment differences after 4 weeks for any other secondary end-points including resolution of heartburn (60.6% esomeprazole vs 60.5% omeprazole; P = 0.995) and proportion of heartburn-free days (72.6% esomeprazole vs 70.9% omeprazole; P = 0.354) or nights (85.7% esomeprazole vs 83.2% omeprazole, P = 0.069). KQ2: "Sex, age (<65 vs ≥65 years), race, and H. pylori status had no meaningful effect on treatment outcome in either group. However, there was a trend toward higher healing rates for women than for men and for patients aged ≥65 years than for those <65 years in both treatment groups. "
Comments:

Compliance:
Compliance rates were similar for the esomeprazole and omeprazole treatment groups (89.8% and 88.3%, respectively).

Adverse Events: Number (%) of patients with adverse events occurring in ≥2.0% of either group

	Esomeprazole 20 mg once daily (n=585)		Omeprazole 20 mg once daily (n=588)	
Headache	58	(9.9)	37	(6.3)
Gastritis	31	(5.3)	18	(3.1)

Respiratory infection	27	(4.6)	25	(4.3)
Diarrhea	27	(4.6)	28	(4.8)
Flatulence	21	(3.6)	24	(4.1)
Abdominal pain	16	(2.7)	22	(3.7)
Nausea	16	(2.7)	23	(3.9)
Sinusitis	13	(2.2)	15	(2.6)
Vomiting	12	(2.1)	11	(1.9)
Pharyngitis	9	(1.5)	12	(2.0)

- AEs were reported in similar proportions of the 585 esomeprazole-treated patients (44%) and 588 omeprazole treated patients (43%)
- Serious AEs were reported in 7 patients (1 and 6 in the 20 mg esomeprazole and 20 mg omeprazole groups, respectively), and none were considered by the investigator to be related to treatment with study drug. Of these 7 patients, one discontinued treatment due to the serious AE. Baseline laboratory tests and vital signs were similar in both treatment groups, and all changes were small and comparable between groups.

Applicability: (narrow/wide): Wide	**Comments:** large sample size but applicable to erosive esophagitis only

GERD data extraction form

Author: Liu	**Yr: 2006**	**UI: 16484118**	**Questions addressed: KQ1; KQ2**	**Extractor: MC**

Objective/Topic:
to determine whether there are any gender differences in clinical presentation, diagnostic evaluations and response to endoscopic therapy in patients with gastroesophageal reflux disease

Study design:	**Country/Setting:**	**Funding:**
Retrospective cohort study	US	Hospital funding

Interventions(s):	**Comparator(s):**
Endoluminal gastroplication using the EndoCinch device (Bard Endoscopic Technologies, Billerica, Mass., USA) or the flexible Endoscopic Suturing Device or ESD® (Wilson-Cook Medical Inc., Winston-Salem, N.C., USA). After endoscopic therapy, the patients were instructed to continue taking antisecretory agents for 2 weeks. Dietary recommendations post-ELGP included a liquid diet for the first day after the procedure and then a soft, pureed diet for 2 weeks. Patients were allowed to resume a normal diet after 2 weeks.	• Response to treatment before-and-after endoscopic therapy • Response to endoscopic therapy by gender

Primary outcome(s):	**Other outcome(s):**
Complete response: a complete resolution of heartburn and regurgitation symptoms or extraesophageal manifestations Partial response: elimination of one but not all the extraesophageal symptoms, or reduction in heartburn or regurgitation symptom scores but with continued use of medication	

Inclusion criteria:	**Exclusion criteria:**
Patients with classic symptoms of GERD including heartburn, regurgitation, or both, patients who had a minimum of 3 months' follow-up for the endoscopic anti-reflux procedure	
Symptoms (describe): Heartburn, regurgitation, or both Extra esophageal symptoms, including chest pain (22%), cough (22%), asthma (11.5%), and reflux laryngitis (21%)	**Hiatal hernia (specify whether considered and size used for exclusion):** Men: 41%; women: 31% Length of hiatal hernia – men: 2 cm (1-7); women 3 cm (1-6)
EGD (performed or not and results): Erosive esophagitis – men: 39%; women: 14%	**Esophagitis/stricture/Barrett's:** Barrett's – men: 14%; women: 5%
PH study (performed or not and results): Mean DeMeester scores – men: 54; women: 37	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): LES pressure (mmHg) – Men: 12.8 (3.8-23.6); women: 14.9 (4.9-45)	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
n/a

GERD data extraction form

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: single arm retrospective study ; no adjustment was done for the comparison of gender differences

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 51	**N enrolled: 95**
%Male: 39	**N completed: 95**
Race: no data	**Dropouts/reasons: n/a**
BMI: men=28; women=29	**Follow-up period: 12 months (range 3-36 mo)**
Comments:	

Results

Primary outcome(s): A total of 80% of men and 79% of women with GERD experienced symptomatic improvement or resolution after endoscopic therapy.

	Male (n=37)	Female (n=58)
% patients responded to endoluminal gastroplication		
Total	32	36
Partial	48	43
No reponse	20	21

No significant differences between groups

Secondary outcome(s):

Comments:

Compliance:
No data

Adverse Events:
No data

Applicability: (narrow/wide): narrow	**Comments:** all patients undergone endoluminal gastroplication in one hospital

GERD data extraction form

Author: Lord	Yr: 2009	UI: 19050984	Questions addressed: 2	Extractor: JHL

Objective/Topic: Hiatal Hernia, Lower Esophageal Sphincter Incompetence, and Effectiveness of Nissen Fundoplication in the Spectrum of Gastroesophageal Reflux Disease

Study design: Cohort study	Country/Setting: Australia	Funding: None

Interventions(s): Nissen Fundoplication	Comparator(s):

Primary outcome(s): Symptoms	Other outcome(s):

Inclusion criteria:

- Patients had been treated by laparoscopic Nissen fundoplication at the University of Southern California Keck School of Medicine Department of Foregut Surgery (USC)
- Patients had symptoms suggestive of reflux disease
- Patients with abnormal distal esophageal acid exposure

Exclusion criteria:

- Patients had received acid suppressant medication therapy prior to their initial endoscopy; had undergone Nissen fundoplication less than 1 year previously; had more than one previous antireflux operation; could not be contacted for this study; patients who had not had a preoperative ambulatory pH study at this institution (those with a named esophageal motility disorder or distal esophageal low amplitude hypomotility, defined as a mean contraction amplitude less than 20 mmHg)

Symptoms (describe):

	NERD	Mild ERD	Severe ERD
Heartburn			
None or mild	3 (7.7%)	4 (9.5%)	4 (11.4%)
Moderate/Severe	36 (92.3%)	38 (90.5%)	31 (88.6%)
Regurgitation			
None or mild	14 (35.9%)	18 (42.9%)	7 (20.0%)
Moderate/Severe	25 (64.1%)	24 (57.1%)	28 (80.0%)
Dysphagia			
None or mild	36 (92.3%)	36 (85.7%)	26 (74.3%)
Moderate/Severe	3 (7.7%)	6 (14.3%)	9 (25.7%)

Hiatal hernia (specify whether considered and size used for exclusion):
N=70/116, 60.34%

EGD (performed or not and results): Performed for classification of patients

Esophagitis/stricture/Barrett's:
Barrett's esophagus; one of GERD category (n=44), this group was excluded for this data extraction. Not modifying factor of interest

PH study (performed or not and results): Performed

	NERD	Mild ERD	Severe ERD
Total % time pH<4	7.4 (3.33)	7.1 (5.2)	9.0 (5.6)

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND

Esophageal manometric studies (performed or not and results): Performed

	NERD	Mild ERD	Severe ERD
LES resting pressure (mmHg)	8.4 (8.8)	7 (7.1)	5.5 (4.2)

Other: Classification of patients

- NERD: Patients without record of esophagitis, defined by the presence of erosions or ulcerations (modified Savary Miller classification) at any endoscopy.
- Mild ERD: Patients with no erosive esophagitis at preoperative endoscopy but a history of ERD at a previous endoscopy that had been healed by acid suppressant drug therapy

	• Severe ERD: patients with persistent or nonhealed esophagitis and was diagnosed when esophagitis was found at the preoperative endoscopy in patients who had received at least some acid suppressant therapy

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
No

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: retrospective chart review

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A/rigorous (endoscopy)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 48.52y	**N enrolled: nd**
%Male: 65.52%	**N completed: 116**
Race: ND	**Dropouts/reasons: 0**
BMI: ND	**Follow-up period:** Median duration of follow-up in months: NERD, 25; Mild ERD, 25.5; Severe ERD 24
Comments:	

Results

Primary outcome(s):

Treatment/Comparison:	**Nissen Fundoplication**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
GERD stage						
NERD (n=39) vs. Mild esophagitis (n=42)	NS					
Mild (n=42) vs. Severe esophagitis (n=35)	NS					

Secondary outcome(s):

Comments:.

Compliance: NA

Adverse Events: ND

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Lundell	Yr: 2006	UI: 16480403	Questions addressed: 3	Extractor: WY

Objective/Topic:
To compare gastric mucosal architecture between GERD pts who had omeprazole 20-40mg QD for 7 years or antireflux surgery

Study design:	Country/Setting:	Funding:
RCT	Sweden	No funding received

Interventions(s):	Comparator(s):
Omeprazole 20-40mg QD for 7 years	Antireflux surgery

Primary outcome(s):	Other outcome(s):
Mucosal morphology H pylori infection	

Inclusion criteria:	Exclusion criteria:
Had symptoms of chronic GERD, had esophagitis per EGD	none
Symptoms (describe): No	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): Yes, results not reported	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): All pts responded to 20–40 mg of omeprazole QD for 4-8 weeks
Esophageal manometric studies (performed or not and results): No	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: it was reported to have 211 patients had complete follow-up data but only 168 patients in the analyses

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
X		

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: <50 years: 85 pts 50-64 years: 91 pts >64 years: 35 pts	N enrolled: 310
%Male: 73.9%	N completed: 211 (reported number)
Race: not reported	Dropouts/reasons: 14 adverse events, 4 noncompliance, 10 lost to follow-up, 6 did not comply with the follow-up procedures, 2 other reason, 41 did not continue after the first 5 years
BMI: not reported	Follow-up period: 7 years
Comments: only 96+72=168 in the analyses	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Compliance: Not reported

Adverse Events:
One patient, who had an uneventful post-operative course, died 3 months after the operation due to myocardial infarction. These are primary outcomes. corpus mucosal inflammation, in omeprazole group: 17/96 (11 mild, 5 moderate, 1 severe) corpus mucosal inflammation, in surgery group: 16/72 (10 mild, 2 moderate, 4 severe) glandular atropy of the oxyntic mucosa, in omeprazole group: 5/96 (2 mild, 1 moderate, 2 severe) glandular atropy of the oxyntic mucosa, in surgery group: 3/72 (all mild) gastric mucosal inflammation on the oxyntic mucosa, among H pylori positive pts, in omeprazole group: 13/13 (1 mild, 5 moderate, 7 severe) gastric mucosal inflammation on the oxyntic mucosa, among H pylori positive pts, in surgery group: 12/12 (4 mild, 5 moderate, 3 severe) Argyrophil cell characteristic (hyperplasia), in omeprazole group: 14/96 (5 diffuse, 3 linear, 6 micronodular) Argyrophil cell characteristic (hyperplasia), in surgery group: 4/72 (1 diffuse, 1 linear, 2 micronodular)

Applicability: (narrow/wide): wide	Comments:

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Author: Lundell	**Yr:** 2007; 2009	**UI:** 17256807; 19490952	**Questions addressed: Q1,3**	**Extractor: MC**

Objective/Topic: 7-year (Lundell, 2007) and 12-year (Lundell, 2009) follow up of a comparative trial of omeprazole with open anti-reflux surgery in patients with chronic GERD – SOPRAN study

Study design: RCT, multicenter	**Country/Setting:** Nordic countries	**Funding:** AstraZeneca

Interventions(s): open anti-reflux surgery: Nissen (primarily), semi-fundo, and others	**Comparator(s):** Omeprazole 20 mg or 40 mg or 60 mg daily Dose adjustment to either 40 or 60 mg omeprazole in patients who had a relapse of symptoms with 20 mg daily

Primary outcome(s): not applicable because the 7-yr and 12-yr follow-up analyses were not originally planned	**Other outcome(s):** 7-year and 12-year follow up with treatment failure as the primary outcome variable. Treatment failure, was defined as the presence of at least one of the following criteria: moderate or severe heartburn or acid regurgitation during the previous 7 days before a hospital visit; oesophagitis of at least grade 2; moderate or severe dysphagia or symptoms of odynophagia in combination with mild heartburn or acid regurgitation; requirement for omeprazole treatment for more than 8 weeks after antireflux surgery to control reflux symptoms, or need for reoperation; after randomization to omeprazole, being considered by the physician to require antireflux surgery to control symptoms; and patient opting for antireflux surgery during the course of the study for any reason, despite randomization to omeprazole. Quality of life assessments: Assessed once a year using Psychological and General Well-Being index and the disease-specific instrument Gastrointestinal Symptom Rating Scale (GSRS)

Inclusion criteria: chronic GERD symptoms with concomitant esophagitis by endoscopy	**Exclusion criteria**: no esophagitis
Symptoms (describe): Results were not described in 2007 or 2009 paper	**Hiatal hernia (specify whether considered and size used for exclusion):** No exclusion
EGD (performed or not and results):yes Results were not described in 2007 or 2009 paper	**Esophagitis/stricture/Barrett's:** At 7 years, Barrett's - PPI 18%; surgery 14% at baseline At 12 years, Barrett's - PPI 18%; surgery 17% at baseline
PH study (performed or not and results): yes Results were not described in 2007 or 2009 paper	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No data
EMS (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) **No, more lost to follow up in surgery group.**

Quality Assessment for RCTs: C due to large lost to follow up	
Blinding: yes, "particular care was taken that the operating surgeon took no part in the postoperative evaluation of that particular patient,"	**Allocation concealment:** yes
Intention-to-treat: yes	**Method of Randomization:** randomization carried out by a blinded computer based system
Other comments: patients were stratified for each center in blocks of ten subjects. Large dropout at both 7-yr and 12-yr follow up. It seems that the long-term follow-up study (beyond 5 years) was not originally planned	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
	B	

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: • At 7-year follow-up, patients' baseline median age (range) Surgery (n=99): 51 (19-73) Omeprazole (n=119): 55 (22-76) • At 12-year follow-up, patients' baseline median age (range) Surgery (n=59) 50 (19-73) Omeprazole (n=78): 52 (28-76)	**N enrolled:** 344, only 310 were randomized; 155 randomized to surgery; 155 randomized to omeprazole; 144 had surgery
Gender: surgery Males 76% omeprazole Males 74%	**N completed:** • 99 in the surgery group and 119 in omeprazole group completed the 7-year follow-up • 59 in the surgery group and 78 in omeprazole group completed the 12-year follow-up
Race: no data	**Dropouts/reasons:** • At 5-year follow-up (reported in original article, Lundell 2001, in previous report)- 9 refused operation; 1 had no esophagitis; 1 had bronchial carcinoma (therefore the operation was cancelled); 1 died of MI 3 months post-op; 3 withdrawn due to unacceptable adverse events; 2 due to non-compliance, 1 to other reasons, 6 were lost to follow up, and 10 refused to comply with the follow-up procedures; In the medical arm, 1 patient never had omeprazole, 10 withdrawn due to unacceptable adverse events; 2 due to non-compliance, 1 to other reasons, 4 were lost to follow up, and 4 refused to comply with the follow-up procedures. • Between 5-year and 7-year follow-up – 6 patients were withdrawn from the omeprazole group and 1 from the antireflux surgery group • Beyond 5-yr follow-up – Primary due to logistic and other technical reasons at the time of prolongation of the study protocol.
BMI: no data	**Follow-up period:** from year 5 up to 12 years
Comments: 34/344 patients had incomplete response to omeprazole during the run-in period and were offered surgery, therefore, only 310 were randomized	

Results

Primary outcome(s):

Secondary outcome(s):

- Analysis of the cumulative rate of treatment failures revealed superiority for antireflux surgery over time (P=0.002, log rank test). Up to 12-yr follow-up (survival analysis), 53% remained in sustained remission in the surgical arm compared with 40% in the medical arm.

Reasons for treatment failure during 7-year follow-up:

	Omeprazole (n=154)	Surgery (n=144)
Symptoms with oesophagitis	4	4
Symptoms without oesophagitis	54	21
Endoscopic oesophagitis	16	17
Treatment failure for other reasons	7	8
Censored before 7 years	20	34
Completed 7 years without relapse	53	60

- In patients with symptomatic and/or endoscopic recurrence, an increase in omeprazole dose was allowed; this resulted in a smaller difference in treatment failure rates between the two groups, but antireflux surgery was still superior (P=0.045)

Obstructive symptoms such as dysphagia, flatulence and inability to belch were reported more frequently after antireflux surgery than for omeprazole therapy (P = 0·006, P = 0·001 and P = 0·001 respectively). The incidence of these complaints remained stable over the 7-year follow-up.

- Up to 12 years follow-up, the main reflux symptoms of heartburn and regurgitation were significantly more comment in PPI than surgery group (HR=1.73, 95%CI 1.6-1.9 and HR=2.38, 95% CI 2.1-2.7, respectively).
- During the 12 years of follow-up, 21 of the 155 patients initially randomized to PPI were referred for fundoplication (14%). In total, 52 of the 144 surgical patients (36%) were treated with PPI for more than 8 weeks, with a slow but steady increase over time.
- The GSRS mean scores for the 2 treatment arms were very similar and at a level is considered to be normal.

Comments:

These two articles are 7-yr and 12-yr follow-up of a RCT by Lundell 2001 (in previous report)

Adverse Events: see 1998 paper for acute AEs.

Long-term safety (up to 12 years follow-up):

- There were no surgery-related deaths. In the surgical arm, more AEs were listed as procedural complications (including hernia, postoperative infections, etc.). One patient randomized to surgical arm was found to have esophageal cancer 12 years after fundoplication, compared with none in those treated with PPI. This patient had a Barrett's diagnosed at initial endoscopy for inclusion in the study. The presence of BE (with intestinal metaplasia but with the absence of dysplasia) had been documented 3 years before the endoscopic diagnosis of esophageal cancer.
- Fatal outcome and heart-related cause of AEs were more common in the PPI group than in the surgical group. 8 patients in the PPI group died of heart-related causes, and 9 experienced non-fatal heart attacks. 2 surgical patients died of heart-related causes, and 2 experienced non-fatal MI. These data were from FDA database, and claimed that FDA concluded that baseline differences and other confounding factors (eg, withdrawal from the surgical group and/or receiving both therapies) could have biased the safety data.

Applicability: (1/2/3): Wide	**Comments:**

GERD data extraction form

Author: Lundell	Yr: 2008	UI: 18469091	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
Compare laparoscopic antireflux surgery (LARS) and esomeprazole in managing gastro-esophageal reflux disease

Study design: RCT	Country/Setting: Multicenter, in 11 European countries, centers were academic units or affiliated with a university	Funding: AstraZeneca

Interventions(s):	Comparator(s):
laparoscopic antireflux surgery (LARS), within 3 months of randomization	esomeprazole 20mg q day, for 3 years if symptom was not controlled after 8 weeks, dose increased to 40mg q day for 8 weeks, then to 20mg bid day for 8 weeks or back to 20mg q day

Primary outcome(s):	Other outcome(s):
Time to treatment failure	GERD symptom control Quality of life

Inclusion criteria:	Exclusion criteria:
Oesophagitis no more than LA grade B GERD symptoms no more than mild	Hx of oesophageal, gastric or duodenal surgery, hx or current Zollinger-Ellison syndrome, primary oesophageal disorders, inflammatory bowel disease, dysplastic changes in a columnar-lined oesophagus or abnormal GI absorption, significant concomitant disease, potential for poor compliance
Symptoms (describe): Heartburn None 35.02% Mild 23.99% Moderate 24.35% severe 16.60% Acid regurgitation None 46.38% Mild 20.54% Moderate 24.54% severe 8.44%	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): Yes grade A 24.18% grade B 24.55% grade C 3.64% grade D 0.16% No oesophagitis 47.46%	Esophagitis/stricture/Barrett's: Barrett's: 9.92%
PH study (performed or not and results): yes	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): yes
Esophageal manometric studies (performed or not and results): no	Other: H pylori status assessed, not reported Hx of GERD <1yr 29.63%

GERD data extraction form

	Hx of GERD 1-5yr	50.75%
	Hx of GERD >5yr	19.11%

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: B (please select one and delete others)	
Blinding: no	Allocation concealment: no
Intention-to-treat: yes, per-protocol for efficacy data	Method of Randomization: unclear, in blocks of 4
Other comments: dropout >20%; pt blinding not possible	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 45.09	N randomized: 554
%Male: 71.84	N completed: 412
Race: not reported	Dropouts/reasons: adverse events (1 in LARS before surgery, 2 in LARS after surgery, 10 in esomeprazole), ineligible (1 in LARS before surgery, 2 in esomeprazole), “study-specific discontinuation” (1 in LARS before surgery, 10 in LARS after surgery, 1 in esomeprazole), lost to follow-up (2 in LARS before surgery, 6 in LARS after surgery, 7 in esomeprazole), lack of therapeutic response (16 in LARS after surgery, 15 in esomeprazole), other (35 in LARS before surgery, 10 in LARS after surgery, 23 in esomeprazole),
BMI:27.25	Follow-up period: 3 years
Comments: There was a 3-month run-in period when all pts took esomeprazole 40mg q day. Out of the 288 pts randomized to undergo LARS, only 248 were operated. Unsure why there were “ineligible” pts after randomization.	

Results
Primary outcome(s): Time to treatment failure Percentage of pts in remission after 3 years, ITT LARS: 90% Esomeprazole: 93% P=0.25 Percentage of pts in remission after 3 years, per-protocol LARS: 90% Esomeprazole: 95% P=0.045
Secondary outcome(s): Among the esomeprazole group, at 3 years, 23% of pts were on an increased dose of esomeprazole; 8% on the maximum allowed dose schedule. Heartburn: throughout the study, there was a decrease in LARS group, and similar level in esomeprazole group. Overall, there was more heartburn in esomeprazole group (p<0.001)(Figure 4A) Acid regurgitation: throughout the study, there was a decrease in LARS group, and similar level in esomeprazole group. (Figure 4B) Dysphagia: mostly mild, more common in LARS group post-op (p<0.001) (Figure 4C)

Flatulence: more common in LARS group post-op (p<0.001) (Figure 4D)

Quality of life scores

	LARS (mean ± SD)	Esomeprazole (mean ± SD)	P between groups***
Quality of life in reflux and dyspepsia*, vitality score	Baseline: 6.28 ± 1.08 3 years: 6.90 ± 0.31	Baseline: 6.21 ± 1.22 3 years: 6.53 ± 0.85	P<0.001
Quality of life in reflux and dyspepsia*, food and drink	Baseline: 6.16 ± 1.16 3 years: 6.85 ± 0.4	Baseline: 6.19 ± 1.12 3 years: 6.38 ± 0.91	P<0.001
Gastrointestinal symptom rating scale**, reflux	Baseline: 1.81 ± 1.07 3 years: 1.18 ± 0.42	Baseline: 1.73 ± 1.03 3 years: 1.63 ± 0.88	P<0.001

* 7= no problem, 6= minimal problems
** 1= no discomfort, 2= minimal discomfort
*** ANOVA

Comments:

Compliance:
NA

Adverse Events:
0.8% of LARS pts and 3.8% of esomeprazole discontinued study due to adverse events.
There was no perioperative mortality, 3% morbidity within hospital stay or within 30 days post-op.
One pt died from pneumonia in the esomeprazole group.
There were two reports of myocardial infarction (1 in each arm)

	Refused LARS (n=40) n (%)	LARS (n=248) n (%)	Esomeprazole (n=266) n (%)
Injury, poisoning, procedural	1 (2.5)	15 (6.0)	2 (0.8)
Gastrointestinal disorders	0	12 (4.8)	5 (1.9)
Musculoskeletal/connective tissue	0	2 (0.8)	8 (3.0)
Infections and infestations	1 (2.5)	3 (1.2)	6 (2.3)
General disorders	0	5 (2.0)	4 (1.5)
Cardiac disorders	1 (2.5)	4 (1.6)	3 (1.1)
Neoplasms, benign/malignant	0	2 (0.8)	6 (2.3)
Reproductive system including breast	0	1 (0.4)	4 (1.5)
Respiratory, thoracic, mediastinal	0	5 (2.0)	1 (0.4)
Vascular disorders	0	3 (1.2)	3 (1.1)
Hepatobiliary disorders	1 (2.5)	3 (1.2)	0
Any serious adverse events	4 (10)	55 (21)	42 (14.3)

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Lutfi	**Yr: 2005**	**UI: 15624052**	**Questions addressed: 1, 3**	**Extractor: JHL**

Objective/Topic: Three year's experience with the Stretta procedure

Study design: Prospective one-arm study	**Country/Setting:** US	**Funding:** ND

Interventions(s): Stretta	**Comparator(s):**

Primary outcome(s): • GERD outcomes • esophageal acid exposure	**Other outcome(s):**

Inclusion criteria: • Presented at the Vanderbilt University Medical Center for the surgical evaluation of GERD since August 2000	**Exclusion criteria:** • a hiatal hernia >3 cm, a lower esophageal sphincter (LES) pressure <8 mmHg, Barrett's esophagus, active grade 3 or 4 esophagitis (Los Angeles classification), American Society of Anesthesiologists (ASA) 4, age <18 years, and pregnancy
Symptoms (describe): ND	**Hiatal hernia (specify whether considered and size used for exclusion):** considered, a hiatal hernia >3 cm
EGD (performed or not and results): Not performed	**Esophagitis/stricture/Barrett's:** Patients with Barrett's esophagus, active grade 3 or 4 esophagitis (Los Angeles classification) were excluded.
PH study (performed or not and results): Performed, no results	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** ND
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: High drop-out rates (21%)

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A (24-h pH study)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46.8y	**N enrolled:** 77
%Male: 44.7%	**N completed:** 61
Race: ND	**Dropouts/reasons:** 21%

BMI: ND	**Follow-up period:** 26.2 months
Comments:	

Results
Primary outcome(s): • "Twenty-six patients were completely off PPI at follow-up (43%). • Patients taking ≤ 50% of their original dosage and those off medications entirely were considered to be responders (39 patients, or 64%). Those who remained on the same preoperative dosage or reduced their original dose by <50% were considered to be nonresponders (36%). • The overall satisfaction rate was 73%. There was a significant improvement in Quality of Life in Reflux and Dyspepsia Patients (QOLRAD) score for the whole group. The average preoperative score was 3.6 ± 1.1, but it increased significantly to 5 ± 1.5 postoperatively ($p < 0.001$). • Twenty-four patients (40%) of those completing the questionnaires agreed to undergo the 24-h pH study; there was a statistically significant improvement in distal acid exposure time (7.8 ± 2.6% to 5.1 ± 3.3; $p = 0.001$) and Johnson-DeMeester score (40.2 ± 17.6 to 29.5 ± 20.5; $p = 0.041$) after the Stretta."
Secondary outcome(s):
Comments:

Compliance: NA

Adverse Events:
• No reported long-term procedure-related complications (e.g., dysphagia, stricture, or disabling gas bloat) • Significant complications possibly related to Stretta treatment occurred in one patient with diabetes who developed transient gastroparesis 2 weeks after the procedure.

Applicability: (narrow/wide): Wide	**Comments:**

KQ3 result template and instruction: Please use the primary GERD extraction form. Please indicate if adverse events were the primary outcome, and report the data in the adverse events section. Do make an attempt to extract n/N for the adverse event (subjects affected/total population at risk).

Author: Madan	Yr: 2006	UI: 16769279	Questions addressed: 3	Extractor: WY, JHL

Objective/Topic:
To define risks of 4 endoluminal therapies for GERD: radiofrequency ablation (Stretta), injection (Enteryx), suture (EndoCinch or Endoscopic Suturing Device)

Study design:	Country/Setting:	Funding:
Review of the Manufacturer and User Facility Device Experience (MAUDE) Database from the U.S. Food and Drug Administration's (FDA) Center for Devices and Radiological Health website	US	

Interventions(s):	Comparator(s):
• Stretta • Enteryx • EndoCinch • Endoscopic Suturing Device	

Primary outcome(s):	Other outcome(s):

Inclusion criteria:	Exclusion criteria:
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Other comments:

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:	N enrolled:
%Male:	N completed:
Race:	Dropouts/reasons:
BMI:	Follow-up period:
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Compliance:

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Adverse Events:
Total of 50 adverse events were reported.
These are the adverse events reported. Number of pts that suffered from these events were not reported in most cases:
Fever: unknown number of pts affected/at risk
Chest pain: unknown number of pts affected/at risk
Inability to swallow: unknown number of pts affected/at risk
Bloating: unknown number of pts affected/at risk
Gastraporesis: unknown number of pts affected/at risk
Shortness of breath: unknown number of pts affected/at risk
Dysphyagia: unknown number of pts affected/at risk
Stenosis: unknown number of pts affected/at risk
Dehydration: unknown number of pts affected/at risk
Device malfunction: unknown number of pts affected/at risk
Grounding pad burn: unknown number of pts affected/at risk
Atrial fibrillation: unknown number of pts affected/at risk
Pneumoperitoneum: unknown number of pts affected/at risk
Increase in reflux: unknown number of pts affected/at risk
Reported or suggested perforation: 38% of adverse events
Improper injection: unknown number of pts affected/at risk
Embolization of injectate: 3 pts
Pleural effusion: unknown number of pts affected/at risk
Pericardial effusion: unknown number of pts affected/at risk
Pneumomediastinum: unknown number of pts affected/at risk
Aspiration: unknown number of pts affected/at risk
Pneumonia: unknown number of pts affected/at risk
Hospitalization: 64% of adverse events
Esophageal leak: unknown number of pts affected/at risk
Subsequent procedure required: 16 pts (9 repeat endoscopy, 6 dilation, 4 pericardiocentesis, 2 thoracentesis, 1 thoracostomy tube, 1 percutaneous drainage, 1 pericardial window, 1 laparoscopic esophageal repair, 1 thoracotomy, 5 surgery for esophageal leak/perforation/bleeding)
Hemorrhage: 4 pts
Death: 8 (3 in the radiofrequency ablation– based group, 5 in the injection-based group).

****The denominator is difficult to obtain because even the manufacturers usually only keep sales data and not necessarily patient-use data. It has been estimated that approximately 3150 EndoCinch (C. R. Bard, Inc., Billerica, MA), 6000 Stretta, and 1700 Enteryx (Enteric Technologies, Foster City, CA) procedures have been performed. By using these estimates, a minimal complication rate can be estimated as .1% for EndoCinch, .4% for Stretta, and 1.5% for Enteryx.

Applicability: (narrow/wide): wide	Comments:

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

GERD data extraction form

Author: Mahmood	**Yr: 2006**	**UI: 16542276**	**Questions addressed: Q1**	**Extractor: DM**

Objective/Topic: Comparison of effects of Transesophageal endoscopic placation with laparoscopic Nissen fundoplication (LNF) on symptom severity scores, endoscopy, 24 h esophageal pH and esophageal manometry, and quality-of-life assessments

Study design: Non-randomized, Comparative	**Country/Setting:** St. James Hospital, Dublin, Ireland	**Funding:** n.d.

Interventions(s):	**Comparator(s):**
Trans-Esophagealendoscopic Plication (TEP) - EndoCinch	Laparascopic Rossetti Nissen fundoplication (LNF)

Primary outcome(s):	**Other outcome(s):**
1) **Heartburn symptom score** = heartburn frequency * Heartburn severity. *Heartburn severity* - visual analog scales 0 = no discomfort **to** 10 = incapacitating pain. *Heartburn frequency* 0 = none 1= occasional (<3/wk) brief episodes controlled by antacids, 2 = frequent (3–5/wk) 3 = daily (6–7/wk). 2) **Regurgitation symptom score** 0 = none 1 = mild, occasional episodes, mostly postprandial and not predictable 2 = moderate (3–5/wk), frequent episodes, predictable by posture 3 = severe (6–7/wk), episodes interfering with work and social activities.	1) **Endoscopy** – assessed degree of esophagitis (non-erosive reflux disease, or LA grade A or B), and the presence and size of any hiatus hernia. 2) **Twenty-four-hour Esophageal pH Monitoring -** Standard parameters were recorded including total percentage of the time pH <4, upright and supine percentages, total number of episodes, and DeMeester acid score. 3) **Esophageal Manometry** 4) **Quality of Life Assessment** - by a special questionnaire (QOLRAD) measuring five parameters - emotional distress, sleep disturbances, food/drink problems, physical/social functioning, and vitality 5) **Consumption of PPIs** 6) **Assessment of Complications -** The complication rate for dysphagia, difficult to vomit and belch were assessed

Inclusion criteria:	**Exclusion criteria:**
All patients with persistent GERD symptoms that were dependent on continuous treatment with PPIs for their relief. Also included were patients were experiencing breakthrough symptoms while on PPIs. 24 Hr esophageal pH monitoring demonstrated pH < 4 after discontinuing PPIs for 10 days, and antacids for 48 h before the test. Patients that agreed to be followed up for at least 12 months post procedure and also agreed to have repeat endoscopy and 24-h esophageal pH studies post procedure.	Age <18 yr; dysphagia; body mass index (BMI) > 40; previous gastric or thoracic surgery; esophageal stricture; Barrett's esophagus (specialized intestinal metaplasia over any length); patients on immunosuppressant drugs; patients with severe comorbid illness or contraindications for general surgery.
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):** Hiatus hernia was assessed but not excluded LNF: 6 /24 (3 > 5 cm), TEP 6/27 (< or equal 2 cm)
EGD (performed or not and results): Performed; baseline levels of esophagitis and their grades are not reported	**Esophagitis/stricture/Barrett's:** *Esophagitis:* Not reported *Barret's Esophagus:* LNF: 0/24

	TEP: 0/27
PH study (performed or not and results): Performed; baseline levels of pH DeMeester scoring (Not reported in the paper, it has been interpreted by the extractor from the graphical output) LNF: 40 (range 25-140) TEP: 35 (range 20-75)	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** n.d
EMS (performed or not and results): Performed	**Other:**

EMS Variable	LNF	TEP
% Upright	16.7± 2.1	12.7±1.1
% Supine	13±4.7	5.5±1.3
No episodes	162±17	177±14.2
% Total	15.5±2.3	10.2 ± 0.9
Acid score	56.6±8.9	38.9±3.4
LOSP	6.4 ± 1.2	9.3±1.8
Amplitude	55.6 ± 6.7	66.3±7.2

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: EndoChin group results had been published previously (Mahmood 2003) and were summarized in 2005 GERD report. The authors claimed current study is a prospective non-randomized contemporaneous comparison study but it is obvious that the two groups were not recruited, assessed, and followed in the same manner. Comparisons between the two groups are problematic. There is an inherent selection bias as most of the subjects recruited into the LNF group were referred patients.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: LNF: mean 36 yr (range 17–68) TEP: mean 39 yr (range 22–62)	**N enrolled:**
%Male: LNF: 66.6% TEP: 55.5%	**N completed:** LNF: 24 TEP: 27
Race: n.d.	**Dropouts/reasons:**
BMI: LNF: mean 25 (range 17–33) TEP: mean 26 (range 21–34)	**Follow-up period:** LNF: mean 12 months post-procedure (range 10–18) TEP: mean 12 months post-procedure (range 11–14)
Smoking history: n.d.	**Comments:**

GERD data extraction form

Results
Primary outcome(s): There was significant improvement in the heartburn symptom score (frequency×severity) in both groups (LNF $p<0.0001$and TEP $p < 0.0001$) post procedure, which was maintained for at least a mean duration of 12 months, and was significantly better in the LNF group ($p = 0.0383$) The regurgitation frequency also significantly improved in both groups (LNF $p < 0.0001$ and TEP $p < 0.0001$), which was also maintained for at least 12 months ($p = 0.208$) Note: data reported in figures only.
Secondary outcome(s): 1) **Endoscopy:** In the TEP group, plications were found to be in position as recorded at the time of the procedure in 22 patients; in 3 patients one of the two plications had vanished and in 2 patients both plications had gone. There was no evidence of worsening of the degree of esophagitis in any of these patients. 2) **Esophageal pH and Manometry**: a. Mean DeMeester acid score showed a significant improvement post procedure in both the groups (LNF $p = 0.0003$ and TEP $p < 0.05$) but was significantly better in the LNF group ($p = 0.0007$) b. Ninety-one percent of patients in the LNF group achieved normal pH as compared to 48% in the TEP group. c. Both procedures were also effective in the reduction of the percentage of esophageal pH values <4 in the upright position (LNF $p < 0.0001$ and TEP $p = 0.0047$) and in the number of reflux episodes occurring in 24 h (LNF $p < 0.0001$ and TEP $p = 0.0007$) and this effect was significantly better in the LNF group d. The manometric studies revealed no significant difference in pre- and post-procedure LES pressures in the TEP group but were significantly improved in the LNF group in addition to the amplitude of contractions. 3) **Consumption of PPIs:** The requirement for PPIs was reduced to 13% (n = 3/24) in the LNF and to 37% (n = 10/27) in the TEP group at 12-month post-procedure 4) ***Quality-of-Life Assessment:*** There was a significant improvement in all five quality-of-life parameters at 12-month post-procedure as compared to baseline in both groups**,** but no significant difference between the two groups ($p = 0.1070$)
Comments: The between group comparisons are biased as there is an inherent selection bias.

Compliance:

Adverse Events:
Complications at 1-Yr Follow-Up **LNF:** In the LNF group 4 patients (15%) had new onset dysphagia (2 cases moderate, 2 cases severe that required dilatation). Side effects of LNF included a difficulty in vomiting in 25% (n = 6), with 4 unable to vomit, and 41% (n = 10) also had difficulty in belching (33% had some difficulty and 8% were unable to belch). **TEP:** There were no complications in the TEP group at 1-yr follow-up. However, the early post-operative transient complications included sore throat, vomiting, abdominal pain, chest soreness, and bloating and mild dysphagia. All the above complaints resolved spontaneously within 72 h. Three patients had significant bleeds. Two patients received one unit of blood each and were admitted overnight. Both remained hemodynamically stable throughout this period and were discharged home the next day. One patient had a gastric mucosal tear, which required no further attention.

Applicability: (narrow/wide): Narrow	**Comments:**

GERD data extraction form

GERD data extraction form

Author: Malfertheiner	Yr: 2005	UI: 15888776	Questions addressed: 2	Extractor: JHL

Objective/Topic: Prognostic influence of Barrett's oesophagus and Helicobacter pylori infection on healing of erosive gastroesophageal reflux disease (GORD) and symptom resolution in non-erosive GORD

Study design: Prospective, multicenter, open cohort study	**Country/Setting:** Germany, Austria and Switzerland	**Funding:** ND

Interventions(s): **ERD patients: 40mg esomeprazole for 4-8 weeks** **NERD patients: 20mg esomeprazole for 2-4 weeks**	**Comparator(s):**

Primary outcome(s): • Healing of erosive gastroesophageal reflux disease (GORD) • Symptom resolution in non-erosive GORD	**Other outcome(s):**

Inclusion criteria: "….patients >18 years of age with ERD or NERD from 1253 centers in Germany, Austria, and Switzerland from May 2000 until February 2001; Patients from hospital endoscopy clinics or from specialized endoscopy units where they underwent endoscopy with the objective of distinguishing between ERD and NERD. Similar numbers of patients from each category in blocks of four (that is, two consecutive NERD and two consecutive ERD patients) were included from each centre to facilitate long term comparison of the groups. Patients diagnosed at the index endoscopy as having BO…"	**Exclusion criteria:** "…continuous treatment with any acid suppressant drug for more than seven days within the four weeks prior to the study, history of gastrointestinal surgery (except simple closure of an ulcer), gastro-oesophageal malignancies and/or ''alarm symptoms'' of malignancy, evidence of alcohol or drug addiction, or limited language skills. In addition, H pylori eradication therapy was not allowed during the initial treatment phase."
Symptoms (describe): A burning feeling and pain behind the breastbone (considered to reflect heartburn)	**Hiatal hernia (specify whether considered and size used for exclusion): ND**
EGD (performed or not and results): Performed, ND	**Esophagitis/stricture/Barrett's:** ERD group: 453/3245, 14.0% NERD group: 69/2970, 2.3%
PH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) No (NERD or ERD patients)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

GERD data extraction form

Quality Assessment Non-RCTs: B
Comments: Used different dose of Esomeprazole by group

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X (endoscopy)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: ERD group: 54.5y NERD group: 53.0y	**N enrolled: 6509**
%Male: ERD group: 60.6% NERD group: 45.0%	**N completed:** ERD group: 3245 NERD group: 2970
Race: ND	**Dropouts/reasons:** 294 patients (213 because of insufficient source data verification, 30 because of missing informed consent, two because of age less than 18 years, 11 due to incomplete CRF data, and 38 were screened and not treated.
BMI: ERD group: 27.3 NERD group: 26.6	**Follow-up period:** ERD patients: 4-8 weeks NERD patients: 2-4 weeks
Comments:	

Results

Primary outcome(s):

Treatment/Comparison:	**Esomeprazole**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure***
			Off PPIs	**Off all meds**		
ERD patients by week 8						
LA classification A/B vs. C/D						*90.3% vs. 76.9%, p*<0.001
Sex Male vs. Female						NS
Age (y) < 60 vs. ≥ 60						NS
BMI classification <30 vs. 30+						NS
NERD patients by week 4						
LA classification A/B vs. C/D						NA
Sex Male vs. Female						NS
Age (y) < 60 vs. ≥ 60						NS
BMI classification <30 vs. 30+						NS

Secondary outcome(s):

Comments: *endoscopic healing of erosive reflux disease by week 8 for ERD patients/ complete heartburn resolution in NERD patients by week 4

GERD data extraction form

Compliance: ND

Adverse Events: ND

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Manning	Yr: 2006	UI: 16872031	Questions addressed: 2, 3	Extractor: JC

Objective/Topic: To review a single surgeon's experience w/ laparoscopic Nissen fundoplication and to determine which factors, if any are likely to influence long term outcome.

Study design: Prospective	Country/Setting: Ireland/Single hospital	Funding: nd

Interventions(s): laparoscopic Nissen fundoplication	Comparator(s): none

Primary outcome(s): GERD symptoms	Other outcome(s):

Inclusion criteria: Pts with GOR and operated on by single surgeon over a 5-yr period	Exclusion criteria: n/d
Symptoms (describe): **Symptomatic outcome** Excellent-w/o symptoms Good-occasional sx of reflux, no med needed Fair-frequent sx of reflux, meds needed Poor-sx of reflux equal to or more than pre-op **Long-term outcome was classified as either good or poor:** Poor: all pts whose were the same or worse than pre-op AND those who were not happy with the results of the operation. Good: all other cases	Hiatal hernia (specify whether considered and size used for exclusion): Considered, 39% found to have hiatus hernia--not used for exclusion
EGD (performed or not and results): Performed, categorized according to Savary Miller grading with note made of lower esophageal biopsies routinely taken. Pre-op: 30% normal, 52% Grade I or II esophagitis, 8% grade III or IV change, 10% grade V change.	Esophagitis/stricture/Barrett's: nd
pH study (performed or not and results): 24-hr ambulatory pH monitoring performed. Mean DeMeester Socre was 94.24/	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): Past medical history, medications and response of symptoms to medications were recorded.
Esophageal manometric studies (performed or not and results): Not performed	Other:

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding: n/a	Allocation concealment: n/a
Intention-to-treat: n/a	Method of Randomization: n/a
Other comments: n/a	

Quality Assessment Non-RCTs: C
Comments: subjective symptomatic outcome compared retrospectively analyzed medical records to determine if pre-operative parameters were predictive of outcome.

Diagnostic Quality: A/rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 44	N enrolled: 124 examined pre-op; 110 had complete data for analysis
%Male: 70%	N completed: 102 completed follow-up
Race: nd	Dropouts/reasons: nd
BMI: nd	Follow-up period: median: 33 months
Comments:	

Results
Primary outcome(s): **Symptomatic outcome (no baseline comparison)** Excellent: 45% Good: 22% Fair: 17% Poor: 6% **Long Term Outcomes (Poor* vs. Good**) compared to pre-operative parameters** *Poor: all pts whose were the same or worse than pre-op AND those who were not happy with the results of the operation. **Good: all other cases Male to female ratio significantly lower in poor outcome group (.8 vs. 2.6, p=0.001) and mean follow-up time was significantly longer (56.4 vs. 32.7 months, p<0.001) than good outcome group. High BMI (p=.97), normal endoscopy or severe esophagitis, presence of hiatus hernia or those suffering complications were no more likely to have poor outcome than other patients. Age (p=.901), DeMeester score, endoscopy findings, hiatal repair, dilatation post-op, conversion to open procedure and complications all N/S between Good and Poor outcome groups.
Comments: Outcomes subjectively rated using Good/Poor criteria. Overall 89.2% of pts reported satisfaction with results of tx. 6.9% regretted having procedure.

Compliance: 8 pts underwent crural approximation at time of surgery. Two cases were converted to an open procedure.

GERD data extraction form

Adverse Events: 2 pts developed port site hernias post-op. One pt. had laparoscopic release of wrap due to persisting dysphagia. Conversion to open: 2/124 (2%)

Applicability: (narrow/wide): narrow	Comments: Single site, single surgeon non randomized case study

GERD data extraction form

Author: Mardani	Yr: 2009	UI: 19016274	Questions addressed: 1,3	Extractor: WY

Objective/Topic:
to determine the long-term results of total Nissen fundoplication with or without division of the short gastric vessels in a 10- year RCT

Study design:	Country/Setting:	Funding:
RCT	Sweden	nd

Interventions(s):	Comparator(s):
Laparoscopic total fundoplication with division of the short gastric vessels	Laparoscopic total fundoplication without division of the short gastric vessels

Primary outcome(s):	Other outcome(s):
QoL per Psychological GeneralWell-Being (PGWB) index and the Gastrointestinal Symptom Rating Scale (GSRS)	GERD symptoms

Inclusion criteria:	Exclusion criteria:
With GERD	none
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's: With division: 1 pt Without division: 0 pt
PH study (performed or not and results): % time at pH<4 With division: 11.5% Without division: 13.2%	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other: Antisecretory medication use With division: 14 pt Without division: 15 pt

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: C	
Blinding: no	Allocation concealment: no
Intention-to-treat: yes	Method of Randomization: nd
Other comments: unclear recruitment criteria	

Quality Assessment Non-RCTs:
Comments:

GERD data extraction form

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		x

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:nd	N enrolled:99
%Male: 51	N completed:82
Race:nd	Dropouts/reasons: 7 died, 2 refused to followup, 8 lost to followup
BMI:	Follow-up period: 10 y
Comments:	

Results
Primary outcome(s): Total score of Health-related QoL per generic PGWB index at 10 years (mean ± SEM) With division:100 ± 17.2 Without division: 92.7 ±21.4 P = 0.151 GSRS reflux syndrome score at 10 years (mean ± SEM) With division: 1.4±0.7 Without division: 1.9±1.4 P = 0.170 GSRS Dysphagia syndrome score at 10 years (mean ± SEM) With division: 2.0±1.5 Without division: 2.4±1.6 P = 0.406
Secondary outcome(s): No reflux symptoms With division: 38 out of 42 pt Without division: 31 out of 40 pt P = nd Heartburn With division: 4 out of 42 pt Without division: 9 out of 40 pt P = 0.207 Acid regurgitation With division: 4 out of 42 pt Without division: 7 out of 40 pt P = 0.463 Medication use at baseline With division: 14 pt Without division: 15 pt P = nd

GERD data extraction form

Medication use post-surgery With division: 7 pt Without division: 7 pt P = 0.79 Composite dysphagia scores at 10 years (mean ± SEM) With division: 8.7 ± 1.7 Without division: 10.5 ± 2.1 P = 0.58 % time at pH < 4 at 1 year (mean ± SEM) With division: 1.3% ± 0.9 Without division: 1.2% ± 0.4 P = 0.909
Comments:

Compliance: NA

Adverse Events: Gas bloat (49 patients in the group with division and 39 in group without division; *P* = 0·153) (*Fig. 2*), ability to belch (24 patients in the group with division and 19 in group without division; *P* = 0·697) vomit (6 in the group with division and 6 in the group without division; *P* = 1·000).

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Mehta	**Yr: 2006**	**UI: 17114017**	**Questions addressed: Q1; Q3**	**Extractor: MC**

Objective/Topic: This is 7-yr follow-up of a RCT by Mahon, 2005 (included in 2005 GERD report)

Study design:	**Country/Setting:**	**Funding:**
Non-RCT	UK	No data

Interventions(s): Original RCT was comparing Nissen with PPI for 12 months. After the first year, patients who had undergone surgery were kept under long-term review. Those in the PPI arm were offered the chance to undergo surgery or to remain on optimal PPI medication. Group 1: Laparoscopic Nissen fundoplication. Group 2: Patients received 1-year PPI in RCT phase, who later opted to received laparoscopic Nissen fundoplication	**Comparator(s):** Group 3: Patients received 1-year PPI in RCT phase, who remaining on PPI. The majority of patients were on regular omeprazole (53%) at a mean dosage of 20 mgs/day. 27% were on lansoprazole at a mean dosage of 28 mgs/day, 10% were on another type of PPI, and the other 10% were on a combination of two or more PPIs.

Primary outcome(s): DeMeester symptom score questionnaire	**Other outcome(s):**

Inclusion criteria: 16-70 yrs; reflux based on EGD and/or 24-h pH study with good symptom correlation (>50% heartburn associated with acid reflux). This long-term follow-up non-RCT only included 183 (out of 217) patients in Norwich.	**Exclusion criteria:** significant esophageal dysmotility, BMI>35
Symptoms (describe): Symptoms of GERD for at least 6 mos and on PPI for at least 3 mos	**Hiatal hernia (specify whether considered and size used for exclusion):** LNF: 94%; PPI: 93%
EGD (performed or not and results): Performed (Reported in Mahon, 2005 article)	**Esophagitis/stricture/Barrett's:** No data
PH study (performed or not and results): Mean DeMeester LNF (n=91): 3.5 PPI then surgery (n=54): 3.3 PPI alone (n=38): 2.4	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No data
Esophageal manometric studies (performed or not and results): Performed (Reported in Mahon, 2005 article)	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) No. Patients opted to receive surgery after 1-year PPI treatment had significantly higher DeMeester symptom scores at 12 months (end of RCT) than patients received surgery or PPI alone.

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: Questionnaire response rate was 79%. Patients opted to receive surgery after 1-year PPI treatment had

significantly higher DeMeester symptom scores at 12 months (end of RCT) than patients received surgery or PPI alone.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 47 (range 24-69)	**N enrolled: 183**
%Male: 69	**N completed: 145 (calculated based on the 79% response rate)**
Race: no data	**Dropouts/reasons: no response to the follow-up symptom questionnaire.**
BMI: mean weight=80 (range 61-126) kg	**Follow-up period: median 6.9 years (range, 4.3-8.3)**
Comments:	

Results

Primary outcome(s):

Mean (SD) DeMeester symptom scores

	12 mo	Median 6.9 yr*
LNF (n=91)	0.9 (1.4)	1.1 (1.9)
PPI then surgery (n=54)	2.3 (2.3)	0.8 (1.4)**
PPI alone (n=38)	1.1 (1.5)	0.9 (1.0)

*response rate=79%

**significant change in score from 12 mo (Mann-Whitney test, $P < 0.01$)

Secondary outcome(s):

Comments:

Compliance:

Adverse Events:

Nissen fundoplication -

- 2 patients suffered splenic bleeding and 2 had inadvertent esophageal injury. These were dealt with laparoscopically and there were no postoperative sequelae.
- In the early postoperative period, 2 patients suffered wrap migration requiring laparoscopic correction and 4 patients had dysphagia within the first 3 months, requiring endoscopic esophageal dilation.

PPI -

- A proportion of patients (10%) suffered side effects of headache, diarrhea, vomiting, or abdominal pain, requiring alteration of the PPI type.
- A further 18% required dosage escalation during the trial period to relieve GERD symptoms.

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Meier	**Yr: 2007**	**UI: 17613919**	**Questions addressed:**	**Extractor: JHL**

Objective/Topic: Improvement of objective GERD parameters after radiofrequency energy delivery

Study design: Open-label, prospective study	**Country/Setting:** Europe	**Funding:** ND

Interventions(s): Stretta	**Comparator(s):**

Primary outcome(s): medication use, satisfaction, GERD health-related quality of life, GERD symptoms	**Other outcome(s):**

Inclusion criteria: • Patients with a history of GERD symptoms ranging from 1 to 36 years • Either self-referred or recruited from the outpatient endoscopy unit from May 2001 to June 2003 • Patients were at least partly responsive to daily proton-pump inhibitors (PPIs) and had a long history of GERD	**Exclusion criteria:** • Patients under 18 years of age, pregnant, poor surgical candidates (ASA III-IV), or if they had a sliding hiatal hernia >2.5 cm, grade III or IV esophagitis (Savary-Miller Classification), long-segment Barrett's metaplasia, dysphagia, a pacemaker, coagulopathy, high-grade dysplasia, cancer, or collagen vascular disease
Symptoms (describe): ND	**Hiatal hernia (specify whether considered and size used for exclusion):** Patients with hiatal hernia (None, 40.7%; < 2 cm, 50.8%; > 2 cm, 8.5%)
EGD (performed or not and results): Performed, no results	**Esophagitis/stricture/Barrett's:** Patients with esophagitis (None, 93.3%; I, 5.0%; II, 1.7%; III, 0%; IV, 0%)
PH study (performed or not and results): Performed, no results	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): Performed, no results	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: GERD patients were poorly defined.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
C (Patients were at least partly responsive to daily proton-pump inhibitors and had a long history of GERD		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 47	**N enrolled:** 60
%Male: 51.7	**N completed all follow up tests:** 40
Race: ND	**Dropouts/reasons:** mainly refuse the 24-h pH metry
BMI: ND	**Follow-up period:** 12 months

GERD data extraction form

Comments:

Results
Primary outcome(s): Medication use • At 12 months 38.3% were still not using any medication for GERD symptoms and 36.7% had reduced their medication intake. Satisfaction after Stretta treatment • At baseline only 26.7% were satisfied with GERD symptom control, while 73.3% of patients were not satisfied. • The percentage of satisfied patients increased from baseline to 46.7% at 12 months. Only 35% of patients were dissatisfied 12 months after Stretta treatment. • This is also reflected in the satisfaction score, which improved significantly one year after treatment, from 2 to 4 ($p < 0.0001$). GERD symptoms • Baseline mean LES pressure increased significantly from 14.8±9.1 at baseline to 16.7±10.0 mmHg 12 months after treatment with persistent normal esophageal peristalsis ($p=0.002$; n=32). • Mean total reflux time decreased significantly from 16.7±12.8% before to 8.8±6.6% one year after treatment ($p=0.001$; n=34) • The mean DeMeester score improved from 72.9±63.0 to 35.1±28.6 at 12 months ($p= 0.003$; n= 26). • The mean heartburn score at baseline was 2.2±1.5 (on medication, n=59) and 3.4±1.1 (off medication, n=59). This improved significantly after 6 and 12 months to 1.3±1.3 ($p<0.05$; n=58 and n= 49, respectively). Quality of life and overall physical and mental health • The mean GERDHRQL score changed significantly from 12.9± 10.4 (on medication) and 19.2±9.0 (off medication) at baseline to 6.6±7.3 twelve months after treatment ($p< 0.0001$; n=49). • The physical and mental health summary scores as assessed by the SF36 questionnaire also improved from baseline to 12 months after treatment ($p<0.001$, n=48 and $p< 0.05$, n=48, respectively).
Secondary outcome(s):
Comments:

Compliance: NA

Adverse Events: ND

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Metz	Yr: 2009	UI: 19210298	Questions addressed: 1,2,3	Extractor: WY

Objective/Topic:
To evaluate the efficacy and safety of dexlansoprazole MR 30 mg and 60 mg QD with placebo for the maintenance of healed erosive esophagitis

Study design:	Country/Setting:	Funding:
RCT	US and non-US, 94 centers	Takeda Global Research & Development Center, Inc.

Interventions(s):	Comparator(s):
(1) dexlansoprazole MR 30 mg QD (2) dexlansoprazole MR 60 mg QD	placebo

Primary outcome(s):	Other outcome(s):
The proportion of patients who maintained healed EO for 6 months per endoscopy	percentage of days without daytime or nighttime heartburn per daily diary percentage of nights without heartburn per daily diary mean severity of heartburn percentage of days without rescue medication use severity of GERD symptoms per investigator self--reported QOL symptom severity per validated questionnaires adverse events

Inclusion criteria:	Exclusion criteria:
Age 18 years or older Healed erosive esophagitis Previous participation in erosive esophagitis healing trials	Positive Helicobacter pylori status
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: C	
Blinding: y	Allocation concealment: n
Intention-to-treat: y	Method of Randomization: central telephone system

GERD data extraction form

Other comments: % dropout appeared to be high (50%) , but the majority of “withdrawal” was due to relapse, which is one of the outcomes. ITT was defined as all randomized patients who had no gap >7 days between the previous healing and current maintenance trials and who received at least1 dose of study drug in the current trial

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 48.18	N enrolled: 445
%Male: 48%	N completed: 221
Race: White: 89.89% Black: 4.72% Asian: 2% Native Hawaiian or pacific islander: 0.22% Multiracial 1.57%	Dropouts/reasons: relapse (n= 127), adverse event (n=16), protocol violation (n=1), loss to followup (n=16), withdrew consent (n=45), other (n=19)
BMI: 30.5	Follow-up period: 6 months
Comments:	

Results

Primary outcome(s):
The proportion of patients who maintained healed EO for 6 months per endoscopy
Dexlansoprazole MR 30 mg 74.9%
Dexlansoprazole MR 60 mg 82.5%
Placebo 27.2%
P<0.00001

The proportion of patients who maintained healed EO for 6 months per endoscopy

	LA grade of A or B prior to healing (n=313)	LA grade of C or D prior to healing (n=122)
Dexlansoprazole MR 30 mg	80%	63%
Dexlansoprazole MR 60 mg	82%	85%
Placebo	30%	15%

Median time to recurrence of EO
Dexlansoprazole MR 30 mg 42 days (P=0.00087 between dexlansoprazole MR 30 mg vs. placebo)
Dexlansoprazole MR 60 mg 61 days (P=0.0015 between dexlansoprazole MR 60 mg vs. placebo)
Placebo 30 days

Secondary outcome(s):
Mean of the proportion of 24-hour heartburn free days
Dexlansoprazole MR 30 mg 96% (P<0.0025 between dexlansoprazole MR 30 mg vs. placebo; NS between 30mg and 60mg groups)
Dexlansoprazole MR 60 mg 91% (P<0.0025 between dexlansoprazole MR 60 mg vs. placebo; NS between 30mg and 60mg groups)
Placebo 29%

Mean of the proportion of nights without heartburn
Dexlansoprazole MR 30 mg 99% (P<0.0025 between dexlansoprazole MR 30 mg vs. placebo)
Dexlansoprazole MR 60 mg 96% (P<0.0025 between dexlansoprazole MR 60 mg vs. placebo)
Placebo 72%

GERD data extraction form

The proportion of days without use of rescue medication
Dexlansoprazole MR 30 mg 98%
Dexlansoprazole MR 60 mg 96%
Placebo 44%

Proportion of patients with no heartburn at 6 months
Dexlansoprazole MR 30 mg 67%
Dexlansoprazole MR 60 mg 63%
Placebo 17%

Heartburn at 1 month and at 6 months: less severe for both dexlansoprazole MR groups than placebo (P < 0.0025)

Acid regurgitation at 1 month and at 6 months: less severe for both dexlansoprazole MR groups than placebo (P < 0.0025)

Dysphagia at 1 month and at 6 months: less severe for dexlansoprazole MR 30mg group than placebo (P < 0.0025); no difference between dexlansoprazole MR 60mg group and placebo.

Belching at 1 month and at 6 months: less severe for both dexlansoprazole MR groups than placebo (P < 0.0025)

Epigastric pain at 1 month and at 6 months: less severe for both dexlansoprazole MR groups than placebo (P < 0.0025)

The diet and food habits subscale of the PAGI-QoL scores: “significant improvement” for both dexlansoprazole MR groups compared with placebo

The total and heartburn/regurgitation subscale of the PAGI-SYM scores: “significant improvement” for both dexlansoprazole MR groups compared with placebo

Comments:

Compliance:
nd

Adverse Events:
Number of patients with adverse events

	Placebo (n=147)	Dexlansoprazole MR 30mg (n=140)	Dexlansoprazole MR 60mg (n=158)
With at least 1 adverse events	43	66	83
Gastritis	7	2	8
Upper respiratory tract infections	1	14	17
Dyspeptic signs and symptoms	6	3	4
Gastrointestinal and abdominal pains	5	3	5
Oesophageal ulcers and perforation	4	0	0
Diarrhea	1	5	8
Musculoskeletal and connective tissue signs and symptoms	2	3	8
Joint related signs and symptoms	1	7	0

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Mickevicius	Yr: 2008	UI: 18398651	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
Compare effectiveness of Nissen (1.5- or 3-cm wrap) vs Toupet (1.5- or 3-cm wrap) laparoscopic fundoplication

Study design:	Country/Setting:	Funding:
RCT	Lithuania, hospital	Not reported

Interventions(s):	Comparator(s):
Nissen (1.5- or 3-cm wrap) laparoscopic fundoplication, and follow-up at 6 months and 12 months	Toupet (1.5- or 3-cm wrap) laparoscopic fundoplication, and follow-up at 6 months and 12 months

Primary outcome(s):	Other outcome(s):
Dysphagia	Degree of esophagitis

Inclusion criteria:	Exclusion criteria:
18-80 years old With GERD symptoms, esophagitis, and hiatal hernia treated with PPIs at least 2 months before surgery	none
Symptoms (describe): no	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): See baseline data in results section	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): DeMeester score >14.72 for all pts	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other: Mean duration of GERD: 7.1 ± 7.7 yr

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: C/Poor (please select one and delete others)	
Blinding: no	Allocation concealment: no
Intention-to-treat: no	Method of Randomization: not reported
Other comments: no description/reason for dropouts	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 52.5 ± 13.6	N enrolled: 153
%Male: 48.37%	N completed: 127

GERD data extraction form

Race: not reported	Dropouts/reasons: not reported
BMI: 52.5	Follow-up period: 12 months
Comments:	

Results

Primary outcome(s):
Dysphagia, percentage of pts*

	Nissen		Toupet	
	Before operation (n=76)	12 months post-op (n=64)	Before operation (n= 77)	12 months post-op (n=63)
Grade 0-1 (no symptoms, minor)	69.80%	82.81%	77.93%	87.99%
Grade 2 (mild)	17.10%	15.64%	18.17%	12.67%
Grade 3 (moderate)	9.20%	1.55%	3.89%	0%
Grade 4-5 (severe, very severe)	3.90%	0%	0%	0%

*no statistical significance

Secondary outcome(s):
Degree of esophagitis, percentage of pts*

	Nissen		Toupet	
	Before operation (n=76)	12 months post-op (n=64)	Before operation (n= 77)	12 months post-op (n=63)
No esophagitis	0%	93.75%	0%	93.66%
Grade A	57.95%	6.25%	49.37%	6.34%
Grade B	30.25%	0%	38.95%	0%
Grade C	9.20%	0%	7.79%	0%
Grade D	2.60%	0%	3.89%	0%

*no statistical significance

Esophageal manometry and 24-hr pH-metry (in 58 pts, 38%) after 12 months: tone of LES significantly increased ($p<0.05$) and DeMeester score significantly decreased ($p<0.05$). No significant difference found between groups. (no numerical data presented for this outcome)

	Nissen		Toupet	
	Before operation (n=76)	12 months post-op (n=26)	Before operation (n= 77)	12 months post-op (n=32)
DeMeester score	48.15	2.58	51.33	8.56
Pressure of the LES (mmHg)	8.1	11.48	4.91	11.19

Treatment failure, number of pts:

	Nissen	Toupet
Prelapse of haital hernia with persistent esophagitis	4	1
Persistent esophagitis, PPI tx	5	7
Total	9	8

Comments:
No clear distinction of which outcome is primary or secondary.
Results were presented stratified by 1.5cm and 3cm group. Data were combined before extraction.
Data from 6-month post-op are available but not extracted in this form.

GERD data extraction form

Compliance: NA

Adverse Events: Post-op complications: post-op bleeding from short gastric blood vessels (n=2), pneumothorax during surgery and post-op lung atelectasis (n=1), esophageal perforation and mediastinitis and death (n=1), cardiac arrhythmias during post-op period (n=1), thrombophlebitis of the deep leg veins (n=1), post-op pnuemonia (n=1)

Applicability: (narrow/wide): narrow	Comments: in Lithuania, no funding source information

GERD data extraction form

Author: Mine	Yr: 2005	UI: 16105122	Questions addressed: Q1; Q3	Extractor: MC

Objective/Topic: to clarify the difference in quality of GERD treatment with PPIs and H2-RA in step-down protocol using lansoprazole

Study design:	Country/Setting:	Funding:
RCT	Japan	No data

Interventions(s):	Comparator(s):
Group 1: 15 mg of lansoprazole once daily for 16 weeks Group 2: 30 mg of lansoprazole once daily for 8 weeks followed by another 8-week treatment with 20 mg of famotidine twice daily	Group 3: 30 mg of lansoprazole once daily for 8 weeks followed by another 8-week treatment with 15 mg of lansoprazole once daily Rescue therapy was instituted for subjects who continued to show symptoms related to gastroesophageal reflux after 12 weeks of completion of therapy. If patients on H2-RA agents experienced symptomatic recurrence, they were treated with PPI maintenance therapy.

Primary outcome(s):	Other outcome(s):
Ordinal scales for grading the severity of GERD symptoms	Endoscopic assessment: LA classification Endoscopic ultrasonography analysis

Inclusion criteria:	Exclusion criteria:
Patients with symptomatic GERD	None stated
Symptoms (describe): heartburn, regurgitation, and/or dysphagia	**Hiatal hernia (specify whether considered and size used for exclusion):** No data
EGD (performed or not and results): Los Angeles classification: mostly Grade A No significant difference was found between the grade O, grade A and grade B groups.	**Esophagitis/stricture/Barrett's:** No data
PH study (performed or not and results): No data	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No data
Esophageal manometric studies (performed or not and results): No data	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: C/Poor	
Blinding: no data	**Allocation concealment: no data**
Intention-to-treat: yes	**Method of Randomization: no data**
Other comments: methods are poorly described, small sample size	

Quality Assessment Non-RCTs:
Comments:

GERD data extraction form

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	X (patient enrollment was poorly described)	

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 61.3	**N enrolled: 43**
%Male: 46.5	**N completed: 43**
Race: Asian (assumed)	**Dropouts/reasons: no dropouts**
BMI: no data	**Follow-up period: 16 weeks**
Comments:	

Results

Primary outcome(s):

	Lansoprazole 15 mg (n=14)		Lansoprazole 30mg/Famotidine 20 mg (n=14)		Lansoprazole 30mg/ Lansoprazole 15 mg (n=15)	
	Pre	16 wk	Pre	16 wk	Pre	16 wk
Heartburn						
0	9	13	4	7	3	15
1	5	1	8	6	9	0
2	0	0	2	1	3	0
3	0	0	0	0	0	0
Regurgitation						
0	2	14	0	3	0	14
1	11	0	13	11	13	1
2	1	0	1	0	2	0
3	0	0	0	0	0	0
Dysphagia						
0	10	14	12	14	9	15
1	2	0	1	0	6	0
2	2	0	1	0	0	0
3	0	0	0	0	0	0

Secondary outcome(s):

- In the no step therapy group with a lansoprazole dose of 15 mg, 6 patients of grade A improved to grade O (no mucosal break), one patient of grade B improved to grade A, and one patient of grade C improved to grade A after 16 weeks.
- In the group with a stepped down to famotidine dose, 4 patients of grade A improved to grade O, 3 patients of grade B improved to grade A, 2 patients of grade C improved to grade A, whereas 1 patient of grade O changed to grade A.
- In the group with a stepped down lansoprazole dose (from 30 mg to 15 mg), 7 patients of grade A improved to grade O, 2 patients and 1 patient of grade B improved to grade O and grade A, respectively, 2 patients of grade C improved to grade A, and 1 patient of grade D improved to grade A.

Comments:

Compliance:
No data

Adverse Events:
“None of the patients reported any troublesome side-effects throughout the study”

Applicability: (narrow/wide): narrow	Comments: small sample size; Asian only

GERD data extraction form

Author: Monnikes H;Bardhan KD;Stanghellini V;Berghofer P;Bethke TD;Armstrong D;	**Yr: 2004**	**UI:** 17489031	**Questions addressed: Comparison of different medical therapies**

Objective/Topic: Psychometric evaluation and validation of GERD symptom patient self-assessment instrument (ReQuest) in response to PPI treatment at -3, 0, 7, 14, 21, 28 days

Study design:	**Country/Setting: Germany**	**Funding:**

Interventions(s): Pantoprazole 20 mg or 40 mg for 28 days	**Comparator(s): Pantoprazole 20mg vs. 40 mg.**

Primary outcome(s): Assessment of GERD symptoms (ReQuest dimensions include general well being, acid complaints, upper abdominal stomach complaints, lower abdominal digestive complaints, nausea, sleep disturbances and other complaints) post PPI treatment. Gastrointestinal Symptom Rating Scale (GSRS)	**Other outcome(s):**

Inclusion criteria: Patients with endoscopically confirmed erosive GERD	**Exclusion criteria: Those who definitely did not take any medication; protocol violators, i.e., pts who had at least one missing baseline value 3 days prior to start of treatment**
Symptoms (describe): general well being, acid complaints, upper abdominal stomach complaints, lower abdominal digestive complaints, nausea, sleep disturbances and other complaints; GI symptoms; Psychological well-being	**Hiatal hernia (specify whether considered and size used for exclusion): not specified—check original study**
EGD (performed or not and results): Endoscopically confirmed GERD—see study phase 1—get article	**Esophagitis/stricture/Barrett's: not specified—check original study**
PH study (performed or not and results): not specified—check original study	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** not specified—check original study
EMS (performed or not and results): not specified—check original study	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

GERD data extraction form

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
Endoscopy---A/		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: not specified—check original study	N enrolled: 421
%Male: not specified—check original study	N completed: 349
Race: not specified—check original study	Dropouts/reasons: one missing value at baseline. Persons terminating the study prematurely due to adverse events assessed as likely or definitely related to the medication and due to low efficacy---data available at phase 1.
BMI: not specified—check original study	Follow-up period: -3, 0, 7, 14, 21, 28 days
Smoking history: not specified—check original study	Comments:

Results
Primary outcome(s): GI Symptoms decreased And general well being increased after 28 days tx. 40mg more
Secondary outcome(s):
Comments:

Adverse Events: see phase 1 study

Applicability: (1/2/3):????	Comments:

GERD data extraction form

Author: Montgomery	Yr: 2006	UI:17101568	Questions addressed: 1, 3	Extractor: SI

Objective/Topic: Compare EndoCinch with Sham procedure in pts with GERD

Study design: RCT	Country/Setting: Sweden	Funding: Karolinska Institute Research Funds and others

Interventions(s): EndoCinch	Comparator(s): Sham

Primary outcome(s): reflux symptoms	Other outcome(s): LES and acid exposure

Inclusion criteria: typical symptoms of GERD requiring daily PPIs; endoscopically verified insufficient gastroesophageal flap-valve with or without esophagitis; and objectively verified GERD with total or upright esophageal acid exposure time >4%	Exclusion criteria: ASA >2; hiatal hernia of at least 3 cm; Barrett's esophagus, previous antireflux surgery or severe esophageal dysmotility
Symptoms (describe): typical symptoms of GERD	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results): y Grade A 3/46 Grade B 1/46 no esophagitis 42/46	Esophagitis/stricture/Barrett's: excluded Barrett's
pH study (performed or not and results): y total time% pH<4 = 5.92	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): not considered
Esophageal manometric studies (performed or not and results): y LES pressure 10.9 mm Hg	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) y

Quality Assessment for RCTs: B	
Blinding: pts blinded	Allocation concealment: n
Intention-to-treat: n	Method of Randomization: nd; stratified to BMI < or >25
Other comments: small sample size, no power calculation	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 41.5 y	N enrolled: 46
%Male: 33%	N completed: 43
Race: nd	Dropouts/reasons: 3 excluded from Sham: 1 pregnancy, 2 with severe symptoms requiring antireflux surgery
BMI: 24.4	Follow-up period: 3 mo and 12 mo
Comments:	

Results				
Primary outcome(s): GI Symptom Rating Scale (GSRS) (Fig 1 in paper): significant improvement in symptoms compared to Sham at 3 mo, but not at 12 mo SF36 Physical and Mental, no significant difference between groups at 12 mo				
Secondary outcome(s):		Baseline	12 mo	
Total time% pH <4	EndoCinch	5.95 (3.78-6.73)	4.7 median (IQR 3.18-7.13)	NS
	Sham	5.90 (4.63-7.08)	7.4 (4.03-12.45)	NS
LES	EndoCinch (mm Hg)	11.6 (6.5-16.8)	9.9 (5.9- 13.9)	NS
	Sham	10.3 (6.6-15.8)	14 (11.6-19.0)	NS
Decrease in PPI use	(doses per wk, equipotent to omeprazole 20 mg per dose)			
	EndoCinch	7	1 median (IQR 0-7)	
	Sham	7	3 (0.5-7)	
Off PPI	EndoCinch	0/46	10/43	
	Sham	0/46	5/43	
Comments:				

Compliance:

Adverse Events: no complications in either arm, minor side effects like sore throat, mild dysphagia and epigastric pain were reported (actual incidence not reported)

Applicability: (narrow/wide): narrow	Comments: unclear where these patients came from

GERD data extraction form

Author: Morgan	Yr: 2007	UI: 18080054	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
Compare continuous therapy and on-demand therapy with rabeprazole 20mg for GERD maintenance

Study design:	Country/Setting:	Funding:
Randomized, open-label, controlled study	Canada, 23 sites	Janssen-Ortho Inc

Interventions(s):	Comparator(s):
Rabeprazole 20mg q day continuous therapy (COT) for 6 months, limit supplemental antacid usage	Rabeprazole 20mg on-demand therapy (ODT) for 6 months, limit supplemental antacid usage ODT: take rabeprazole on the first day of symptoms, and 1 dose q morning on subsequent days until symptoms resolved

Primary outcome(s):	Other outcome(s):
Percentage of heartburn-free days in 6 months	• Heartburn duration • Supplemental antacid use • GERD symptom evaluation (occurrence, frequency of symptom occurrence, symptom severity, symptom distress or bother) • Heartburn control satisfaction • Quality of life

Inclusion criteria:	Exclusion criteria:
25-65 years old Confirmed GERD per response to 4-week PPI therapy At least 3 months of hx of GERD Heartburn as predominant GERD symptom Postmenopausal and using birth control and negative urine pregnancy test (for women)	Hypersensitivity to rabeprazole or any substituted benzimidazole, hx of using histamine2 receptor antagonist in the 2 weeks before screening, hx of significant GI conditions (with vomiting, bloody stool, anemia, dysphasia), hx of Barrett's esophagus, esophageal stricture, pyloric stenosis, gastric or duodenal ulcer, infectious or inflammatory conditions of small or large intestine, malabsorption syndromes, obstruction, GI malignancy, prior gastric or intestinal surgery, uncontrolled chronic constipation, conditions that likely interfere with health during the study, use of continuous concurrent tx for upper or lower GI conditions, use of other antacids or acid suppressive medication, use of high-dose systemic corticosteroids, pregnancy or lactation (women)
Symptoms (describe): Heartburn: None: 82.16% Mild (present, no or little discomfort, can be ignored): 29.84% Moderate (cannot be ignored, does not affect daily routine): 22.07% Severe (some interference with daily routine): 0% Very severe (disabling, significantly interferes with daily routine): 0%	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): no	Esophagitis/stricture/Barrett's: no

GERD data extraction form

PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): Response to PPI treatment at baseline was satisfactory in 42% and completely controlled in 57%
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: B/acceptable (please select one and delete others)	
Blinding: no	Allocation concealment: no
Intention-to-treat: yes	Method of Randomization: not described
Other comments: pt blinding is not possible in this treatment design. Minor error/inconsistencies in reports.	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 48.02	N randomized: 268
%Male: 50.58	N completed: 234
Race: % white 96.53%	Dropouts/reasons: 9 poor heartburn control, 8 lost to follow-up, 6 adverse event, 5 withdrew consent, 2 noncompliant, 2 protocol violation, 1 pregnancy, 1 other % of withdrawal due to inadequate heartburn control not different between COT and ODT groups
BMI: 30	Follow-up period: up to 6 months
Comments:	

Results
Primary outcome(s): Percentage of heartburn-free days COT: 90.3% ODT 64.6% P<0.0001 Percentage of heartburn-free or mild days COT: 95.8% ODT: 84.3% P<0.0001
Secondary outcome(s): Percentage of weeks with 2 days or less of heartburn, of max severity or mild COT: 84% ODT: 41% P<0.0001 Heartburn episodes (consecutive days with heartburn)

COT: 7±9.1
ODT: 26±15.7
P<0.0001

Mean heartburn episode duration
COT: 1.4±2
ODT: 4.4±15.7
P=0.0319

Mean treatment episode duration (consecutive days of medication in response to symptoms) in ODT: 4.5±15.8 days
Mean interval between treatments in ODT: 9.7±22 days

Change in GERD symptoms assessment scale (higher score, less symptom control) (figure 3)

	Change within COT from baseline	Change within ODT from baseline	Difference between COT and ODT
Number of symptoms	Decreased, Sig	Increased, Sig	Sig
Frequency	Increased, NS	Increased, NS	NS
Severity	No change	Increased, Sig	Sig
Bother/distress	Increased, NS	Increased, Sig	NS

*Sig: p<0.05, NS: p>0.05

Change in quality of life (higher score, poorer quality) (figure 4)

	Change within COT from baseline	Change within ODT from baseline	Difference between COT and ODT
Daily activity	Decreased, NS	Increased, Sig	Sig
Clothing	Decreased, NS	Increased, Sig	Sig
Diet and food habits	Decreased, NS	Increased, Sig	Sig
Relationships	Decreased, Sig	Decreased, NS	NS
Psychological well-being	Decreased, NS	Increased, Sig	Sig
Total score	Decreased, NS	Increased, Sig	Sig

*Sig: p<0.05, NS: p>0.05

Supplemental antacid usage, number of tablets/day
COT: 0.1±0.3
ODT: 0.3±0.4
P=0.0023

Percentage of weeks with satisfactorily or completely controlled heartburn
COT: 96%
ODT: 84%
P<0.001 in figure 2, p<0.0001 in text

Percentage of weeks with satisfied or very satisfied heartburn control
COT: 92%
ODT: 76%
P<0.001 in figure 2, p<0.0001 in text

Overall effect of medication on heartburn control was “good” or “very good”, assessed by pts
COT: 89%
ODT: 83%
P=0.2803

Overall effect of medication on heartburn control was “good” or “very good”, assessed by MDs
COT: 89%
ODT: 81%

P=0.1173

Overall Satisfied or very satisfied with heartburn control, per pts
COT: 92%
ODT: 79%
P=0.007

Comments:
Discrepancy in p-value reported for ratings of heartburn control and satisfaction between figure 2 and text.
Numerical data for figure 3 and figure 4 not available in text.

Compliance:
COT: treatment taken on 97% of the study days
ODT: drug taken on 45% of the study days, about 1 dose/2.2 days

Adverse Events:
Sinusitis
COT: 4, <3%
ODT: 8, 6.1%
Upper respiratory infection
COT: 12, 8.8%
ODT: 9, 6.9%
Common cold
COT: 5, 3.7%
ODT: 6, 4.6%
Bronchitis
COT: 6, 4.4%
ODT: 5, 3.8%
Diarrhea
COT: 5, 3.7%
ODT: 3, <3%
Headache
COT: 3, <3%
ODT: 4, 3.1%
Flu
COT: 1, <3%
ODT: 4, 3.1%

Adverse events that led to withdrawal (in 4 pts in COT and 1 pt in ODT): aggravation of palpitation (n=1), memory impairment (n=1), abdominal cramps (n=2), stomach ache (n=1), bloating (n=1), diarrhea (n=2)

Adverse event “possibly related to” treatment that led to withdrawal: memory impairment
Adverse events “probably related to” treatment: abdominal cramps, stomach ache, bloating, diarrhea
Serious adverse events not related to treatment: post-op tonsillectomy hemorrhage, malignant melanoma, a fib, headache, skin cancer, intestinal infection
No change in vital signs or weight

Note: in the list of adverse events that led to withdrawal, abdominal cramps were counted twice – not sure if there were 2 or 4 pts.

Applicability: (narrow/wide): wide	Comments:

Author: Morgenthal	Yr: 2007	UI: 17562117	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
To evaluate long term outcomes after laparoscopic Nissen fundoplication

Study design:	Country/Setting:	Funding:
Cohort, data collected prospectively	US	Not reported

Interventions(s):	Comparator(s):
Laparoscopic Nissen fundoplication	NA

Primary outcome(s):	Other outcome(s):
Symptom score	

Inclusion criteria:	Exclusion criteria:
Had laparoscopic Nissen fundoplication at Emory University Hospital between November 1992 and December 1995	
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:46.8 (at surgery)	N enrolled: 312
%Male:57	N completed: 166 (number of patients with at least 6 years of follow-up)

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

Race: nd	Dropouts/reasons: 29 died before 6-year follow-up, 1 refused to participate,
BMI: preop: 27.9; at follow up: 29.2	Follow-up period: 11.1 yr (median) 6.1-13.3 yr (range)
Comments:	

Results
Primary outcome(s): Mean change in total symptom score: -4.93 Mean change in heartburn symptom score: -1.68 Mean change in regurgitation symptom score: -1.10 Mean change in dysphagia symptom score: -0.69 Mean change in chest pain symptom score: -0.47 Mean change in hoarseness symptom score: -0.37 Mean change in cough symptom score: -0.42 Mean change in asthma symptom score (among all patients): -0.06 Mean change in asthma symptom score (among 22 asthma patients): -1.09 Note: all scores are based on a 4-point scale. 0=none and 3=severe.
Secondary outcome(s):
Comments:

Compliance: NA

Adverse Events: 18 revisional antireflux procedure 22 attempted redo laparoscopic Nissen fundoplication (one with Collis gastroplasty) 2 converted to open Nissen fundoplication, 1 open Nissen fundoplication 3 laparoscopic Toupet fundoplications (one with Heller myotomy).

Applicability: (narrow/wide): narrow	Comments:

For KQ3, we will examine all the studies already included in addressing questions 1 and 2. We will also screen in all studies, including case reports, cohorts, comparative studies, and reviews in which the specific focus was on adverse events and complications after medical, surgical, or endoscopic interventions for GERD.

GERD data extraction form

Author: Mosler	**Yr**: 2008	**UI**: 18629586	**Questions addressed**: 1, 3	**Extractor**: JC

Objective/Topic: Compare efficacy of endoluminal gastroplication (ELGP) using Endocinch w/ and w/o adjuvant cautery

Study design: RCT	**Country/Setting**: U.S./Single center	**Funding**: ND

Interventions(s): endoluminal gastroplication (ELGP) with adjuvant bicap cautery	**Comparator(s)**: endoluminal gastroplication (ELGP)

Primary outcome(s): 12 months after the procedure, the pts answered questions concerning adverse effects related to the procedure since prior eval, current meds used for the tx of GERD, their GERD symptom score, 24-h pH probe monitoring, upper endoscopy for evaluation of esophagitis, and plication persistence. At 24 months post procedure, the pts answered questions concerning heartburn sx and current meds for tx of GERD.	**Other outcome(s)**:

Inclusion criteria: symptomatic GERD (defined as heartburn frequency >= 3 times/week) when not taking medication, with or without erosive esophagitis (i.e., grade 0–2 Savary–Miller scale); symptomatic symptom reduction with the use of antisecretory medications, H2 blockers, or PPIs (equated as follows: Esmeprazole 20 mg = Lansoprozole 30 mg = Omeprazole 20 mg = Pantoprazole 40 mg = Rabeprazole 20 mg); and abnormal 24-h pH less than 4 for more than4%of the total time or more than 2% of supine time after discontinuation of all GERD medications except antacids for 7 days.	**Exclusion criteria:** age younger than 18 years, pregnancy (active or intended during the study period), dysphagia, general health status not permitting general surgery or endoscopic therapy and/or American Society of Anesthesiology (ASA) class 3 or higher, Savary- Miller grade 3 or 4 esophagitis, body mass index (BMI) greater than 40 kg/m2, prior gastroesophageal surgical procedures, GERD refractory to PPIs, hiatal hernia exceeding 3 cm, or daily immunosuppressant therapy.
Symptoms (describe): Heartburn was scored on a scale of 0 (none), 1 (occasional), 2 (frequent), or 3 (daily).	**Hiatal hernia (specify whether considered and size used for exclusion)**: Considered, greater than 3 cm excluded.
EGD (performed or not and results): Perfomed. 10 patients in the cautery group had grade 0 esophagitis (modified Savary–Miller scale) at baseline. In the no cautery group, three patients had grade 2 and five patients had grade 0 esophagitis.	**Esophagitis/stricture/Barrett's**: Pts. with Barrett's oesophagus or oesophageal stricture excluded (Savary-Miller grade 3 or 4 esophagitis). See exclusion criteria.
pH study (performed or not and results): transnasal catheter ambulatory pH monitoring for a minimum of 16 h after discontinuation of GERD medications for 7 days. The probe tip was placed 5	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Pts encouraged to take antisecretory medications if needed. **Medication use**

cm above the position manometrically cephalad of the LES.	Cautery group: The baseline medications were daily PPI for three patients, daily PPI plus antacids or metoclopramide for two patients, PPI twice daily for three patients, and an H2-blocker twice daily for one patient. No cautery: The baseline medications were daily PPI for five patients, PPI twice daily for two patients, and PPI four times daily for one patient.
Esophageal manometric studies (performed or not and results): transnasal catheter ambulatory pH monitoring for a minimum of 16 h after discontinuation of GERD medications for 7 days. The probe tip was placed 5 cm above the position manometrically cephalad of the LES.	Other: Medical/surgical history also obtained

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: A/B	
Blinding: Yes, single blinding. The patients were blinded as to their randomization category for the first 12 months of the study.	Allocation concealment: Randomization was accomplished by opaque sealed envelopes in blocks of four.
Intention-to-treat: ND	Method of Randomization The 18 patients who met the study enrollment criteria were randomized to either suturing alone or suturing with adjuvant cautery.
Other comments:	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: mean 51.8	N enrolled: 18
%Male: 78%.	N completed: 15
Race: ND.	Dropouts/reasons: 3: One patient was lost to follow-up evaluation at 12 months, and two more patients were lost to follow-up evaluation after 24 months, all in the no cautery group. One patient died of unrelated causes.
BMI: ND	Follow-up period: 2 year for primary outcomes, 1 year for secondary outcomes
Comments:	

GERD data extraction form

Results

Primary outcome(s):

Follow-up time	Mean symptom score		Mean total % time pH<4		Daily PPI/H2-blocker or 2nd antireflux procedure		Plications intact	
	Cautery	No cautery	Cautery	No cautery	Cautery	No cautery	Cautery	No cautery
Baseline	2.70	2.75	12.1	20.6 (14.4)[a]	10/10	8/8	9 of 27 patients[b]	8 of 20 patients
1 Year 2	2.0	2.43	7.3	12.3 (11.1)[a]	6/10	3/7 (1 LTF)	10/27 (37%)	3/20 (15%)
Years	2.70	2.60	Not done	Not done	9/10	5/5 (3 LTF)	No repeat endoscopy	No repeat endoscopy

LTF, lost to follow-up evaluation
a Exclude 1 outlier patient
b Exclude 1 Nissen patient

Endoscopy Score
Endoscopy at 12 mo showed esophagitis score for five (56%) of nine pts in cautery group increased from grade 0 to 1 or 2.

In the no cautery group, esophagitis score for one (14.3%) of seven pts increased from grade 0 to grade 2. Six pts showed no changes in esophagitis score. One pt was lost to follow- up evaluation.

LES pressure
The mean baseline LES pressure was 14.2 mmHg (range, 0–23.5 mmHg) in cautery group and 13.4 mmHg (range, 0–29.1 mmHg) in no cautery group.

At 12 months, mean LES pressure was 13.4 mmHg (range, 0–35.8 mmHg) in the cautery group and 18.6 mmHg (range, 7.5–37.9 mmHg) in the no cautery group ($p>0.05$).

Secondary outcome(s):

Comments:

Compliance:
Pts undergoing a second antireflux procedure during the follow-up period were considered study failures and scored 3.

Adverse Events:
Most patients experienced a mild sore throat after ELGP.

Two major hemorrhages occurred 2 or 3 days after ELGP (one each in the cautery and no cautery groups). Both pts experienced hemoglobin drop greater than 5 mg/dl, and each received 2 to 4 units of blood. Emergency endoscopy showed active bleeding from suture line. Each pt was treated successfully with epinephrine injection, and no rebleeding occurred.

Applicability: (narrow/wide): Narrow	Comments: Small sample size, strict inclusion/exclusion criteria

GERD data extraction form

Author: Noar	**Yr**: 2007	**UI**: 17321232	**Questions addressed**: 1, 2, 3	**Extractor**: JC

Objective/Topic: To assess symptom and medication changes after the Stretta procedure during a 4-year follow up period in drug refractory pts.

Study design: Retrospective cohort	**Country/Setting**: Community practice—single practitioner performing Stretta	**Funding**: n/d

Interventions(s): Stretta	**Comparator(s)**: None

Primary outcome(s): Change in symptom scores, GERD quality of life parameters, medication usage	**Other outcome(s)**: Complications

Inclusion criteria: Significant GERD with persistent sx of heartburn and regurgitation despite twice daily PPI	**Exclusion criteria:**.Pts with stenosis, stricture or ulceration of the pyloric valve, pregnancy, poor surgical risk (American Surgical Association Grade >III), achalasia, previous non-Nissen esophageal or gastric surgery, collagen vascular disease or severe uncontrolled medical illness.
Symptoms (describe): Symptom assessment—heartburn severity, pt satisfaction (GERD QoL)--with GERD health-related quality of life questionnaire.	**Hiatal hernia (specify whether considered and size used for exclusion)**: not considered
EGD (performed or not and results): Performed on some and graded according to Los Angeles classification, grade A or higher (All pts had GERD dx confirmed by finding erosive esophagitis at) upper endoscopy or abnormal acid contact time detected at ambulatory esophageal pH testing)	**Esophagitis/stricture/Barrett's**: Stricture of the pyloric valve excluded—see Exclusion Criteria. 39% of pts w/ Barrett's 33% of pts w/ Esophagitis
pH study (performed or not and results): Performed on some (All pts had GERD dx confirmed by finding erosive esophagitis at) upper endoscopy or abnormal acid contact time detected at ambulatory esophageal pH testing)	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** See inclusion criteria—All pts had significant GERD with persistent sx of heartburn and regurgitation despite twice daily PPI. All pre-stretta medication maintained for 6-8 weeks after procedure to maintain baseline and allow time for complete healing.
Esophageal manometric studies (performed or not and results): Not described.	Other: Gastric emptying scans were performed on all patients—31 of 109 demonstrated abnormal emptying. Medication use assessed with assistance of pt diaries and detailed questions addressing use of all GERD meds.

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) n/a—no comparator

GERD data extraction form

Quality Assessment for RCTs: n/a	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: Retrospective cohort—No comparator

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: mean (s.d) 51 (13)	N enrolled: 109
%Male: 62%	N completed: 93 at 48-month follow-up
Race: n/d	Dropouts/reasons: 2 pts deceased and 1 refusal to comply—SEE COMPLIANCE BELOW
BMI: mean (s.d) n/d	Follow-up period: 48 months
Comments: Weight-kg mean (sd): 77 (10)	

Results

Primary outcome(s):

Comparison of clinical parameters at various follow-up intervals show significant changes in all measures

Parameter	Baseline		Follow-up (mo)				
	Off medication	On medication	12	24	36	48	P value
GERD HRQoL	27.8	20.5	6.8	4.6	6.7	7.1	.001
Heartburn	3.6	2.6	0.9	0.7	1.06	1.18	.001
Satisfaction	1.4	2.2	3.97	4.4	3.8	3.8	.001
Percent without PPI	100	0	82	83	77	75	.05

Secondary outcome(s): Subgroup analysis performed b/w pts with and without erosive esophagitis at initial assessment as to their satisfaction outcomes. At baseline no significant diff in t satisfaction while on medications before Stretta. At 1-yr follow up that was significant improvement in satisfaction in both groups—no diff b/w groups. Results maintained throughout 4 years with no significant differences b/w groups.

Comments: At 48 month follow up pts were divided into 4 med use categories: 1) no meds; 2) as needed antacids/over the counter PPI; 3) daily PPI; 4) 2x daily PPI. At 48 months 85% of pts had reduced their med requirements by half or eliminated it completely. Other pts were in categories 3 and 4.

Compliance: 13 pts not satisfied with initial result and went on to request a second procedure—6 had a Nissen fundoplication and 7 had a 2nd stretta procedure. All failed pts were treated on an intent to treat basis and their last value sores carried forward to 4 years for complete data analysis.

Adverse Events: Minor complications occurred after the procedure including 11 cases (10.1%) of dyspepsia, 27 chest discomfort (25%) and 2 minor gastric bleeding (1.8%). Complications resolved within 2 weeks without sequlelae. No serious complications were noted after the procedure or in long term follow up.

Applicability: (narrow/wide): narrow	Comments: Case series, non-RCT, no comparator, single site, single practitioner setting.

GERD data extraction form

Author: Nocon	**Yr: 2007**	**UI: 17311605**	**Questions addressed: KQ2**	**Extractor: MC**

Objective/Topic:
To describe the long-term pattern of GERD medication use in GERD patients receiving routine care.

Study design:	**Country/Setting:**	**Funding:**
Cohort study	Germany, Austria, and Switzerland	AstraZeneca

Interventions(s):	**Comparator(s):**
Long-term observational follow-up of an 8-week RCT comparing different regimens of esomeprazole. Patients were asked the medication used and symptom in the 3 months prior to the follow-up questionnaire.	Association between patient characteristics and predominant form of treatment (i.e., treatment taken for three or more years during the 4-year follow-up period)

Primary outcome(s):	**Other outcome(s):**
Predominant form of treatment: continuous PPIs, PPI on-demand, other GERD medication, or no GERD medication for most of the study period	

Inclusion criteria:	**Exclusion criteria:**
Patient with physician-diagnosed GERD	
Symptoms (describe): Mean GERD symptom score = 17	**Hiatal hernia (specify whether considered and size used for exclusion):** No data
EGD (performed or not and results): Based on LA classification: Non-erosive reflux disease (n=2970) Mold erosive reflux disease (n=2634) Severe erosive reflux disease (n=611)	**Esophagitis/stricture/Barrett's:** No data
PH study (performed or not and results): No data	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Not reported in current paper. This is a Long-term observational follow-up of a 8-week RCT
Esophageal manometric studies (performed or not and results): No data	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: prospective study but self-reported outcomes and univariate analyses only

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 54	**N enrolled: 6215**
%Male: 53	**N completed:** year 1, 85% (n = 5269) in year 2, 81% (n = 5017) in year 3, and 78% (n = 4855) in year 4
Race: no data	**Dropouts/reasons:** no medication data were available
BMI:	**Follow-up period:** 4 years
Comments:	

Results

Primary outcome(s):
Percent of no medication used during the follow-up:

	Year 1	Year 2	Year 3	Year 4
Non-erosive reflux disease	31%	31%	32%	34%
Mild erosive reflux disease	24%	24%	25%	26%
Severe erosive reflux disease	16%	18%	18%	17%

Non-erosive reflux disease (Year 1: n = 2624, Year 2: n = 2496, Year 3: n = 2378, Year 4: n = 2324)
Mild erosive reflux disease (Year 1: n = 2335, Year 2: n = 2249, Year 3: n = 2140, Year 4: n = 2053)
Severe erosive reflux disease (Year 1: n = 545, Year 2: n = 524, Year 3: n = 499, Year 4: n = 478)

Treatment/Comparison:	Odds ratio (95%CI) of no medication used during 4-year follow-up period of a 8-week RCT using esomeprazole					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Continuous use of PPIs	**Off all meds**		
Age			1.03 (1.02, 1.04)			
Sex (Female vs. Male)			No effect			
BMI			1.03 (1.01, 1.06)			
Symptoms (baseline GERD symptom score)			1.04 (1.03, 1.05)			
Esophagitis (Severe ERD or mild ERD vs. NERD)			Severe: 3.69 (2.65, 5.12) Mild: 1.96 (1.63, 2.37)			

Secondary outcome(s):

Comments:
Univariate analyses only

Compliance:
Not applicable

Adverse Events:
No data

GERD data extraction form

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Norman	Yr: 2005	UI: 15924594	Questions addressed: KQ1,3	Extractor: MC

Objective/Topic: clinical effectiveness and safety of continuous esomeprazole, 'on-demand' esomeprazole and continuous ranitidine treatment strategies

Study design:	Country/Setting:	Funding:
RCT	Norway, 281 clinics	No data

Interventions(s): 4 weeks of control phase followed by a 6-month follow-up phase All patients received esomeprazole 40 mg once daily for 4 weeks. After the control phase, patients who were symptom free were randomized to 6 months treatment with one of the following regimens: Esomeprazole 20 mg od continuously, esomeprazole 20 mg on-demand or ranitidine 150 mg twice daily (bid) continuously.	**Comparator(s):** Throughout the follow-up phase, if relapse in symptoms, patients who were receiving either of the esomeprazole treatments were prescribed a 4-week treatment course of esomeprazole 40 mg od, and patients receiving ranitidine were prescribed a 4-week treatment course of ranitidine 300 mg bid. If after this 4-week treatment course, patients were symptom free, they would resume the long-term treatment they were originally randomized to.

Primary outcome(s): • patient satisfaction with treatment strategy • time on each allocated treatment strategy • time to first relapse • reported symptoms of GERD	**Other outcome(s):**

Inclusion criteria: Over 18 years of age with symptoms suggestive of GERD (heartburn as the predominant symptom with or without acid regurgitation) for 3 days or more in the 7 days before the start of the study	**Exclusion criteria:** none
Symptoms (describe): 11.4% had mild heartburn, 70.7% had moderate heartburn and 17.9% had severe heartburn	**Hiatal hernia (specify whether considered and size used for exclusion):** No data
EGD (performed or not and results): No data	**Esophagitis/stricture/Barrett's:** No data
PH study (performed or not and results): No data	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** All response to 40 mg esomeprazole once daily for 4 weeks
Esophageal manometric studies (performed or not and results): No data	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) yes

Quality Assessment for RCTs: B	
Blinding: no blinding.	**Allocation concealment: no**
Intention-to-treat: yes	**Method of Randomization: yes**

Other comments: This is an open trial so both patients and physicians were aware of treatment allocations. All patients reported outcomes with no blinding. Change treatment regimen if relapse to simulate the real life situation.

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
	x	

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 51 (ranged 18-88)	**N enrolled: 1902**
%Male: 55.1	**N completed: 1648**
Race: no data	**Dropouts/reasons: 254 (**12%) patients dropout 125 dropout due to adverse event (esomeprazole on-demand n = 16, esomeprazole continuous n = 52 and ranitidine continuous n = 57)
BMI: no data	**Follow-up period: 6 months**
Comments: 2156 patients entered the control phase; 1902 were symptom free and randomized	

Results
Primary outcome(s): • Percentage of patients with no heartburn following 6-months of treatment - Esomeprazole 20 mg continuous (*n* = 658): 72.2% Esomeprazole 20 mg on-demand (*n* = 634): 45.1% Ranitidine 150 mg bid (*n* = 610): 32.5% P<0.0001 between groups • Percentage of patients with no acid regurgitation following 6-months of treatment - Esomeprazole 20 mg continuous (*n* = 658): 78% Esomeprazole 20 mg on-demand (*n* = 634): 62% Ranitidine 150 mg bid (*n* = 610): 45.7% • The time on allocated treatment strategy for the esomeprazole continuous and on-demand treatment groups was significantly longer (p < 0.0001) than for ranitidine (170, 171 and 125 days, respectively). • The percentage of patients who experienced at least one relapse during the study was significantly lower for both the esomeprazole 20 mg continuous strategy (7.0%) and the esomeprazole on-demand strategy (10.9%) than for the ranitidine continuous (34.4%) strategy (p < 0.0001)
Secondary outcome(s):
Comments:

Compliance: A total of 387 patients (esomeprazole continuous n = 73, esomeprazole on-demand n =64 and ranitidine continuous n = 250) were discontinued from the study due to a lack of efficacy

Adverse Events: Patients having any adverse event: Esomeprazole 20 mg ODT: 16/634 (2.5%); Esomeprazole 20 mg CT 52/658 (7.9%); Ranitidine 150 mg CT: 57/610 (9.3%) The most frequently reported adverse events during the study in the esomeprazole on-demand, esomeprazole continuous and ranitidine groups were diarrhea (3, 9 and 12 events, respectively), headache (6, 7 and 12 events, respectively) and nausea (5, 6 and 18 events, respectively).

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Oelschlager	Yr: 2008	UI: 17970835	Questions addressed: 1,2,3	Extractor: JHL

Objective/Topic: Long-term outcomes after laparoscopic antireflux surgery

Study design: Surgical cohort study (retrospective)	Country/Setting: US	Funding: None

Interventions(s): Laparoscopic antireflux surgery	Comparator(s):

Primary outcome(s): • Symptom control • Predictors for symptom improvement and resolution	Other outcome(s):

Inclusion criteria: "….patients who had a primary LARS for GERD performed at the University of Washington between September 1993 and September 1999."	Exclusion criteria: Patients operated on because of a paraesophageal hernia or failed prior antireflux procedure
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion): Hiatal hernia, n=160 (56%)
EGD (performed or not and results): Performed	Esophagitis/stricture/Barrett's: Esophagitis, n=168 (58%) Barrett's esophagus, n=51 (18%)
PH study (performed or not and results): Performed, DeMeester score 78.2 ± 71.2	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND
Esophageal manometric studies (performed or not and results): LES pressure (mmHg) 12.8 ± 8.8, Ineffective esophageal motility, n=37 (13%)	Other:

Presenting symptom	
Heartburn	260 (90%)
Regurgitation	193 (67%)
Dysphagia	123 (43%)
Chest pain	86 (30%)
Bloating	41 (14%)
Cough	88 (31%)
Hoarseness	63 (22%)

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B
Comments: Retrospective study

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A/rigorous (endoscopy)		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 47y	N enrolled: 288

GERD data extraction form

%Male: 21%	**N completed: 288**
Race: ND	**Dropouts/reasons: NA (retrospective study)**
BMI: ND	**Follow-up period: median follow-up 69 months**
Comments:	

Results

Primary outcome(s):

- "At 69 months, the majority of patients maintained improvement or resolution of heartburn (90%), regurgitation (92%), and dysphagia (75%) when compared to before LARS."

Treatment/Comparison:						
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Univariate analysis						
	Primary symptom improvement (%)					
Sex	NS					
Heartburn	*p*=0.01					
Dysphagia	NS					
Primary symptom: respiratory	*p*=0.02					
Bloating	NS					
Abdominal pain	NS					
Esophagitis (any severity)	NS					
Severity of acid reflux	NS					
Esophageal motility	NS					
Hiatal hernia	NS					
Multivariate analysis						
	Primary symptom resolution (%)					
Male	*OR 0.52 (95%CI, 0.29, 0.94)*					
Dysphagia	*OR 2.17 (95%CI, 1.18, 3.98)*					
Age	*OR 1.03 (95%CI, 1.01, 1.58)*					

*Variables included in analysis: type of surgery—Nissen *versus* Toupet; esophagitis; hiatal hernia; Barrett's esophagus; LES pressure; peristalsis >80%; manometry; ineffective esophageal motility; DeMeester score; DeMeester score >50; % exposure time; % exposure time upright; heartburn; bloating; abdominal pain; respiratory symptoms as primary presenting symptom; presence of respiratory symptoms.

Secondary outcome(s):

Comments:

Compliance: NA

Adverse Events:

- Ten patients (3%) have required reoperations.
  - 2 for acute complications; 1 for gastric perforation (postoperative day #3); 1 for acute herniation of the fundoplication (postoperative day #3)
  - 8 patients with reoperation had a revision Nissen fundoplication for chronic problems: either dysphagia (N = 1) or recurrent GERD (N = 7). One patient subsequently underwent a gastrectomy for recurrent GERD after failure of the re-do Nissen.
- 27 patients (9%) developed a new onset of bloating; 32 (11%) patients developed new or increased diarrhea; 7 patients (2%) developed new onset dysphagia; 1 patient has required revisional surgery for dysphagia.

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Olberg	Yr: 2005	UI: 15932167	Questions addressed: 1,3	Extractor: JHL

Objective/Topic: Long-term outcome of surgically and medically treated patients with GERD

Study design: A matched-pair follow-up study	Country/Setting: Norway	Funding: AstraZeneca AS, Norway

Interventions(s):	Comparator(s):
• Open or laparoscopic fundoplication	• Controls treated medically

Primary outcome(s):	Other outcome(s):
• GERD symptoms	• Health-related quality of life

Inclusion criteria:	Exclusion criteria:
Patients • Patients operated on with fundoplication because of GERD at St. Olav's Hospital (SOHO) and at Levanger Hospital (LH) in the period 1992-99 • SOHO 215 patients 209 patients (a 360° fundoplication ad modum Nissen-Rosetti) + 6 patients (hemifundoplication ad modum Toupet) Matching controls • "… Comparability with regard to hospital, sex, age (± 5 years for those 50 years or above and ± 10 years for those < 50 years), follow-up time (gastroscopy in the same year as operated on or ± 1 year if none was found), highest grade of esophagitis recorded at the time of operation or earlier, graded according to Savary & Miller (regarding Barrett's esophagus as a separate grade), and presence of hiatus hernia or Barrett's esophagus."	**Matching controls** • "Serious disease representing a contraindication against operation, alcoholism, reduced mental function incompatible with completing questionnaires and later operation with fundoplication. It was not possible to find a suitable control for 90 operated patients (43 from SOHO and 47 from LH)."
Symptoms (describe): ND	**Hiatal hernia (specify whether considered and size used for exclusion):** SOHO 87.3%, LH 100%
EGD (performed or not and results): ND	**Esophagitis/stricture/Barrett's:** Esophagitis Grade 0/I/II/III/IV (%) • SOHO 8.8/28.4/51.0/8.8/2.9 • LH 6.5/3.9/36.4/35.1/18.2 Barrett's esophagus • SOHO 2.9%, LH 6.5%
PH study (performed or not and results): ND	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): ND	**Other:** Matching controls: medical treatments vary based on the severity of GERD and the general practitioner. "Patients with no or only mild esophagitis were first given a 1-3 months' treatment course with an H2RA and advised of subsequent on-demand use if satisfactory relief was obtained. If no satisfactory relief was achieved the next step would be continuous, intermittent or on-demand treatment with a PPI. In the majority of patients with mild reflux disease, however, follow-up and further treatment were the responsibility of the submitting general practitioner."

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
No (matched pair, surgically vs. medically treated patients)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: • No information on diagnostic tests for GERD • 179 pairs, 102 from SOHO + 77 from LH; "…no significant differences between operated patients and controls with regard to the matching criteria, smoking status, and the presence of concurrent disease. Disease history in both hospitals, however, was significantly longer in operated patients than in controls ($p < 0.05 – p < 0.001$)."

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
C/Poor (No data)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: SOHO 54y, LH 54.5y	**N enrolled:** • SOHO 215 operated patients • LH 158 operated patients
%Male: SOHO 63.7%, LH 81%	**N completed: SOHO 102 pairs, LH 77 pairs**

Race: ND	**Dropouts/reasons:**
	St Olavs Hospital
	215 operated patients (OPR): 162 OPR with matched control + 43 OPR without matched control + 10 OPR excluded; Died 2 and 3 years after the operation for reasons unrelated to the operation or GERD (n=2), mentally retarded (n=1), had eosophagectomy as a result of Barrett's esophagus and severe dysplasia (n=1), demanded that the fundoplication be reversed (n=1), not possible to classify their preoperative degree of esophagitis (n=3), alcoholism (n=1), an erroneously indicated age of 8 years in the archive (n=1)
	• OPR (Total n=162): 135 responders + 27 non-responders
	  o 135 responders: 125 completed data + 10 (excluded)
	  o 125 complete data: 102 with paired control + 23 without paired control
	• Controls (Total n=162): 126 responders + 36 non-responders
	  o 126 responders: 123 completed data + 3 (excluded)
	  o 123 complete data: 102 with paired OPR + 21 without paired OPR
	Levanger Hospital
	158 operated patients (OPR): 158 OPR with matched control + 47 OPR without matched control + 3 OPR excluded; died 5 years after the operation for a reason unrelated to the operation or GERD (n=1), not possible to classify their preoperative degree of esophagitis (n=2)
	• OPR (Total n=108): 102 responders + 6 non-responders
	  o 102 responders: 102 completed data + 0 (excluded)
	  o 102 complete data: 77 with paired control + 25 without paired control
	• Controls (Total n=108): 82 responders + 26 non-responders
	  o 82 responders: 80 completed data + 2 (excluded)
	  o 80 complete data: 77 with paired OPR + 3 without paired OPR

BMI: ND	**Follow-up period: SOHO 71.5 months (mean), LH 79 months (mean)**

Comments:

Results

Primary outcome(s):

- **Drug use for patients operated on with fundoplication and their paired controls from St. Olav's Hospital (SOHO) and Levanger Hospital (LH). Difference tested with the χ^2 test.**

	SOHO (n=102 pairs)			LH (n=77 pairs)		
	Operated	Controls	Diff	Operated	Controls	Diff
Antireflux drugs the previous week (%)	19.8	76.5	p < 0.001	18.2	77.9	p < 0.001
Anti-reflux drugs the previous year (%)	27.7	88	p < 0.001	29.9	84.4	p < 0.001
Continuous use the previous week	11.9	52.9	p < 0.001	5.2	57.1	p < 0.001
PPI the previous week (%)	11	45.9	p < 0.001	6.5	54.5	p < 0.001
PPI the previous year (%)	17	56.1	p < 0.001	7.8	61	p < 0.001
The previous week H2RA (%)	1	20.4	p < 0.001	1.3	11.7	p < 0.001
H2RA the previous year (%)	2	21.4	p < 0.001	1.3	14.3	p < 0.001
Other anti-reflux drugs the previous week (%)	7	9.2	ns	7.8	11.7	ns
Other anti-reflux drugs the previous year (%)	8	10.2	ns	15.6	9.1	ns

- **Gastrointestinal Symptom Rating Scale (GSRS) and Psychological General Well-Being Index (PGWB) scores in patients operated with fundoplication and their paired controls, difference tested with the Wilcoxon signed-rank test.**

	SOHO (n=102 pairs)			LH (n=77 pairs)		
	Operated	Controls	Diff	Operated	Controls	Diff
GSRS						
Abdominal pain	2.0 (1.8 -2.1)	2.3 (2.1-2.5)	p < 0.05	2.1 (1.9-2.2)	2.2 (2.0-2.4)	ns
Reflux	1.3 (1.2-1.4)	2.5 (2.3-2.7)	p < 0.001	1.4 (1.2-1.6)	2.5 (2.3-2.8)	p < 0.001
Diarrhea	2.1 (1.9-2.4)	2.0 (1.8-2.2)	ns	1.9 (1.6-2.1)	1.9 (1.6-2.1)	ns
Indigestion	2.8 (2.5-3.0)	2.4 (2.2-2.6)	p < 0.05	2.7 (2.5-2.9)	2.5 (2.3-2.8)	ns
Constipation	1.8 (1.6-2.0)	1.8 (1.6-2.0)	ns	1.8 (1.5-2.0)	1.8 (1.6-2.1)	ns
Total GSRS	2.2 (1.9-2.2)	2.2 (2.0-2.3)	ns	2.0 (1.9-2.2)	2.2 (2.0-2.4)	ns
PGWB						
Anxiety	24 (23-25)	23 (22-24)	ns	24 (23-25)	24 (23-24)	ns
Depression	15 (15-16)	15 (15-16)	ns	16 (15-16)	15 (15-16)	ns
Pos. well-being	15 (15-16)	15 (14-16)	ns	16 (15-16)	15 (15-16)	ns
Self-control	15 (15-16)	15 (14-16)	p < 0.05	16 (15-16)	15 (14-15)	ns
General health	14 (13-14)	13 (12-13)	ns	14 (13-14)	13 (12-14)	ns
Vitality	16 (16-17)	16 (15-17)	ns	16 (15-17)	16 (15-17)	ns
Total PGWB	100 (97-104)	97 (93-100)	ns	101 (98-104)	98 (94-102)	ns

- **GSRS and PGWB scores for patients operated on with fundoplication and their paired controls, belonging to pairs without concurrent disease, difference tested with the Wilcoxon signed-rank test.**

	SOHO (n=24 pairs)			LH (n=19 pairs)		
	Operated	Controls	Diff	Operated	Controls	Diff
GSRS						
Abdominal pain	1.7 (1.4-2.1)	2.2 (1.7-2.6)	ns	2.2 (1.7-2.6)	2.2 (1.9-2.6)	ns
Reflux	1.1 (1.0-1.3)	2.6 (2.1-3.2)	p < 0.001	1.6 (1.1-2.1)	2.6 (2.0-3.2)	p < 0.01
Diarrhea	2.3 (1.8-2.8)	2.0 (1.5-2.4)	ns	2.0 (1.5-2.4)	2.0 (1.5-2.6)	ns
Indigestion	2.7 (2.2-3.1)	2.2 (1.8-2.6)	ns	2.5 (2.0-2.9)	2.4 (2.0-2.8)	ns
Constipation	1.5 (1.3-1.7)	1.4 (1.2-1.7)	ns	1.8 (1.3-2.3)	1.8 (1.3-1.7)	ns
Total GSRS	2.0 (1.7-2.2)	2.2 (1.7-2.4)	ns	2.1 (1.7-2.4)	2.2 (1.9-2.5)	ns
PGWB						
Anxiety	26 (25-27)	23 (21-25)	p < 0.05	24 (22-26)	22 (20-25)	ns
Depression	16 (16-17)	16 (15-17)	ns	15 (14-17)	16 (14-17)	ns
Pos. well-being	17 (16-19)	15 (14-16)	p < 0.05	16 (14-17)	15 (13-17)	ns
Self-control	17 (16-17)	15 (13-16)	p < 0.01	16 (14-17)	15 (14-16)	ns
General health	16 (15-17)	14 (12-15)	p < 0.01	14 (13-15)	14 (13-15)	ns
Vitality	19 (19-20)	16 (14-18)	p < 0.01	16 (14-18)	16 (14-17)	ns
Total PGWB	112 (107-117)	99 (91-106)	p < 0.01	101 (93-108)	97 (89-105)	ns

Secondary outcome(s):

Comments:

Compliance: NA

GERD data extraction form

Adverse Events:		
	Laparoscopy n=215 (%)	**Open n=158 (%)**
Peroperative		
- pneomothorax	6	
- intraabd. Bleeding		2
SUM	6 (2.8)	2 (1.3)
Early postoperative		
- gastric perforation	1	
- bleeding, transfusion	2	
- crural rupture		1
- pulmonary embolism	1	
- lung infection	8	4
- wound infection		2
- acute paraesoph. Herniation	3	
SUM	15 (7.0)	7 (4.4)
Late postoperative		
- ventral hernia		2
- port site hernia	13	
- diaphragmatic hernia		1
- paraesophageal herniation	9	
- slipped Nissen	6	1
- disrupted Nissen or Toupet	3	
SUM	31 (14.4)	4 (2.5)
Complications total	52 (24.2)	13 (8.3)
Reoperations	17 (7.0)	5 (3.2)

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Ozawa	Yr: 2009	UI: 19440812	Questions addressed: 1	Extractor: WY

Objective/Topic: to evaluate the effectiveness and safety of endoluminal gastroplication (ELGP) with EndoCinch

Study design: Prospective cohort	Country/Setting: Japan, Multicenter	Funding: nd

Interventions(s): endoluminal gastroplication (ELGP) with EndoCinch	Comparator(s): NA

Primary outcome(s): GERD symptoms Medication use Esophagitis grade Durability of plication Adverse events	Other outcome(s):

Inclusion criteria: when not taking antisecretory medications: a QUEST symptom score of ≥ 4 and endoscopic Los Angeles classification grade A, B, or C esophagitis	Exclusion criteria: Younger than 18 years, hiatal hernia > 2 cm in length, body mass index 40 kg/m2, history of surgery for esophageal or gastric diseases, history of portal hypertension or esophageal varices, esophageal stenosis or dysphagia, lack of response to PPI therapy
Symptoms (describe): Mean QUEST score: 9.0 ± 2.9	Hiatal hernia (specify whether considered and size used for exclusion): Mean length at baseline: 1.5±0.5cm
EGD (performed or not and results): LA grade A: 27 pts LA grade B: 15 pts LA grade C: 6 pts	Esophagitis/stricture/Barrett's:
PH study (performed or not and results): Performed.	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results): Performed.	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:

GERD data extraction form

Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:58±15	N enrolled:48
%Male: 64.58	N completed: 48
Race: nd	Dropouts/reasons: NA
BMI: 23.3±3.3	Follow-up period: 2 yr
Comments:	

Results

Primary outcome(s):

	Baseline	2 year	P (baseline vs. 2 yr)
Heartburn frequency score	3.8±0.6	1.5±0.7	<0.0001
Heartburn severity score	3.9±1.0	1.5±0.9	<0.0001
Heartburn symptom score	14.9±4.6	2.7±2.9	<0.0001
Complete resolution of heartburn	NA	66% of all patients	
Discontinued use of PPI or H2RA	NA	66% of all patients 63% of PPI-dependent patients	
Discontinued or reduced use of PPI or H2RA by more than 50%	NA	76% of all patients 74% of PPI-dependent patients	
Endoscopic LA classification changed to grade O	NA	80% of all patients	
Any improvement in endoscopic LA classification	NA	83% of all patients	

	Baseline	3 months	P (baseline vs. 3 mo)
% time in 24-hr with esophageal pH <4 (N=27)	23.3±26.3	10.4±9.6	0.014
Lower esophageal sphincter pressure (mmHg)	36.2±17.3	35.4±22.5	Nd
Lower esophageal sphincter length (cm)	3.4±1.2	3.1±1.0	nd

Secondary outcome(s):
Compared with patients who lost all plications, patients with more than 1 plication remaining had higher rates of complete resolution of heartburn, had higher rates of discontinued PPI or H2RA use, were more likely to show improvement of endoscopic LA classification to grade O.

Comments:
Data at 3 months, 6 months, 1 year, and 1.5 year follow-up are also reported, but not extracted here.

GERD data extraction form

Compliance: NA

Adverse Events: Ozzing at the suture site: 6 patients (12.5%) Slight pharyngeal pain post-op: 1 patient (2%) Death: 0 patient

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Pace	**Yr: 2005**	**UI:** 16024305	**Questions addressed: 1,3**	**Extractor: JHL**

Objective/Topic: To investigate the comparative efficacy of rabeprazole and omeprazole in patients with reflux oesophagitis

Study design: RCT	**Country/Setting: Italy**	**Funding: Janssen-Cilag, Italy**

Interventions(s): rabeprazole 20mg once daily	**Comparator(s):** omeprazole 20mg once daily

Primary outcome(s):	**Other outcome(s):**
• Healing of mucosal damage • Reflux symptoms • Time of action of intervention for symptom relief	• Overall assessment for reflux symptoms • General well-being

Inclusion criteria:	**Exclusion criteria:**
• For the curative phase: (i) male and/or female outpatients aged ≥18 years; (ii) presence of oesophagitis of grades I–III (according to the four-degree Savary–Miller classification) at an endoscopy during the last 7 days prior to inclusion in the trial; (iii) a minimum heartburn score of 2 for both frequency and intensity at daytime and/or nighttime; (iv) a history of at least 3 months of oesophagitis-like symptoms and heartburn for at least 3 days in each of the 2 weeks prior to inclusion. • For the maintenance phase: (i) complete healing of oesophagitis confirmed by endoscopy at the end of the curative phase; (ii) relief of reflux symptoms, defined as a score ≤1 for both frequency and intensity of daytime and nighttime heartburn.	(i) oesophagitis of infectious origin or caused by exogenous acid or alkaline substances; (ii) grade IV oesophagitis according to Savary–Miller; (iii) Zollinger–Ellison syndrome; (iv) presence of an active gastroduodenal ulcer or previous oesophageal, gastric or biliary surgery (including vagotomy); (v) primary oesophageal motility disorders; (vi) recent treatment with PPIs (within 2 weeks) and previous (for more than five consecutive days in the 2 weeks prior to trial entry) or concomitant therapy with H2-receptor antagonists, prokinetic agents, anticholinergics or mucosal protective agents; (vii) pregnancy or breast-feeding female; (viii) severe liver and/or renal disease, end-stage heart or lung disease; (ix) cancer or HIV infection; (x) daily use of NSAIDs; alcoholism or drug abuse.
Symptoms (describe): regurgitation, heartburn and other complaints (epigastric pain/burning, dysphagia, nausea, nocturnal coughing and nocturnal wheezing	**Hiatal hernia (specify whether considered and size used for exclusion): ND**
EGD (performed or not and results): Performed	**Esophagitis/stricture/Barrett's:** Baseline characteristics of patients

	Rabeprazole (N=277)	Omeprazole (N=272)
Patients with a first episode of oesophagitis (n, %)	186 (67.2%)	200 (73.5%)
Oesophagitis grade (n, %)		
Grade 0	3 (1.1%)	3 (1.1%)
Grade I	188 (67.9%)	192 (70.6%)
Grade II	71 (25.6%)	62 (22.8%)
Grade III	15 (5.4%)	15 (5.5%)

PH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

GERD data extraction form

Quality Assessment for RCTs: B/acceptable	
Blinding: Yes	**Allocation concealment: No**
Intention-to-treat: Yes	**Method of Randomization: Yes**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		
A (endoscopic evidence of mild to severe oesophagitis + moderate to very severe reflux symptoms)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 47.4y	**N enrolled: 560**
%Male: 68.1%	**N completed: at 4 weeks (n=442)**
Race: ND	**Dropouts/reasons:**

	Rabeprazole (n=283)	Omeprazole (n=277)
Discontinued total N	25	22
Loss to follow-up	7	2
Consent withdrawn	12	12
Adverse events	5	6
Not valid data/Other	1	2

BMI: 26.4

Follow-up period:

1. Curative phase: (i) patients received one tablet of rabeprazole 20 mg + one omeprazole-placebo capsule once daily or vice versa (ii) Patients who did not improve the symptoms and were cured endoscopically after 1 month, received the curative treatment for an additional 4 weeks
2. Maintenance phase: patients improved reflux symptoms and complete endoscopic healing → a low dose (10 mg once daily) of rabeprazole for a maximum duration of 48 weeks

Comments:

Results

Primary outcome(s):

- Endoscopic healing at endpoint (8 weeks): rabeprazole group (n=228/233, 97.9%), omeprazole group (n=231/237, 97.5%) completely healed ($p < 0.0001$ at Blackwelder's test, it means the equivalence between the two drugs is statistically significant)
- Reflux symptoms
  - "The mean time to the first day with satisfactory heartburn relief was significantly shorter for the rabeprazole group patients ($n = 271$) (2.8±0.2 days, mean ± S.E.M.) than with the omeprazole group patients ($n = 271$) (4.7±0.5 days) ($p = 0.0045$ at log-rank test)."
  - "Mean time to complete heartburn relief was similar: 7.2 days in the rabeprazole group ($n = 271$) and 8.4 in the omeprazole group ($n = 271$) ($p = 0.1342$ at log-rank test)."

Secondary outcome(s):

- % of patients graded their overall assessment for reflux symptoms as very good or good (8 weeks): 7 → 90 % (rabeprazole group), 5.5 → 90.7% (omeprazole group)
- % of patients for general well-being (8 weeks): 41.7 → 89.3 % (rabeprazole group), 43.5 → 86.3% (omeprazole group)

Comments:

Compliance: ND

Adverse Events:

- Acute phase: "no significant difference between treatment groups in single adverse events occurring during the acute phase, with the sole exception of headache; it was reported more frequently in the omeprazole than in the rabeprazole group (4.8% n = 13/17 versus 1.4% n = 4/17, p = 0.0241, at the Chi-square test)…. Serious adverse effects in the curative phase occurred in only three patients, all belonging to the omeprazole group, but were not related to omeprazole therapy in itself in all instances."
- Maintenance phase: "severe adverse effects occurred in 12 patients. There was no adverse event with an incidence greater than 2%, and only few events with an incidence greater or equal to 1%, such as flu (1.8%), fever (1.0%), hypertension (1.0%), headache (1.8%), dyspepsia (1.2%), diarrhea (1.2%), sciatalgia (1.4%) and abdominal pain (1.2%)."

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Pace	**Yr: 2005**	**UI: 16098002**	**Questions addressed: 1**	**Extractor: JHL**

Objective/Topic: Quality of life in acute and maintenance treatment of non-erosive and mild erosive GERD

Study design: Open, RCT, multicentre study	**Country/Setting:** Italy	**Funding:** AstraZeneca

Interventions(s): Esomeprazole 20mg (continuous)	**Comparator(s):** Esomeprazole 20mg (on demand)

Primary outcome(s): • Quality of life in reflux and dyspepsia (QOLRAD)	**Other outcome(s):** • Patient satisfaction

Inclusion criteria: • Conducted in Italy between March 2001 and February 2002	**Exclusion criteria:** • Patients with grade II-IV oesophagitis, according to Savary-Miller's classification
Symptoms (describe): • "Population epigastric pain was classified as absent in 12.8% of patients, mild in 30.1%, moderate in 46.8% and severe in 10.2%. Regurgitation was absent in 16.0% of patients, mild in 30.3%, moderate in 44.1% and severe in 9.4%. Heartburn was absent in 0.4% of patients, with 4.0% of patients experiencing it for <4 days/week. Heartburn severity was mild in 21.0% of patients, moderate in 67.2% and severe in 11.4%. Less frequently present was dysphagia, classified as absent in 67.1% of patients, mild in 20.4%, moderate in 10.2% and severe in 1.9%."	**Hiatal hernia (specify whether considered and size used for exclusion): ND**
EGD (performed or not and results): Performed • Normal – 28.7% • Savary–Miller I 70.5% • Savary–Miller II & III 0.8%	**Esophagitis/stricture/Barrett's: ND**
PH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: C/Poor	
Blinding: No	**Allocation concealment: No**
Intention-to-treat: Yes	**Method of Randomization: Yes**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous		
x (Endoscopy)		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 46.9y	**N enrolled: 6017**
%Male: 49.9%	**N completed: 5265**
Race: Caucasian 98.9%	**Dropouts/reasons:** 752 patients (12.5% of the enrolled, during the run-in period before randomization); loss to follow-up (3.5% of the enrolled, 28.3% of the discontinued cases), insufficient efficacy (2.9% of the enrolled, 22.9% of the discontinued cases), adverse event (2.3% of the enrolled, 18.8% the discontinued cases) and consent withdrawal (2.2% of the enrolled, 17.8% of the discontinued cases)
BMI: ND	**Follow-up period:** Total 26 weeks (i) Acute phase: esomeprazole 40mg/d for 4weeks (for all patients) (ii) Maintenance phase: esomeprazole 40mg/d continuous or demand for 22 weeks
Comments:	

Results
Primary outcome(s): Quality of life in reflux and dyspepsia (QOLRAD) • "The analysis of covariance performed on QOLRAD dimensions scores at last assessment with scores at randomization as covariate showed a marginally but statistically significantly superior improvement in the continuous treatment arm than in the on-demand arm for all dimensions ($P < 0.0001$)."
Secondary outcome(s): Treatment satisfaction: • Acute phase: "96.2% of the 5502 patients with data available were classified as satisfied (score 1–4), with 64.4% of patients were classified as very satisfied (score 1–2)"
Comments: "Baseline homogeneity was tested at randomization with analysis of variance: a statistically significant difference between the two groups was detected for three dimensions, emotional, physical/social and vital."

Compliance: Mean drug consumption per patient: 179.9 tablets (continuous treatment), 98.5 tablets (on-demand treatment)

Adverse Events: No specific information (2.3% of the enrolled, 18.8% the discontinued cases)

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Pai	Yr: 2006	UI: 17009401	Questions addressed: 1, 3	Extractor: DM

Objective/Topic: Compare S-pantoprazole (20 mg /day) with racemic Pantoprazole (40 mg/day) in the treatment of gastroesophageal reflux disease (GERD)

Study design: RCT	**Country/Setting: India**	Funding: Emcure Pharm for tablets

Interventions(s): 20 mg S-pantoprazole once daily for 28 days	Comparator(s): 40 mg racemic pantoprazole once daily for 28 days

Primary outcome(s):	Other outcome(s):
The severity of heartburn, acid regurgitation, dysphagia bloating and nausea scores as per VAS scoring *Heartburn, acid regurgitation, bloating and nausea scores: 0= none, no symptom; 1= mild, occasional symptoms that did not affect normal activities; 2= moderate, frequent symptoms or symptoms that affected normal activities; 3= severe, constant symptoms.* *Dysphagia scores: 0= normal; 1= occasional sticking of solids; 2= swallowing semisolids and Pureed food; 3= swallowing liquids only.*	Proportion of patients with at least 50% improvement of symptom scores

Inclusion criteria: 18 to 65 years old; clinical GERD	**Exclusion criteria:** known hypersensitivity to pantoprazole; Any major hematologic, hepatic, metabolic, gastrointestinal or endocrine disorder requiring any other anti-GERD medication; pregnant or lactating women; women of child bearing age not practicing effective method of contraception
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): Not done in all patients. **Esophagitis:** S-pantoprazole gp: n=21/29 Racemic pantoprazole gp: n=17 /25 **Erosions:** S-pantoprazole gp: n=2/29 Racemic pantoprazole gp: 6 /25	Esophagitis/stricture/Barrett's: see EGD
pH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results): no	Other:

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
y

Quality Assessment for RCTs: **C/poor**	
Blinding: pts were blinded	Allocation concealment: no
Intention-to-treat: no drop out	Method of Randomization: computer generated
Other comments: no power calculations, baseline characteristics not adequately reported, poor diagnostic quality	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		X

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 42.3	N enrolled: 369
%Male: 62	N completed: 369
Race: nd	Dropouts/reasons:
BMI: nd	Follow-up period: 28 days
Comments:	

Results

Primary outcome(s):
Heartburn, Regurgitation, dysphagia bloating and nausea assessed by VAS

Outcome	**Intervention**	**Baseline**	**28 days**	**p value**
Heartburn	Racemic pantoprazole	1.8 ± 0.8	0.6 ± 0.9	< 0.0001
	S-pantoprazole	1.9 ± 0.8	0.6 ± 0.8	
Regurgitation	Racemic pantoprazole	1.6 ± 0.9	0.5 ± 0.8	< 0.0001
	S-pantoprazole	1.7 ± 0.9	0.4 ± 0.6	
Dysphagia	Racemic pantoprazole	0.3 ± 0.6	0.1 ± 0.4	< 0.001
	S-pantoprazole	0.5 ± 0.8	0.1 ± 0.4	
Bloating	Racemic pantoprazole	1.4 ± 0.9	0.5 ± 0.8	< 0.0001
	S-pantoprazole	1.4 ± 1	0.3 ± 0.6	
Nausea	Racemic pantoprazole	1.4 ± 1	0.4 ± 0.8	< 0.0001
	S-pantoprazole	1.3 ± 1	0.4 ± 0.7	

Secondary outcome(s):

Proportion of patients showing improvement of heartburn scores at 28 days
Racemic pantoprazole: 74.4%
S-pantoprazole: 85.5%
P=0.01

Proportion of patients showing improvement of acid regurgitation scores at 28 days
Racemic pantoprazole: 82.4%
S-pantoprazole: 92.9%
P=0.004

GERD data extraction form

Proportion of patients showing improvement of bloating scores at 28 days
Racemic pantoprazole: 76.5%
S-pantoprazole: 86.7%
P=0.03

Patients with esophagitis

Outcome	Intervention	Baseline	28 days	p value (between groups)
Esophagitis	Racemic pantoprazole	17/25 (68%)	7/25 (28%)	NS
	S-pantoprazole	21/29 (72.4)	9/29 (31)	
Erosions	Racemic pantoprazole	6/25 (2.4%)	6/25 (2.4%)	NS
	S-pantoprazole	2/29 (0.7)	3/29 (1%)	

Comments:

Compliance:

Adverse Events: no adverse events observed in either group

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Pai	Yr: 2007	UI:17696229	Questions addressed: 1, 3	Extractor: SI

Objective/Topic: compare dexrabeprazole 10 mg once daily with rabeprazole 20 mg once daily in the treatment of GERD

Study design: RCT	Country/Setting: India	Funding: Emcure Pharm

Interventions(s): dexrabeprazole 10 mg once daily for 28 d	Comparator(s): rabeprazole 20 mg once daily for 28 d

Primary outcome(s): heartburn and regurgitation VAS score improvement	Other outcome(s):

Inclusion criteria: 18 to 65 years old; clinical GERD	Exclusion criteria: known history of hypersensitivity to any PPIs or history of infectious or inflammatory conditions of the intestine like bowel disease, malabsorption syndromes, intestinal obstruction, GI malignancy, gastric or intestinal surgery (vagotomy), Barrett's esophagus, esophageal stricture, pyloric stenosis, and scleroderma, pregnant and lactating females, abnormal laboratory tests at baseline (including liver enzymes greater than twice the upper limit of normal), patients refractory to a 2-mo course of H_2-blocker or PPI therapy for GERD treatment, patients who took PPI within 14 d of screening or a H_2-blocker or prokinetic agent within 7 d of screening, patients who required daily use of NSAIDs, oral steroids, aspirin or who were unable to discontinue the use of anti-cholinergics, cholinergics, spasmolytics, opiates or sucralfate and patients with poorly controlled associated disease (such as heart disease, coagulation disorders, thyroid disorders)
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): no esophagitis 6/50 (12%) Grade A 8/50 (16%) Grade B 36/50 (72%)	Esophagitis/stricture/Barrett's: Barrett's esophagus, esophageal stricture were excluded
pH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): patients refractory to a 2-mo course of H_2-blocker or PPI therapy for GERD treatment were excluded
Esophageal manometric studies (performed or not and results): no	Other:

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
y

Quality Assessment for RCTs: C/poor	
Blinding: pts were blinded	Allocation concealment: no
Intention-to-treat: no drop out	Method of Randomization: computer generated
Other comments: small sample size; details of visual analog scale for GERD symptoms not provided; no power calculations	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		X

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 37.5	N enrolled: 50
%Male: 72	N completed: 50
Race: nd	Dropouts/reasons:
BMI: wt 62.3 Kg	Follow-up period: 28 d
Comments:	

Results
Primary outcome(s): heartburn assessed by VAS (full range of this scale not reported) baseline 28 d Dexrabeprazole 64.8 ± 5.1 (SD) 30 ± 11.5 rabeprazole 64.4 ± 8.7 32 ± 9.5 regurgitation assessed by VAS (full range of this scale not reported) baseline 28 d Dexrabeprazole 64 ± 8.1 (SD) 24 ± 10 rabeprazole 57.6 ± 9.7 29.2 ± 11.9 Differences between groups not significant
Secondary outcome(s): Proportion of patients showed at lest 50% improvement of regurgitation scores (?28 d) Dexrabeprazole 96% rabeprazole 60% P<0.05 Patients with esophagitis baseline 28 d Dexrabeprazole 21/25 8/25 rabeprazole 23/25 15/25
Comments: statistical analysis incompletely reported

GERD data extraction form

Compliance:

Adverse Events: no adverse events observed in either group

Applicability: (narrow/wide): wide	Comments:

Author: Paulssen	**Yr:** 2008	**UI:** 18938771	**Questions addressed: 1,3**	**Extractor: DM**

Objective/Topic:
Safety of EndoCinch gastroplication in GERD patients

Study design:	**Country/Setting:**	**Funding:**
Cohort (?Prospective)	Norway/ Hospital	Nd

Interventions(s):	**Comparator(s):**
Bard EndoCinch endosuturing system	None

Primary outcome(s):	**Other outcome(s):**
1) Satisfaction score *1: no reduction in symptoms* *2: some reduction* *3: significant, yet not total reduction* *4: total absence of heartburn.* **2)** Heartburn severity score was calculated as symptom frequency (F) multiply by symptom severity (S) **3)** Regurgitation score *0: no regurgitation;* *1: mild; occasional episodes, mostly postprandial and usually predictable (1-2 days per week)* *2: moderate; frequent episodes (3-5 days per week), predictable by posture* *3: severe; daily episodes interfering with work and social activities (6-7 days per week)*	Acid suppression index: the number of normal daily doses of acid suppressants taken per week (DD/w).

Inclusion criteria:	**Exclusion criteria:**
symptomatic GORD confirmed at least once by findings of erosive oesophagitis at gastroscopy, or by positive 24-h ambulatory pH measurement.	**nd**
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):** Mean hiatal hernia length in cm (s.d.): 1.8 (1.19)
EGD (performed or not and results): Endoscopic grade oesophagitis, Savary-Miller No erosions 75 (63.0%) Grade I 28 (23.5%) Grade II 9 (7.6%) Grade III 1 (0.8%) Grade IV 5 (4.2%)	**Esophagitis/stricture/Barrett's:** See EGD
PH study (performed or not and results): 24-h oesophageal pH<4,% (s.d.) 11.7 (7.37)	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or	**Other:**

not and results): Lower oesophageal sphincter (LOS) measurements Mean LOS length in centimetres (s.d.): 3.5 (1.36) Mean LOS pressure, mmHg (s.d.) 9.7 (3.76)	

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: B/acceptable	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C/Poor
Comments: Significant loss to follow up

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46 y	**N enrolled: 119**
%Male: 62%	**N completed: 80 (20 offered a second procedure, and not included in the data extracted)**
Race:	**Dropouts/reasons:**
BMI: 27.6 kg/m^2	**Follow-up period: Mean 41 months (27-55 months)**
Comments:	

Results

Primary outcome(s):

	Baseline	**12 month**	**Long term follow up**
Heartburn severity score	21.4 (4.72)	13.4 (8.98) *	8.5 (8.43) *
Satisfaction score n (%)			
No improvement	37 (31.9)	30 (36.1)	40 (50)
Some improvement	33 (28.4)	17 (20.5)	17 (21.3)
Significant improvement	28 (24.1)	25 (30.1)	14 (17.5)
Full remission	18 (15.5)	11 (13.3)	9 (11.3)
Regurgitation score n (%)			
No regurgitation	44 (37)	43 (53.1)	53 (66.3)
Mild regurgitation	31 (26.1)	24 (29.6)	17 (21.3)
Moderate regurgitation	21 (17.6)	10 (12.3)	6 (7.5)
Severe regurgitation	23 (19.3)	4 (4.9)	4 (5)

* $p < 0.01$

Secondary outcome(s):

	Baseline	**12 month**	**Long term follow up**
PPI use (daily doses/wk)	8.7 (4.60)	5.0 (5.81) *	6.4 (6.23)

Comments:

Compliance:

Adverse Events:
Two patients (1.6%) acquired oesophageal fungal infections 1 patient (<1%) had to have one suture removed because of difficulty in swallowing

Applicability: (narrow/wide): narrow	**Comments: Small sample size**

GERD data extraction form

Author: Pessaux	Yr: 2005	UI:16230543	Questions addressed: 1,3	Extractor: SI

Objective/Topic: report on a cohort of patients who had laparoscopic anti-reflux surgery

Study design: retrospective multicenter cohort	Country/Setting: France	Funding: nd

Interventions(s): Nissen, Toupet partial posterior, partial anterior	Comparator(s): none

Primary outcome(s): Visick scores	Other outcome(s):

Inclusion criteria: unclear; 1593/2684 pts who had GERD and received laparoscopic antireflux surgery were eligible for 5 or more years of follow up; 1340 responded to notification of follow up; 1116 had complete medical examination; 224 completed only a phone survey	Exclusion criteria: unclear
Symptoms (describe): mean duration 6.8 y	Hiatal hernia (specify whether considered and size used for exclusion): 304/1340 (22.7%) had hiatal hernia
EGD (performed or not and results): 1049/1285 (81.6%) had esophagitis	Esophagitis/stricture/Barrett's:
PH study (performed or not and results): in 815/1340	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results): in 924/1340	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
no

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: study eligibility criteria incompletely reported; not all patients had actual medical examination follow up

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 49.3 ± 13.6	N enrolled: 2684
%Male: 61	N completed: 1340
Race: nd	Dropouts/reasons: nd
BMI: nd	Follow-up period: 7.1 ± 1.5 y
Comments:	

Results
Primary outcome(s): Visick grade Grade 1 878/1340 (65.5%) Grade 2 370/1340 (27.6%) Grade 3 59/1340 (4.4%) Grade 4 33/1340 (2.5%)
Secondary outcome(s): dysphagia 68/1340 (5.1%) gas bloat 101/1340 (7.5%) resume med for antireflux 122/1340 (9.1%) needed another surgical procedure 59/1340 (4.4%)
Comments:

Compliance:

GERD data extraction form

Adverse Events:

no death occurred

conversion rate to open anti-reflux surgery 112/1340 (8.4%)

postoperative complication 35/1340 (2.6%) see table 3 in paper

> 5yrs

Dysphagia 68/1340 (5.1%)

Gas bloat syndrome 101/1340 (7.5%)

*Intraoperative and 30-d postoperative complications

Complication	**No. of Patients (N = 1340)**
Intraoperative complications	
Bleeding	20
Gastric perforation	1
Esophageal perforation	4
Pneumothorax	4
Total (%)	**29** (2.1)
Postoperative complications	
Venous thrombosis or pulmonary embolism	2
Paraesophageal herniation	2
Pneumonia	11
Pleural effusion	5
Urinary infection	3
Persistent esogastric perforation	2
Wound infection	3
Hematoma	5
Abdominal abscess	1
Cardiac arrhythmia	1
Total (%)	**35** (2.6)

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Peura	Yr: 2009	UI: 18726153	Questions addressed: 1,3	Extractor: SI

Objective/Topic: compare lansoprazole with ranitidine in long-term maintenance of erosive esophagitis

Study design: RCT	Country/Setting: US	Funding: Takeda Inc.

Interventions(s): oral lansoprazole 15 mg daily for up to 1 y	Comparator(s): oral ranitidine 150 mg twice daily for up to 1 y

Primary outcome(s): time to recurrence of esophagitis	Other outcome(s): changes in the severity of symptoms, time to recurrence of heartburn, improvements in QoL

Inclusion criteria: at least 18 y/o; endoscopically proven erosive esophagitis (Grade ≥2 using the modified Hetzel–Dent grading scale) without coexisting duodenal ulcer and/or gastric ulcer ≥3 mm in diameter; patients had to have endoscopically proven healed erosive esophagitis (Grade 0 or 1) at the end of an 8-week acute treatment period	Exclusion criteria: required more than occasional use (≤10 days/month) of NSAIDs; pts who received a PPI within 4 weeks prior to starting the acute phase of the study were not permitted to enroll
Symptoms (describe): before acute treatment phase 68-77% day heartburn; 43-56% night heartburn before randomization 91% asymptomatic	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): y before randomization: acute treatment phase grade 2 58.7% grade 3 33% grade 4 8.3% either grade 0 or 1 at randomization	Esophagitis/stricture/Barrett's:
pH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): see study protocol
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) y

Quality Assessment for RCTs: B/acceptable	
Blinding: y	Allocation concealment: n
Intention-to-treat: yes but primary analysis was in evaluable patients	Method of Randomization: nd

GERD data extraction form

Other comments:

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 50	N enrolled: 206
%Male: 67.5	N completed: 195 (experienced recurrence or completed 1 y of therapy); 177 evaluable (no protocol violation)
Race: 90% white; 7% black	Dropouts/reasons: nd
BMI: 29	Follow-up period: up to 1 y
Comments:	

Results
Primary outcome(s): evaluable patients analysis healing rate at 1 y lansoprazole 67% (95%CI 56.4-77.6) ranitidine 13% (95%CI 4.4-22.5) median time to recurrence lansoprazole 92 d ranitidine 36 d
Secondary outcome(s): remaining asymptomatic at 1 y lansoprazole 56% (95%CI 56.4-77.6) ranitidine 15% (95%CI 4.4-22.5) Participants >65 y and participants with higher baseline esophagitis were more likely to recur in logistic regression analysis (P=0.01 and 0.02, respectively).
Comments:

Compliance:
Patients treated with lansoprazole remained on maintenance therapy for significantly longer (mean 236.9 days) than patients treated with ranitidine (mean 88.7 days; P B 0.05).

GERD data extraction form

Adverse Events:
treatment- emergent adverse events
lansoprazole 71%
ranitidine 55% P=0.02

overall incidence of adverse events possibly or probably related to treatment
lansoprazole 20%
ranitidine 12% P=NS

headache
lansoprazole 5%
ranitidine 6%

abdominal pain
lansoprazole 5%

serious adverse events not related to study meds
lansoprazole 9
ranitidine 1

discontinued treatment due to adverse events (not related to study drug per investigator)
lansoprazole 2
ranitidine 0

No clinically significant trends were observed in any laboratory parameters.

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Pilotto	Yr: 2007	UI: 17724802	Questions addressed: 1, 2, 3	Extractor: WY

Objective/Topic:
Compare efficacy and tolerability of four PPIs (omeprazole, lansoprazole, pantoprazole, rabeprazole) in elderly patients with esophagitis

Study design:	Country/Setting:	
RCT	Italy, single center	**Funding:** "Ministero della Salute", IRCCS Research Program, Ricerca Corrente 2006-2008, Linea n. 2 "Malattie di rilevanza sociale"

Interventions(s):	Comparator(s):
Omeprazole 20 mg once daily Lansoprazole 30 mg once daily Pantoprazole 40 mg once daily Rabeprazole 20 mg once daily All taken right before breakfast, for 2 months	No real comparator; comparisons were done among the 4 medical treatments

Primary outcome(s):	Other outcome(s):
Rate of healing	GERD symptoms Side effects

Inclusion criteria:	Exclusion criteria:
65 years old or older Had esophagitis grade I to IV, per endoscopy, according to the Savary-Miller classification	history of Zollinger-Ellison syndrome, pyloric stenosis, previous surgery of the esophagus and/or GI tract (except for appendectomy and cholecystectomy), GI malignancy, use of antacids, sucralfate, prokinetics, H2-blockers, and/or PPIs for more than 7 days in the 4 weeks prior to the study
Symptoms (describe): no	Hiatal hernia (specify whether considered and size used for exclusion): 194 pts (60.6%)
EGD (performed or not and results): Yes Grade 1: 96 pts (30%) Grade II: 152 pts (47.5%) Grade III-IV: 72 pts (22.5%)	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other: H pylori infection: 202 pts (66%)

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: B/acceptable

GERD data extraction form

Blinding: no	Allocation concealment: no
Intention-to-treat: yes (both PP and ITT analyses)	Method of Randomization: computer-generated
Other comments: no blinding nor allocation concealment	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 77.4 ± 7.9 yrs (range: 65 - 93)	N enrolled: 320
%Male: 48.8%	N completed: 301
Race: not reported	Dropouts/reasons: adverse events (n=2), low compliance (n=11), refused to have endoscopy post-treatment period (n=6)
BMI: not reported	Follow-up period: 2 months
Comments:	

Results

Primary outcome(s):
Healing rates

Treatment group	PP		ITT	
	% of pts healed	95% CI	% of pts healed	95% CI
Omeprazole (n=80)	81.0 (out of 74 pts)	72.0-89.9	75.0	65.0-84.0
Lansoprazole (n=80)	90.7 (out of 75 pts)	84.1-97.2	85.0	77.0-92.8
Pantoprazole (n=80)	93.5 (out of 77 pts)	87.9-99.0	90.01	83.4-96.5
Rabeprazole (n=80)	94.6 (out of 75 pts)	89.4-99.7	88.82	81.5-95.6

Pantoprazole *vs* Omeprazole: PP analysis: $P = 0.039$, ITT analysis $P = 0.022$
Rabeprazole *vs* Omeprazole: PP analysis: $P = 0.022$, ITT analysis $P = 0.040$

Secondary outcome(s):
Healing rates per esophagitis grade (PP analysis, number of pts healed/total number of pts, %)

Treatment group	Grade I	Grade II	Grade III-IV
Omeprazole	27/33, 81.8%	18/22, 81.8%	15/19, 78.9%
Lansoprazole	25/25, 100%	28/29, 96.5%	15/21, 71.4%
Pantoprazole	20/20, 100%	36/40, 90%	46/48, 95.8%
Rabeprazole	14/14, 100%	46/48, 95.8%	11/13, 84.6%

GERD symptoms disappearance, % of pts

Treatment group	Heartburn	Acid regurgitation	Epigastric pain	Dysphagia	Vomiting	Anemia
Omeprazole	86.9% ($P < 0.05$ Omeprazole *vs* Pantoprazole and Omeprazole *vs* Rabeprazole)	100%	95%	100%	100%	100%
Lansoprazole	82.4% (P=0.0001 Lansoprazole *vs* Pantoprazole, P=0.005 Lansoprazole *vs* Rabeprazole)	75% (P= 0.0001 Lansoprazole *vs* Omeprazole; P<0.05 Lansoprazole *vs* Pantoprazole, Lansoprazole *vs* Rabeprazole)	82.6% (P<0.05 Lansoprazole *vs* Omeprazole & Lansoprazole *vs* Pantoprazole; P=0.0001 Lansoprazole *vs*	100%	100%	100%

			Rabeprazole)			
Pantoprazole	100%	92.2%	95.2%	100%	100%	100%
Rabeprazole	100%	90.1%	100%	100%	100%	100%

Comments:

Treatment/Comparison:	Omeprazole 20 mg once daily Lansoprazole 30 mg once daily Pantoprazole 40 mg once daily Rabeprazole 20 mg once daily					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Healing rates
			Off PPIs	Off all meds		
Esophagitis (any severity)						lower healing rate was observed in patients with grade 1 or 2 esophagitis treated with omeprazole than other PPIs
H pylori positive or negative						No effect

Compliance:
NA

Adverse Events:
Adverse events occurred in 4 pts, among which 2 discontinued the study. Adverse events included urticaria, glossitis, nausea, and headache.

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Pizza	**Yr: 2007; 2008**	**UI: 17278197; 18197944**	**Questions addressed: KQ2; KQ3**	**Extractor: MC**

Objective/Topic:
2007 article aimed to review the outcome of young and elderly patients undergoing laparoscopic antireflux surgery for the treatment of GERD;
2008 article aimed to evaluate whether esophageal dysmotility can influence the outcome of laparoscopic total fundoplication

Study design:	**Country/Setting:**	**Funding:**
Retrospective study (the authors stated this study was prospective because patients' data were collected prospectively)	Italy	No data

Interventions(s):
Nissen-Rossetti fundoplication

Comparator(s):
- Age ≥65 vs. <65 years old
- Comparisons between groups that were based on the character of esophageal peristalsis:
  - Group A: patients with impaired esophageal motility (defined as a mean amplitude < 30 mmHg of swallow induced contractions 5 cm proximal to the LES or more than 30% of peristaltic waves in the distal esophagus were simultaneous in response to voluntary deglutition)
  - Group B: patients with normal esophageal motility (normal amplitude, duration, and velocity of peristaltic waves)
  - Group C: patients with motor dysfunction intermediate between the other two groups (defined as a mean amplitude 30–59 mmHg of swallow induced contractions 5 cm proximal to the LES or less than 30% of peristaltic waves in the distal esophagus were simultaneous in response to voluntary deglutition).

Primary outcome(s):
Changes in symptom scores

Other outcome(s):
Adverse events

Inclusion criteria:
Consecutive patients with GERD underwent laparoscopic Nissen fundoplication.

Exclusion criteria:
none

Symptoms (describe):

	≥65 yr old	(%)	<65 yr old	(%)
Heartburn	44/65	(67.7)	298/355	(83.9)
Acid regurgitation	39/65	(60.0)	277/355	(78.0)
Solid food dysphagia	22/65	(33.80	27/355	(7.6)
Chest pain	18/65	(27.7)	51/355	(14.4)
Respiratory complication (chronic cough, sleep apnoea, asthma, laryngitis)	27/65	(41.5)	19/355	(5.4)

Hiatal hernia (specify whether considered and size used for exclusion):
≥65 group: 58/65 (89.2%)
<65 group: 253/355 (71.3%)
P<0.05 between groups

All symptoms were significantly different between groups	
EGD (performed or not and results): No data	**Esophagitis/stricture/Barrett's:** Barrett's – ≥65 group: 5/65 (7.7%) <65 group: 10/355 (2.8%) P<0.05 between groups
PH study (performed or not and results): Mean % time pH<4: ≥65 group: 9.1% <65 group: 8.2%	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** All patients were off peptic medication for 30 days prior operation.
Esophageal manometric studies (performed or not and results): LES (mmHg) was about 12 in both groups at baseline	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Not applicable

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: retrospective design; for pH outcomes, only 50% of patients provided results.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
	X	

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 42.8 (range 12-80)	**N enrolled: 420** For age comparison: ≥65 group (n=65); <65 group (n=355) For esophageal motility comparison: group A (n=123), group B (n=217); group C (n=80)
%Male: ≥65 group: 40 <65 group: 37	**N completed: 400 (age comparison); 406 (esophageal motility comparison)** For age comparison: ≥65 group (n=62); <65 group (n=338) For esophageal motility comparison: group A (n=118), group B (n=212); group C (n=76)
Race: no data	**Dropouts/reasons:** two patients in ≥65 group died for reason not related to surgery. No reasons for dropout were reported for others.
Mean weight (kg): ≥65 group: 64.4 <65 group: 65.3	**Follow-up period:** ≥65 group: mean 60 mo (range 6-95) <65 group: mean 83.2 mo (range 6-141) Group A: mean 80.1 mo (6-136) Group B: mean 81.9 (6-141) Group C: mean 81.5 (6-121)
Comments: American Society of Anaesthesiologists (ASA) scores were significantly different between age groups (P<0.05): ≥65 group: 2.2 <65 group: 1.82	

GERD data extraction form

Results						
Treatment/Comparison:	**Nissen-Rossetti fundoplication**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Age (≥65 vs. <65)	No effect	No effect (based on 50% patients at 1-year follow-up)				
Esophageal motility (impaired, normal or intermediate dysfunction)	No effect	No effect (based on 68% patients at 1-year follow-up)				
Primary outcome(s): Both groups showed significant improvement in clinical symptom score. At 6 mo, persisting postoperative dysphagia (DeMeester score 2-3) leading to > 15% of weight loss was observed in 11 (3.3%) of 338 patients in <65 yr old group, 2 patients in the group with preoperative impaired peristalsis and 9 in the group with normal esophageal Motility. In ≥65 yr old group, persisting postoperative dysphagia was relieved in 2 (3.2%) of 62 patients, both in group with normal preoperative esophageal peristalsis.						
Secondary outcome(s):						
Comments:						

Compliance: No data

Adverse Events:
Perioperative results
Mortality, 0/420 (0%)
Mucosal tear, 1/420 (0.2%)
Bleeding, 3/420 (0.7%)

2/65 (3%) patients in ≥65 group died.

Postoperative side effects	≥65 yr old	(%)	<65 yr old	(%)	Total (%)
Dysphagia	2/62	(3.2%) [A]	11/338	(3.3%) [B]	13/400 (3.3%)
Heartburn	2/62	(3.2%) [C]	12/338	(3.6%) [D]	14/400 (3.5%)
Hyperflautolence	1/62	(1.6%)	6/338	(1.8%)	7/400 (1.8%)
Early satiety	2/62	(3.2%)	9/338	(2.7%)	11/400 (2.8%)
Bloating	1/62	(1.6%)	3/338	(0.9%)	4/400 (1.0%)
Chest pain	0		2/338	(0.6%)	0/400 (0%)

A. 2 dilation; B. 5 dilation, 6 laparoscopic re-fundoplication; C. 2 reassumed peptic medications; D. 8 reassumed peptic medications, 4 laparoscopic refundoplication.

Postoperative side effects	Group A	Group B	Group C
Dysphagia	4/123	6/217	3/80
Heartburn	4/123	7/217	3/80
Hyperflautolence	2/123	3/217	2/80
Early satiety	5/123	7/217	2/80
Bloating	3/123	4/217	2/80
Chest pain	0	2/217	0

Applicability: (narrow/wide): wide	**Comments:**

First author: Ravi	**Year:** 2005	**UI: 16105534**

Modifying Factor(s): dysmotility defined by 30% wet swallows with any: distal wave <30 mm Hg; simultaneous contractions with amplitudes <30 mm Hg, wave not traversed the entire length of the distal esophagus, or absent peristalsis

Study design: retrospective comparative **Follow up duration:** 6 mo	**Country: Ireland** **Multicenter:** no	**Funding:** nd

Interventions(s): open and laparoscopic Rossetti Nissen fundoplication

Primary outcome(s): symptom outcomes, QOL, manometry and pH	**Other outcome(s):** (if reported)

Baseline characteristics:
GERD definition for the population included: not defined
Age: median 45 (range 16-74 y)
Gender: 44% male
Race: (if available)
Weight: median 73.2 Kg
Severity of symptoms:
Duration of symptoms: median 3 y (range 0.5 to 5)
Frequency of symptoms:
Type of medications: PPIs or H2RAs for ≥6 mo
Acid reflux (by pH study):
Abnormal manometry study:
Esophagitis by endoscopy: 51% no Esophagitis; A (24%); B (8%); C (12%); D (4%)

Significant baseline differences between GroupA and GroupB (and GroupC… etc)

Symptoms:
EGD: all grade D in dysmotility group
EMS: amplitude is higher (50 mm) in normal vs. dysmotility (23 mm)
PH study: median acid reflux score higher in dysmotility (53 vs. 36, P<0.001)
Hiatal hernia:
Meds used in the groups:

Other:

N enrolled per group:	dysmotility 38	normal motility 60	GroupC: (if any)
N completed per group:	38	60	GroupC: (if any)

Outcomes (as reported in the Results)	**Results**		
	dysmotility	normal motility	Difference between groups
Dysphagia, regurgitation, heartburn frequency			NS (see table 1 in paper)
QOL per QOL in Reflux and dyspepsia questionnaire			NS (see table 3 in paper)
DeMeester Score	53 (preop) to 4.2 (postop)	36 (preop) to 2.5 (postop)	NS

LES	6 (preop) to 12.5 (postop)	6 (preop) to 15 (postop)	

Adverse Events: 4/60 patients with normal motility developed ineffective motility after surgery (if reported, please add proportion of patients per adverse event; also separate to minor or major adverse events)
Dysmotility: 22/98 (22.4%) (Normal mortility group: 4/60; Dysmotility group: 18/38)

Quality Assessment:
Description of the biological plausibility for the hypothesis to be tested: yes
Description of inclusion /exclusion criteria and rationale: yes
Documentation of how data were collected and analyzed (eg, blinding): no
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): no
Participant drop-out percentage (>20%?): not applicable
Description of statistical methods in sufficient detail to be replicated: yes
Overall grade: C

Comments: unclear the proportion of eligible controls enrolled in the study

ND: no data

GERD data extraction form

Author: Repici	Yr: 2010	UI: 19902310	Questions addressed: 1,3	Extractor: WY

Objective/Topic:
To evaluate short and mid term outcomes of endoluminal fundoplication with EsophyX

Study design:	Country/Setting:	Funding:
cohort	Italy	nd

Interventions(s):	Comparator(s):
EsophyX	NA

Primary outcome(s):	Other outcome(s):
Esophagitis status	PPI use, LES pressure

Inclusion criteria:	Exclusion criteria:
With esophagitis >6 months, need long term acid suppressive therapy	
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used for exclusion):** <3cm: 55%
EGD (performed or not and results): No esophagitis or LA grade A: 75% LA grade B or C: 25%	**Esophagitis/stricture/Barrett's:**
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results):	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: small sample size

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:48 (26-68)	**N enrolled: 20**
%Male: 75	**N completed: 15**
Race: nd	**Dropouts/reasons:**

BMI: nd	Follow-up period: 12 mo
Comments:	

Results
Primary outcome(s): At 12 months, Improved GERD-HRQL of ≥50%: 73% of patients (11/15)
Secondary outcome(s): At 12 months, off PPI 47% of patients (7/15) LES pressure: no significant change between 12 months and baseline Total reflux esophageal exposures: no significant change between 12 months and baseline Acid reflux esophageal exposures: no significant change between 12 months and baseline
Comments:

Compliance:

Adverse Events: **Hematemoesis: 2 pts**

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Reymunde	Yr: 2007	UI: 17321231	Questions addressed: 1	Extractor: WY

Objective/Topic:
to evaluate the effect of the Stretta procedure for GERD patients on symptom control, quality of life, and medication use

Study design:	Country/Setting:	Funding:
Case series	Puerto Rico	nd

Interventions(s):	Comparator(s):
Stretta procedure	NA

Primary outcome(s):	Other outcome(s):
health-related QOL score for heartburn and regurgitation, and GERD symptoms index	dose and the frequency of medication use

Inclusion criteria:	Exclusion criteria:
Responsive to PPI therapy, confirmed GERD per ambulatory esophageal pH testing or endoscopy finding of erosive esophagitis	Haital hernia >3cm, erosive esophagitis >LA grade B, long segment Barrett's esophagus, LES pressure <5 mmHg, aperistalsis, pregnancy, poor surgical risks, severe dysphagia, previous esophageal or gastric surgery, collagen vascular disease, significant untreated medical problems
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results): yes	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B
Comments: Authors called this study "case-series". It's not much different from other surgical cohort studies.

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: nd	N enrolled: 83
%Male:78	N completed:80
Race: nd	Dropouts/reasons: 3 loss to followup
BMI: nd	Follow-up period: 4 yr
Comments:	

Results

Primary outcome(s):
GERD symptoms

	Baseline	4 yr	P (baseline vs. 4 yr)
Mean GERD symptom score	2.7	0.6	nd
Complete resolution of GERD symptoms (symptom score=0)	NA	68.67% of pts	<0.001
Mean QOL score	2.4	4.3	<0.001

Secondary outcome(s):
69 patients (86.25%) reduced their medications to either antacid as necessary or no medications use.

	Baseline	4 yr	P (baseline vs. 4 yr)
% of pts on GERD medication	100	13.75	<0.001
LA classification grade A	60 out of 83 pts (83.3%)	0 out of 73 pts	nd

Comments:

Compliance:
NA

Adverse Events:
Nd

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Rice	Yr: 2006	UI: 16549692	Questions addressed: 1,3	Extractor: JHL

Objective/Topic: Laparoscopic Anterior 180º Partial Fundoplication

Study design: Prospective surgical cohort	Country/Setting: Australia	Funding: ND

Interventions(s): Laparoscopic Anterior 180º Partial Fundoplication	Comparator(s):

Primary outcome(s): • Overall satisfaction • Symptoms of heartburn and dysphagia • Adverse outcomes	Other outcome(s):

Inclusion criteria: Patients underwent surgery between August 1, 1993, and November 30, 1999, primarily at the Royal Adelaide Hospital and associated private hospitals in Adelaide, Australia.	Exclusion criteria: ND
Symptoms (describe): ND	Hiatal hernia (specify whether considered and size used for exclusion): ND
EGD (performed or not and results): Not performed	Esophagitis/stricture/Barrett's:ND
PH study (performed or not and results): Not performed	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND
Esophageal manometric studies (performed or not and results): Performed, no results	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: No information about the basic characteristics of patients

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
C/Poor (ND)		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: ND	N enrolled: 117
%Male: ND	N completed: 100

GERD data extraction form

Race: ND	**Dropouts/reasons: n=17** • 4 patients not be located at the time of thepresent study • "12 (11%) died during followup…. None of the deaths were linked to the laparoscopic procedure. The causes of death: carcinoma (5 patients [3 colonic, 2 lung]), myocardial infarction (1 patient), cerebrovascular accident (1 patient), bicycle accident (1 patient), suicide (1 patient), "old age" (2 patients), and complications of an open esophageal mucosectomy procedure for severe dysplasia in Barrett esophagus (1 patient)." • 1 patient underwent esophagectomy
BMI: ND	**Follow-up period:** 5-11 years (mean, 6.4 years)
Comments:	

Results
Primary outcome(s): • Heartburn using the analog scale "46 patients had a postoperative score of 0 (no heartburn); 34 had a score of 1, 2, or 3 (occasional minor episodes of heartburn); 11 reported a score of 4 to 6 (moderate heartburn symptoms; and 9 gave a score of 7 or higher (significant troublesome heartburn). Most patients reported a moderate-to-severe heartburn score before surgery" • Dysphagia to liquids and solids using the analog scale "At late postoperative follow-up, patients were less likely to describe dysphagia to liquids and solids compared with preoperative scores" • Overall satisfaction "The mean overall satisfaction score was 8.4 (median score, 9). Forty-five reported a satisfaction score of 10; 35, a score of 7 to 9; 17, a score of 4 to 6; and 3, a score of 3 or less." • 22 patients taking acid-suppressing medications (PPI, 12 patients; H2RA, 10 patients)
Secondary outcome(s):
Comments: No statistical test between before surgery and at late follow-up

Compliance: NA

Adverse Events:
• Death: 12/113 (11%)
• Further surgical procedures were undertaken in 12/113 patients (11%)
  o Two of these were performed immediately using a laparoscopic approach, 2/113 (1.8%)
  o Eight procedures (7%) were performed for recurrent reflux between 8 months and 6 years (median, 4 years) after the original fundoplication.
  o 2 patients: early postoperative dysphagia sufficient to require endoscopic dilatation

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Riedl	Yr: 2009	UI: 19370381	Questions addressed: 2	Extractor: SI

Objective/Topic: to study the impact of preoperative LES on LARS outcome

Study design: retrospective	Country/Setting: Austria	Funding: nd

Interventions(s): laparoscopic antireflux surgery	Comparator(s):

Primary outcome(s): GERD symptoms	Other outcome(s):

Inclusion criteria: Pts with GERD who had laparoscopic Nissen fundoplication (for long history of GERD, complications of GERD, impaired QoL despite medical treatment, or patient preference) who had pre and 1 yr postoperative follow up data	Exclusion criteria: nd
Symptoms (describe): 96.9% had acid reflux; 68% had regurgitation; 13.4% had dysphagia	Hiatal hernia (specify whether considered and size used for exclusion): 95% had hiatal hernia; size was not used for exclusion
EGD (performed or not and results): yes 56% had esophagitis	Esophagitis/stricture/Barrett's:
pH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): all pts were on long-term PPI (40 mg esomeprazole daily)
Esophageal manometric studies (performed or not and results): yes mean DeMeester score 35.02 ± 28.56	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: retrospective, potential selection bias, no power calculation, details of analysis not presented

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 50.3 ± 11.5	N enrolled: 395
%Male: 62	N completed: 351
Race: nd	Dropouts/reasons:
BMI: nd	Follow-up period: 1 yr
Comments:	

Results

Primary outcome(s): GERD symptoms stratified by LES findings

		Group 1 (intraabdominal length <1cm, pressure <8 mm Hg)	Group 2 (<8 mm Hg)	Group 3 (<1 cm)	Group 4 (normal)
Acid reflux	Pre	98.5%	96.9%	95.5%	94.1%
	post	9.2%	7.7%	13.6%	16.2%
Regurgitation	Pre	71%	65.4%	59.1%	69.1%
	post	1.5%	4.6%	4.5%	4.4%
Dysphagia	Pre	13%	10.8%	4.5%	8.8%
	post	7.6%	7.7%	4.5%	8.8%

no significant differences between groups in treatment response, actual P values not reported

Secondary outcome(s):

		Group 1	Group 2	Group 3	Group 4
esophagitis	Pre	62.6%	53.8%	72.7%	44.1%
	post	9.9%	3.8%	4.5%	4.4%
DeMeester score	Pre	38.99±27.78	34.98±30.62	29.42±21.05	31.78±29.93
	post	9.94±14.14	8.5±11.73	8.59±12.23	9.60±16.20
GIOLI	Pre	92.91±18.92	94.22±18.33	94.45±19.77	95.69±15.59
	post	117.89±15.33	119.14±15.14	118.38±15.14	123.81±12.93

no significant differences between groups in treatment response, actual P values not reported

Treatment/Comparison:	intact vs. defective LES					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
LES competence	No effect	No effect			no effect	
LES pressure	No effect	No effect			no effect	
Comments:						

GERD data extraction form

Compliance: nd

Adverse Events: nd

Applicability: (narrow/wide): narrow	Comments:

Author: Rosenthal	Yr: 2006	UI: 17243869	Questions addressed: 3	Extractor: DM

Objective/Topic:
Assess disease-specific symptoms and quality of life of all patients treated by laparoscopic fundoplication

Study design:	Country/Setting:	Funding:
Cohort	Switzerland/Hospital	Nd

Interventions(s):	Comparator(s):
Anti-reflux surgery (Nissen or Toupet fundoplication)	None

Primary outcome(s):	Other outcome(s):
Gastrointestinal quality of life index (GIQLI) [German]	surgery-related questions disease-specific questions

Inclusion criteria:	Exclusion criteria:
All patients undergoing laparoscopic fundoplication between Jan 1992 & Dec 2002	
Symptoms (describe): Heartburn (89%) Regurgitation (83%) Pain (39%) Nausea and vomitus (31%) Dysphagia (20%)	**Hiatal hernia (specify whether considered and size used for exclusion):** Prevalence 92%.
EGD (performed or not and results): erosive esophagitis 77% of the patients Barrett's esophagus in 16%,	**Esophagitis/stricture/Barrett's:** See EGD
PH study (performed or not and results): In 47 patients (25%) – All showed pathologic pH-metric measurements with prolonged overall acid exposure time.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Under conservative treatment, symptoms resolved in 18% and improved in 56% of patients, while they remained unchanged in 26%.
Esophageal manometric studies (performed or not and results): Hypotonic lower esophageal sphincter : 79% nonspecific alterations in tubular esophageal motility: 24% Severe motility disturbance: 2%.	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C/Poor
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 51 (range, 22–88 years)	**N enrolled: 186**
%Male: 64.5	**N completed: 143**
Race:	**Dropouts/reasons: Did not respond to mailed questionnaire**
BMI: mean 27 (range, 20–41)	**Follow-up period: 4.7 years (range, 0.1–10.1 years)**
Comments:	

Results

Primary outcome(s):

The average GIQLI score was 115 (range: 54–144)

Secondary outcome(s):

Symptom	Preoperative (%)	Postoperative (%)
Heartburn	89	24
Regurgitation	83	23
Pain	39	49
Nausea and vomitus	31	25
Dysphagia	20	38

37% of patients complained of new symptoms postoperatively, and 21% occasionally took antireflux medication.

Comments:

Compliance:

Adverse Events:
No deaths
Local complications: 5/186 (2.7%)
Systemic complications occurred in 14/186 (7.5%)

- Medication-induced – 4 (2.2%)
- Urinary tract infection - 3 (1.6%)
- Pulmonary - 3 (1.6%)
- Neuropsychiatric – 2 (1.1%)
- Cardiac – 1 (0.5%)
- Endocrinological – 1 (0.5%)

Reoperations: 6 (3%)

- Refundoplication for telescoping – 2(1%)
- Repositioning and fixation of a paraesophageal hernia – 2(1%)
- Conversion to a Toupet due to dysphagia and/or severe gas bloating symptoms – 2(1%)

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Salminen	**Yr:** 2006	**UI:** 16921296	**Questions addressed: 3**	**Extractor:** JHL

Objective/Topic: Late Subjective Results and Symptomatic Outcome After Laparoscopic Fundoplication

Study design: Surgical cohort	**Country/Setting:** Finland	**Funding:** ND

Interventions(s): Laparoscopic Nissen Fundoplication	**Comparator(s):**

Primary outcome(s): • Subjective symptomatic outcome	**Other outcome(s):** • Subjective evaluation of the surgical result • Use of medication

Inclusion criteria: "Between January 1996 and December 2001, 468 consecutive patients underwent laparoscopic Nissen fundoplication for gastro-esophageal reflux disease of which 464 patients were available for long-term follow-up.."	**Exclusion criteria:** "If the endoscopy showed persistent esophagitis and the patient had no dysphagia; these preoperative investigations were not necessarily performed."
Symptoms (describe): ND	**Hiatal hernia (specify whether considered and size used for exclusion):** ND
EGD (performed or not and results): Performed, ND	**Esophagitis/stricture/Barrett's:** ND
PH study (performed or not and results): Performed, ND	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** ND
Esophageal manometric studies (performed or not and results): Performed, ND	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: No specific information on the baseline characteristics of patients, no statistical test between pre and post-operative assessment

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A/rigorous (endoscopy)		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 53y	**N enrolled:** 468
%Male: 54%	**N completed:** 464
Race: ND	**Dropouts/reasons:** n=4 (died of unrelated causes)
BMI: ND	**Follow-up period:** 51 months (range 20 to 91 mo)
Comments:	

Results

Primary outcome(s):

- Subjective symptomatic outcome 2 to 8 years after surgery

	Absent or Mild symptoms	Moderate symptoms	Severe symptoms
Heartburm/regurgitation/upper abdominal pain	77.1%	10.0%	12.9%
Dysphagia	78.0%	10.7%	11.3%
Bloating/flatulence	27.4%	20.0%	52.6%

Secondary outcome(s):

- Evaluation of the surgical result
  - Excellent (37.2%), Good (32.0%), Satisfactory (20.2%), Fair (5.5%), Poor (5.1%)
- Use of medication, 30% (n=132) taking acid suppression medications postoperatively
  - n=82, proton pump inhinbitors
  - n=13, histamine receptor antagonists
  - n=10, a variety of medications, mainly antacids
  - n=27, not define the used medication

Comments: No information on outcomes before the surgery

Compliance: NA

Adverse Events:
4 patients – death of causes unrelated to surgery
10 patients – converted to open surgery
47 patients – difficulties with swallowing
9 patients – reoperation

Subjective symptomatic outcome 2 to 8 years after surgery

	Absent or Mild symptoms	Moderate symptoms	Severe symptoms
Dysphagia	78.0%	10.7% (n=47)	11.3% (n=50)
Bloating/flatulence	27.4%	20.0% (n=88)	52.6% (n=232)

Immediate postoperative complications in 20 cases (4.5%)

	No. of patients
Bleeding	8
Urinary retention	4
Pneumonia	1
Fever of unknown origin	4
Port sign pain	1
Neural injury of the diaphragm	1
Wrap herniation (early)	1

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Salminen	Yr: 2007	UI: 17667497	Questions addressed: 1;3	Extractor: WY

Objective/Topic:
Compare laparoscopic vs. conventional Nissen fundoplication

Study design:	Country/Setting:	Funding:
RCT	Finland	Turku University Central Hospital research grant

Interventions(s):	Comparator(s):
laparoscopic Nissen fundoplication	conventional Nissen fundoplication

Primary outcome(s):	Other outcome(s):
Esophagitis occurrence	Esophagitis severity Presence of Barrett esophagus, hiatal hernia, and the endoscopic appearance of the plication and lower esophageal sphincter Symptom severity on heartburn, regurgitation and upper abdominal pain, dysphagia, and bloating or increased flatulence Rate of reoperation

Inclusion criteria:	Exclusion criteria:
Recruitment methods were described in another publication	Recruitment methods were described in another publication
Symptoms (describe): no	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): yes	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other: n/a

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Recruitment methods were described in another publication; Assumes yes.

Quality Assessment for RCTs: C/Poor	
Blinding: no	Allocation concealment: no
Intention-to-treat: yes (both ITT and PP analyses done)	Method of Randomization: not reported
Other comments: inconsistency in data reporting. See comments in results section	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 60	N randomized: 110
% male: 58.1%	N analyzed in ITT analysis: 86 pts (including 4 pts in laparoscopic group that converted to open group) N analyzed in PP analysis: 82 pts (73 endoscopies f/u, 9 phone interview f/u only)
Race: not reported	Dropouts/reasons: 16 death unrelated to treatment, 1 reoperated, 3 other medical condition (ovarian cancer, renal cancer, severe dementia), 4 lost-to-follow-up
BMI: not reported	Follow-up period: 11 years
Comments:	

Results

Primary outcome(s):
Presence of esophagitis at follow-up
Open group (n=35): 2 pts (5.7%)
Laparoscopic group (n=38): 2 pts (5.3%)
P=1.000
All of these pts with esophagitis were at grade A.

Secondary outcome(s):

	Open group (n=35)	Laparoscopic group (n=38)	P value
Barrett's esophagus	2 pts, (5.7%) (of which 1 is new-onset)	6 pts, (15.8%) (of which 4 is new-onset)	0.2643
LES evaluated loose	9 pts, (25.7%)	2 pts, (5.3%)	0.0080
Esophageal stricture	1 pts, (2.9%)	0 pt	NA
Hiatal hernia	14 pts, (37.1%)	10 pts, (26.3%)	0.4498
Partial plication disruption	10 pts, (28.6%)	4 pts, (10.5%)	0.0296
Total plication disruption	4 pts, (11.4%)	1 pt, (2.6%)	NA
Ventricular ulcer	2 pts, (5.7%)	2 pts, (5.3%)	NA
Duodenal ulcer	0 pt	1 pt, (2.6%)	NA
Incisional hernias	10 pts, (28.6%)	0 pt	<0.001
Reoperation	3 pts (8.57%) with refundoplication; 1 due to dysphagia from distorted plication, 2 due to disrupted plication	3 pts, (7.9%) 2 had dilatations due to dysphagia, 1 had gastrojejunostomy due ventricle retention	NA

All pts with loose LES had disrupted plication.
H pylori positive: 14 pts
Incisional hernia in all pts was small and asymptomatic.

Symptoms, rated on a scale of 1 (none), 2 (mild), 3 (moderate), 4 (difficult), and 5 (having severe symptoms)*

	Among all pts (n=73)	P, comparing between open and laparoscopic groups
Heartburn or regurgitation (see comments)	None or mild: 60 pts, 73.2% Moderate: 8 pts, 9.8% Difficult: 14 pts, 17%	0.6241
Dysphagia	None: 68 pts, 83% Mild or moderate: 11pts, 13.4% Difficult or severe: 3 pts, 3.6%	0.0682
Bloating and flatulence	None or mild: 29 pts, 35.4% Moderate: 16 pts, 19.5%	0.1734

GERD data extraction form

Difficult or severe: 37 pts, 45.1%

* group specific percentages were presented in figures, not text or tables with numbers

Patient satisfaction, ask pts to state if they would still prefer surgery to medication:

	Open group (n=35)	Laparoscopic group (n=38)	P value
Would still choose surgery	28 pts, 73.7%	36pts, 81.8%	NA
Would abstain from surgery	3pts, 7.9%	5pts, 11.4%	NA
Unsure	7pts, 18.4%	3, 6.8%	NA

Use of acid suppression medication

	Open group (n=35)	Laparoscopic group (n=38)	P value
Any acid suppressant	15 pts, 39.5%	18pts, 40.9%	1.000
Use PPIs	5 pts, 33.3%	5 pts, 26.3%	0.4027

Comments:
unclear which is primary outcome
There appears to be inconsistencies in data presented for heartburn and regurgitation severity. According to figure 3, there are pts with severe (score 5) heartburn and regurgitation, but in text, the % of pts with none to difficult (score 1-4) added up to 100%.

Compliance:
NA

Adverse Events:

	Among all pts (n=73)
Upper abdominal symptoms	None or mild: 60 pts, 73.2% Moderate: 8 pts, 9.8% Difficult: 14pts, 17.0%
Dysphagia	None: 68 pts, 83% Mild or moderate: 11pts, 13.4% Difficult or severe: 3 pts, 3.6%
Bloating and flatulence	None or mild: 29 pts, 35.4% Moderate: 16 pts, 19.5% Difficult or severe: 37 pts, 45.1%

	Open group (n=35)	Laparoscopic group (n=38)
Reoperation	3 pts (8.57%) with refundoplication; 1 due to dysphagia from distorted plication, 2 due to disrupted plication	3 pts, (7.9%) 2 had dilatations due to dysphagia, 1 had gastrojejunostomy due ventricle retention

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Schiefke	Yr: 2005	UI: 15888777	Questions addressed:1	Extractor: WY

Objective/Topic:
To evaluate the efficacy and durability of Endoscopic gastroplication with EndoCinch

Study design:	Country/Setting:	Funding:
Prospective cohort	Germany, single center	nd

Interventions(s):	Comparator(s):
Endoscopic gastroplication with EndoCinch	NA

Primary outcome(s):	Other outcome(s):
GERD symptoms PPI use Esophagitis status LOS pressure Time with pH <4 per 24 hours	

Inclusion criteria:	Exclusion criteria:
Between 18 and 80 years old, chronic heartburn and/or regurgitation >2 years, continuous PPI medication with at least partial symptom response, pathological distal oesophageal acid exposure measured by 24 hour pH monitoring (pH <4 greater than 5.2%/ 24 hours or a DeMeester-Johnson score >14.7)	hiatal hernia >3 cm in length, grade IV reflux oesophagitis, histological Barrett's mucosa, severe dysphagia, previous oesophageal surgery, specific motility disorders, significant untreated medical conditions
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 48 (range: 22-77)	N enrolled: 70
%Male:62	N completed: 56
Race: nd	Dropouts/reasons:10 geographic reasons, 4 declined to follow up
BMI:25.5 (23.4-28.3)	Follow-up period: 18 months
Comments:	

Results

Primary outcome(s):

	Baseline	18 months	P (baseline vs. 18 mo)
Heartburn severity scoring system (HBSS)	58.2 (41-76.3)	36.8 (14.4-46.1)	0.001
Dysphagia	8 pts (11.4%)	5 pts (7.1%)	nd
Regurgitation	21 pts (30%)	23 pts (32.8%)	nd
PPI use (any)	70 pts (100%)	66 pts (94.3%)	nd
H2RA use (any)	0	0	nd
Treatment success (decrease medication doses>50% and patient satisfaction, and improvement in HBSS)	NA	14 pts (20%)	nd
Endoscopic esophagitis grade O	26 pts (37.1%)	32pts (45.7%)	nd
Endoscopic esophagitis grade I	26 pts (37.1%)	27pts (38.6%)	nd
Endoscopic esophagitis grade II	16 pts (22.9%)	9pts (12.9%)	nd
Endoscopic esophagitis grade III/IV	2 pts (2.9%)	2 pts (2.9%)	nd

Secondary outcome(s):

	Baseline	12 months	P (baseline vs. 12 mo)
% time in 24-hr with esophageal pH <4	(out of 68 pts) 9.1	(out of 54 pts) 8.5	0.82
DeMeester score	(out of 68 pts) 32.7	(out of 54 pts) 24.1	0.97
Lower esophageal sphincter pressure (mmHg)	(out of 67 pts) 7.7	(out of 50 pts) 10.3	0.051
Lower esophageal sphincter length (cm)	(out of 67 pts) 3.0	(out of 50 pts) 3.2	<0.05

Comments:

Compliance:
NA

Adverse Events:
nd

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Scholten	Yr: 2005	UI: 16113546	Questions addressed: 1, 3	Extractor: SI

Objective/Topic: compare on-demand pantoprazole with placebo in long term treatment of GERD

Study design: RCT	Country/Setting: Germany, Austria, Netherlands	Funding: ALTANA Pharma AG

Interventions(s): pantoprazole 40 mg on demand once daily for 24 wk	Comparator(s): pantoprazole 20 mg once daily, placebo

Primary outcome(s): heartburn symptom relief	Other outcome(s):

Inclusion criteria: heartburn symptom relief during the last 3 days before end of treatment in a 4 wk open phase study; ≥18 yr; grade 0 or I endoscopic confirmed GERD	Exclusion criteria:
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion): nd
EGD (performed or not and results): Yes	Esophagitis/stricture/Barrett's: grade 0 or I
pH study (performed or not and results): nd	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): heartburn symptom relief during the last 3 days before end of treatment in an open phase study
Esophageal manometric studies (performed or not and results): nd	Other:

Were Inclusion/Exclusion criteria the same for all arms? yes (Specify yes or no and describe differences)

Quality Assessment for RCTs: C	
Blinding: nd	Allocation concealment: no
Intention-to-treat: y	Method of Randomization: nd
Other comments: non-validated symptom score; specific details of adverse events not reported	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 53	N enrolled: 548
%Male: 51	N completed: 465
Race: nd	Dropouts/reasons: lost to follow up; intake of not permitted meds; missing diary entries on 4 consecutive days; lack of efficacy, adverse events
BMI: 27	Follow-up period: 28 wk
Comments:	

Results
Primary outcome(s): Perceived average daily symptom load (heartburn, epigastric pain, acid regurgitation, amount of antacids intake) at 6 mo (ITT) Pantoprazole 40 mg 2.71 Pantoprazole 20 mg 2.91 Placebo 3.93 (P<0.0001 compared to Pantoprazole 40 or 20)
Secondary outcome(s): antacids intake (average number per day) (ITT) Pantoprazole 40 mg 0.33 ± 0.52 Pantoprazole 20 mg 0.45 ± 0.79 Placebo 0.68 ± 0.77 (P=0.0034 compared to Pantoprazole 40 or 20)
Comments:

Compliance:
"high" – 20 pts with missing entries on daily dairies

Adverse Events:
adverse events symptoms: 166/548 pts 5% likely related to study med 1 definitely related to study med 10% severe intensity 20/634 pts had serious adverse events unrelated to study med 9/548 discontinued meds due to adverse events

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Scholten	**Yr:** 2007	**UI:** 17358101	**Questions addressed:** Key question 1 and 3	**Extractor:** Peter Bonis

Objective/Topic: Comparative efficacy of on-demand therapy with esomeprazole versus pantoprazole after induction pantoprazole in patients with endoscopy-negative reflux disease or with reflux oesophagitis (Los Angeles Grade A or B)

Study design: Parallel group RCT	**Country/Setting:** University setting in Germany	**Funding:** Industry supported (manufacturer of pantoprazole)

Interventions(s): Pantoprazole 20 mg plus antacids as needed	**Comparator(s):** Esomeprazole 20 mg plus antacids as needed

Primary outcome(s): Intensity of gastrointestinal symptoms, heartburn, acid eructation and epigastric pain on a four-point scale	**Other outcome(s):** Adverse events

Inclusion criteria: 18 and older adults with endoscopy-negative reflux disease or Los Angeles grade A or B esophagitis who had heartburn of at least moderate intensity on at least 3 consecutive days during the previous week and a history of frequent episodes of GERD-related symptoms (i.e., heartburn possibly with acid eructation) over the previous 3 months. H. pylori status assessed.	**Exclusion criteria:** Higher grades of esophagitis, Barrett's esophagus, peptic ulcer disease, Zollinger Ellison syndrome, peptic ulcer complications, previous gastrointestinal surgery other than appendectomy or cholecystectomy, requirement for H. pylori eradication, pregnancy, severe comorbidity.
Symptoms (describe): Baseline characteristics not described	**Hiatal hernia (specify whether considered and size used for exclusion):** Not described
EGD (performed or not and results): Yes.	**Esophagitis/stricture/Barrett's:** Pantoprazole versus esomeprazole groups, respectively: Grade A esophagitis (60.6 versus 58%), Grade B esophagitis (34.3 versus 33%), non-erosive GERD (5.1 versus 9%).
PH study (performed or not and results): Not described and presumably not done.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Not described
Esophageal manometric studies (performed or not and results): Not described and presumably not done.	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B/acceptable	
Blinding: Patient and outcome assessor blinded	**Allocation concealment:** Not described

GERD data extraction form

Intention-to-treat: Yes	**Method of Randomization:** List
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 54.5 (+/- 12.6) and 52.7 (+/- 13.4) in the pantoprazole versus esomeprazole groups, respectively	**N enrolled:** 236
%Male: 57 and 44%, respectively	**N completed:** 199
Race: 99 and 100% Caucasian, respectively	**Dropouts/reasons:** 9 dropouts (reasons not describe) 46 protocol violations, 36 patients did not enter the on-demand portion of the study, 1 was considered not eligible. Authors present ITT and PP analysis.
BMI: 27.6 +- 4.1 versus 27.3 +/- 4.4, respectively	**Follow-up period:** 24 weeks
Comments:	

Results
Primary outcome(s): After 4 weeks of acute therapy, complete heartburn relief was achieved in 87.3% of patients who received pantoprazole. During the on-demand phase, the mean intensity of heartburn significantly lower with pantoprazole during on-demand period (score 1.32 versus 1.12, p=0.012). Mean intensity of acid eructation not significantly different.
Secondary outcome(s): No significant differences with regard to days with respective symptoms and number of symptom intervals (data not provided). More antacids taken in pantoprazole group (0.31 versus 0.23 tables/day) but not clear if difference was significant.
Comments: All patients received induction with pantoprazole (20 mg) during the acute phase. This may have biased toward the heartburn benefit since patients presumably achieved stable drug levels with pantoprazole during the run-in. Outcome assessors were evaluating patient diaries and thus the degree to which allocation concealment took place would be particularly important, especially considering the funding source. Authors did not perform a sample size determination, thus they may have been underpowered to detect differences in other outcomes. Authors did not assess esophagitis healing.

Compliance: Protocol violations were reported in 46 patients but were not described. Overall, patients took on average of 0.31 tables/day in the pantoprazole group and 0.36 tablets per day in the esomeprazole group.

Adverse Events: Adverse events were observed in 21% versus 23 percent in the pantoprazole versus esomeprazole groups. They were considered to be causally related to the drug in 6 versus 8 percent of the groups, respectively. They were considered to be severe in 7 and 6 percent of the groups, respectively. None of these was considered to be related to the study drug.

Applicability: (narrow/wide): wide	**Comments:** see above.

GERD data extraction form

Author: Schwartz	**Yr: 2007**	**UI: 16763053**	**Questions addressed: Q1; Q2; Q3**	**Extractor: MC**

Objective/Topic: to evaluate the therapeutic efficacy of endoscopic gastroplication in GERD compared with the sham procedure

Study design: RCT, double-blind, single center	**Country/Setting:** Netherlands	**Funding:** one of the authors was supported by a pharmaceutical grant.

Interventions(s): All procedures, both active and sham, were carried out by one and the same endoscopist. • Active gastroplication: the procedure was carried out using two video gastroscopes and the endoscopic suturing device (Endocinch). After endoscopic placement of an oesophageal overtube, two stitches were placed adjacent to one other, using the same thread.	**Comparator(s):** • Sham gastroplication: The sham procedure was carried out using the same equipment, but without the suturing needle and thread loaded. The endoscopist and two trained nurses carried out the same treatment routine as during active treatment for a duration of 40 min, including placement of an overtube, but no mucosal tissue was grasped or stitched.

Primary outcome(s): • Use of PPI: daily PPI dose • Symptom scores for heartburn and regurgitation	**Other outcome(s):** • QoL scores: SF-20 • Oesophageal acid exposure characteristics: 24-h pH monitoring • Lower oesophageal sphincter (LOS) pressure

Inclusion criteria: • Patients with typical persistent symptoms of GERD (heartburn or regurgitation). All patients were at least partially responsive to PPI drugs and had been dependent on PPIs for at least 1 year but considered for non-medical Tx. • Patients were included only when oesophageal pH results were compatible with the diagnosis of GORD—that is, oesophageal pH <4, >5% of the time or a symptom association probability >95%	**Exclusion criteria:** • Age <18 yr old • Severe oesophageal motility disorder on manometry • Hiatus hernia >3 cm in length • History of thoracic or gastric surgery • Oesophagitis grade C or D (LA classification) • Barrett's epithelium • Other severe comorbidities (including cardiopulmonary disease portal HTN • Use of anticoagulant or immunosuppressive drugs or a history of alcohol or drug misuse
Symptoms (describe): heartburn or regurgitation	**Hiatal hernia (specify whether considered and size used for exclusion):** Patients with hiatus hernia >3 cm in length were excluded
EGD (performed or not and results): Oesophagitis grade A or B (LA classification): 40% in Endocinch group; 45% in Sham group	**Esophagitis/stricture/Barrett's:** Excluded Barrett's
PH study (performed or not and results): Time pH<4 (off PPI): 5.6% in Endocinch group; 5.2% in Sham group	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** All patients were at least partially responsive to PPI drugs and had been dependent on PPIs for at least 1 year
Esophageal manometric studies (performed or not and results): LOS pressure, kPa: 1.1 (0.9) in Endocinch group; 1.1 (0.8) in Sham group	**Other:** PPI dose, mg (except 1 patient using H2-receptor antagonist): 40 (20-80) in Endocinch group; 40 (20-40) in Sham group

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) yes

GERD data extraction form

Quality Assessment for RCTs: A	
Blinding: double-blind (see comments)	**Allocation concealment:** numbered envelope was drawn from a set of sealed envelopes containing the allocation on a card
Intention-to-treat: Yes. All patients were analyzed at 3 month (end of double-blind RCT); long-term follow-up results (see comments) was analyzed according to the ITT principle.	**Method of Randomization:** block reanomization
Other comments: This is a double-blind RCT until 3 months of follow-up. Subsequently, patients were unblinded with regard to the Tx they had received. Patients from the sham and observation groups were offered open-label active treatment. In case of treatment failure in the active treatment group the patient was offered a repeat endoscopic treatment, consisting of the addition of one or more gastroplications. Follow-up was continued for up to 12 months after the gastroplication procedure.	

Quality Assessment Non-RCTs: B
Comments: 18% drop out at 12 mo (9/50)

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46	**N enrolled:** 40
%Male: 62.5	**N completed:** 40 @ 3 months (end of double-blind RCT); 33 @ 12 months
Race: no data	**Dropouts/reasons:** no dropouts @ 3 months (end of double-blind RCT) For the 12-month follow-up (open-label period): Incomplete questionnaire (n=3); received antireflux surgery (n=2); enrolled in other trial (n=1); too short follow-up (n=2)
BMI: 26.5	**Follow-up period:** 3 and 12 months
Comments: data the observation group (no treatment) were not extracted	

Results

Primary outcome(s):

At 3 months (end of double-blind RCT) –

- There was a significantly greater reduction in daily PPI use in active patients compared with sham patients (p<0.04, data shown in figure only)
- 13 (65%) patients in the active group responded to intervention (>50% reduction in PPI use) compared with 5 (25%) patients in the sham group (p=0.011 between groups)
- There were 8 (40%) patients in the active group and 1 (5%) patient in the sham group who had reduced PPI use by >95% at 3 months (p=0.02)
- The number of patients that were heartburn-free (frequency <1/month) was 8 (40%) in the active group, 1 (5%) in the sham group and none in the observation group (p=0.02)
- Symptom outcomes:

	Endocinch treatment (n=20)		Sham treatment (n=20)		P Values
	Change (SD)	%	Change (SD)	%	
Heartburn score (frequency x severity, range 0-24, off PPI)	-8.6 (9.0)	-50	-0.9 (4.3)	-6	0.003
Regurgitation score (frequency x severity, range 0-24, off PPI)	-5.2 (8.3)	-32	-1.1 (4.2)	-7	NS

At 12 months (open-label period) –

- The reduction of PPI use in the active treatment persisted at 6 and 12 months, although an increase in drug use

was noted over time (p=0.48). At 12 months, >50% and >95% reductions were achieved in 68% and 29% of the patients, respectively.

Secondary outcome(s):

At 3 months (end of double-blind RCT) –

- SF-20 outcomes –

	Endocinch treatment (n=20)		Sham treatment (n=20)		P Values
	Change (SD)	%	Change (SD)	%	
Physical function	19 (34)	+50	5 (24)	+10	NS
Role function	25 (26)	+40	1 (22)	+2	0.01
Social function	15 (31)	+23	0 (23)	0	NS
Mental health	-2 (20)	-3	0 (8)	0	NS
General health	14 (26)	+40	-1 (17)	+1	0.04
Bodily pain perception	-24 (39)	-34	2 (19)	+3	0.02

- mean oesophageal acid exposure times were decreased in both the active group and, to a slightly lesser extent, the sham group (p=0.02, active; p=0.10, sham)

	Endocinch treatment (n=17)		Sham treatment (n=18)		P Values
	Change (SD)	%	Change (SD)	%	
Acid total (percentage of time oesophageal pH<4, off PPI)	-2.7 (4.4)	-29	-1.9 (4.6)	-20	0.61
LOS pressure (kPa)	-0.0 (0.7)	-1	-0.3 (0.8	-21	0.35

Comments:

Power calculation was performed.

All subjects, including the no treatment group, were analyzed together in open-label period (6 and 12 months) therefore, the results were not extracted here.

Compliance:

No data

Adverse Events: No major adverse events requiring clinical observation. All adverse events were mild and transient, resolving spontaneously within 1 week. Adverse events occurred more frequently in the active group, with the exception of experiencing a sore throat. One patient developed a subcutaneous haematoma as result of a misplaced intravenous line.

	Endocinch treatment n (%)	Sham treatment n (%)
Sore throat	8 (40)	9 (45)
Chest soreness	6 (30)	0 (0)
Dysphagia <7 days	10 (50)	1 (5)
Belching	1 (5)	0 (0)
Abdominal pain	1 (5)	1 (5)
Bloating	2 (10)	0 (0)
Early satiety	1 (5)	0 (0)
Hiccups	1 (5)	0 (0)
Sedation-related	0 (0)	1 (5)

Applicability: (narrow/wide): Narrow	**Comments:** small sample size

GERD data extraction form

Author: Sheu	**Yr: 2007**	**UI: 18702650**	**Questions addressed: KQ2**	**Extractor: MC**

Objective/Topic:
To investigated whether BMI affects the efficacy of esomeprazole in active-phase or subsequent on-demand therapy

Study design:	**Country/Setting:**	**Funding:**
Prospective cohort study	Taiwan	Government

Interventions(s):	**Comparator(s):**
Active-phase therapy: esomeprazole, 40 mg qd., for 8 wk On-demand therapy: 40-mg esomeprazole as a drug tablet, until the fourth month. Only those patients who had maintained a sustained symptomatic response by the eighth week of the active-phase therapy were switched to on-demand therapy.	control: BMI <25 kg/m^2 vs. overweight: BMI 25–30 kg/m^2 vs. obese: BMI >30 kg/m^2

Primary outcome(s):	**Other outcome(s):**
Rate of sustained symptomatic response (SSR): symptoms of both acid regurgitation and heartburn for the last 7 continuous days in any week and thereafter of the active-phase therapy	TEM: number of 40-mg esomeprazole tablets used per month during the on-demand therapy phase in the third or fourth month of the study period. ODT (on-demand therapy) failure: Those patients who were switched to continuous PPI use or who had a follow-up endoscopic exam to confirm progression of erosive esophagitis during the ODT study period were defined as having a failure of ODT.

Inclusion criteria:	**Exclusion criteria:**
Patients who had clinical symptoms of either acid regurgitation, heartburn sensation, or both. These symptoms were defined as GERD and also further classified by panendoscopy as being either grade A or B in severity (LA classification).	• peptic ulcer, pregnancy, or major medical problems (including hypertension, liver cirrhosis, COPD, asthma, diabetes, renal failure, and congestive heart failure) • previous gastric surgery • drug allergy to esomeprazole • perimenopausal women currently using hormone therapy
Symptoms (describe): Acid regurgitation score (range 0-3) - BMI>25: 2.12 BMI 25-30: 2.42 BMI >30: 2.73 Heartburn score (range 0-3) - BMI>25: 2.23 BMI 25-30: 2.51 BMI >30: 2.57	**Hiatal hernia (specify whether considered and size used for exclusion):** BMI>25: 21.1% BMI 25-30: 22% BMI >30: 23.5%
EGD (performed or not and results): LA grade A: 53% LA grade B: 47%	**Esophagitis/stricture/Barrett's:**
PH study (performed or not and results): No data	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** • No patients took PPI or H2Ras within 4 week prior to the endoscopy and active-phase therapy. • Only those patients who had maintained a sustained symptomatic response by the eighth week of the active-phase therapy were switched to on-demand therapy

GERD data extraction form

Esophageal manometric studies (performed or not and results): No data	**Other:** H. pylori – BMI>25: 58.9% BMI 25-30: 58.3% BMI >30: 53.5%

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: prospective study with low rate of lost to follow-up. ITT and multivariate analyses. Inconsistent reporting between text and result table for some results

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: BMI>25: 43.8 BMI 25-30: 43.2 BMI >30: 42.8	**N enrolled: 350 (active-therapy phase); 286 (on-demand phase)**
%Male: BMI>25: 51 BMI 25-30: 52 BMI >30: 51	**N completed: 337 (active-therapy phase); 266 (on-demand phase)**
Race: Asian	**Dropouts/reasons:** Active-therapy phase: discontinued esomeprazole and used other drugs (n=6), moved to other cities (n=3); unknown (n=4) On-demand phase: failed on-demand treatment (n=13); unknown (n=7)
BMI: BMI>25: 180/350 BMI 25-30: 127/350 BMI >30: 42/350	**Follow-up period: 8 weeks (active-therapy phase); 4 months (on-demand phase)**
Comments: Smoking (%) - BMI>25: 20; BMI 25-30: 18.7; BMI >30:18.6	

Results

Primary outcome(s):

Treatment/Comparison:	Active-phase therapy: esomeprazole, 40 mg qd., for 8 wk					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		

BMI (<25, 25-30, vs. >30)	Rate of sustained symptomatic response (SSR) decreased significantly with increasing BMI (ITT analysis): 91.1%, 77.2%, and 65.1%, respectively, for the control, overweight, and obese groups (P < 0.001). OR of SSR (overweight vs. control) = 0.27 (95% 0.13, 0.58). OR of SSR (obese vs. control) = 0.16 (95% 0.06, 0.39) BMI >25 vs. <25: beta coefficient = -0.103 (95%CI -0.106, -0.047) (multivariate analysis)					
Symptoms (heartburn severity)	beta coefficient = -0.072 (95%CI -0.135, -0.009) (multivariate analysis)					
Severity of acid reflux (Acid regurgitation severity)	No effect (multivariate analysis)					
Hiatal hernia (present vs. not)	No effect (multivariate analysis)					

SSR, sustained symptomatic response
Multivariate analysis include the following parameter in the logistic regression model: BMI as overweight and obese, smoking, alcohol use, habitual tea use, habitual coffee use, acid regurgitation severity, heartburn severity, presence of hiatus hernia

Secondary outcome(s):

Treatment/Comparison:	On-demand therapy: 40-mg esomeprazole as a drug tablet, until the fourth month.					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
BMI (<25, 25-30, vs. >30)						ODT failure rates increased significantly with increasing BMI: 2.4%, 5.3%, and 14.2%, respectively, for the control, overweight, and obese groups (P = 0.002) BMI >25 vs. <25: beta coefficient = 1.051 (0.11 SE) (multivariate analysis)
Symptoms (heartburn severity)						No effect (multivariate analysis)

Severity of acid reflux (Acid regurgitation severity)						No effect (multivariate analysis)
Hiatal hernia (present vs. not)						beta coefficient = -0.075 (95%CI -0.137, -0.013) (multivariate analysis) Note: inconsistent with what text described

ODT, on-demand therapy

Comments:
Inconsistent reporting between text and result table

Compliance:
No data

Adverse Events:
No data

Applicability: (narrow/wide): narrow	**Comments: LA grade A and B; Asian only**

GERD data extraction form

Author: Sheu	**Yr: 2008**	**UI: 18702650**	**Questions addressed: KQ2**	**Extractor: MC**

Objective/Topic: To assessed the endoscopic healing rates of reflux esophagitis with Los Angeles grades C and D (RE-CD) using a 6-month esomeprazole, and the demographic factors or genotypes of S-mephenytoin 4'-hydroxylase (CYP2C19) that correlated with the healing of RE-CD

Study design:	**Country/Setting:**	**Funding:**
Prospective cohort study	Taiwan	Government

Interventions(s):	**Comparator(s):**
40 mg of esomeprazole once daily for 6 months	BMI <25 kg/m^2 vs. overweight/obese: BMI >25 kg/m^2

Primary outcome(s):	**Other outcome(s):**
Healing rate of reflux esophagitis Los Angeles grades C and D (RE-CD): • Complete healing group of GE-CD fulfilled both of the following two requirements: (a) complete healing of the esophageal ulcer into scar stage, and (b) total regression of erosive reflux esophagitis to be free from grade A and B by Los Angeles classification. • Improve group: patients with healing of ulcer but still having erosive esophagitis that was grade A or B by Los Angeles classification • Poor healing: ulcer still existed	

Inclusion criteria:	**Exclusion criteria:**
Patients with typical reflux esophagitis clinical symptoms as either acid regurgitation or heartburn sensation and proven with panendoscopy as being either grade C or D in severity (LA classification).	• taken antibiotics, antisecretory agents, including histamine-2 receptor antagonists, and any PPI within 4 wk prior to receiving endoscopy • peptic ulcer, pregnancy, or major medical problems (including hypertension, liver cirrhosis, COPD, asthma, diabetes, renal failure, and congestive heart failure) • previous gastric surgery • drug allergy to esomeprazole • perimenopausal women currently using hormone therapy • current usage of anti-obesity drugs, steroids, or nonsteroidal anti-inflammatory agents
Symptoms (describe): Mean reflux severity score (range 0-6) – 5.23	**Hiatal hernia (specify whether considered and size used for exclusion):** 23.2%
EGD (performed or not and results): LA grade C: 89% LA grade D: 11%	**Esophagitis/stricture/Barrett's:** No data
PH study (performed or not and results): No data	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No patients took PPI or H2Ras within 4 week prior to the endoscopy and active-phase therapy.
Esophageal manometric studies (performed or not and results): No data	**Other:**

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: prospective study with low rate of lost to follow-up. Unclear what parameters were included in the multivariate analysis model.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 53.8	**N enrolled: 125**
%Male: 63.2	**N completed: 113**
Race: Asian	**Dropouts/reasons: no data**
BMI: 26.2	**Follow-up period: 6 months**
Comments: Smoking (%) - 28	

Results

Primary outcome(s):

Treatment/Comparison:	40 mg of esomeprazole once daily for 6 months					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
BMI (>25 vs. <25)						OR of complete healing = 2.3 (95%CI 1.9, 3.5) (multivariate analysis)
Hiatus hernia (present or not)						No effect

Secondary outcome(s):

Comments:
Also report analyses at 1 month but not extracted.

Compliance:
less than 80% of their medication during the follow-up periods were defined as having poor compliance but no data were reported

Adverse Events: No data

Applicability: (narrow/wide): narrow	**Comments:** Los Angeles grades C and D and Asian only

GERD data extraction form

Author: Sjosted	**Yr**: 2005	**UI**: 16091055	**Questions addressed**: 1, 2, 3	**Extractor**: JC

Objective/Topic: Investigate whether esomeprazole 20 mg, taken O-D, is as effective as esomeprazole 20 mg once daily for endoscopic remission over a 6-month period.

Study design: RCT	**Country/Setting**: Sweden/Multicenter	**Funding**: Not reported

Interventions(s): esomeprazole 20 mg once daily.	**Comparator(s)**: esomeprazole 20 mg on-demand.

Primary outcome(s): Severity of individual GERD symptoms	**Other outcome(s)**: Proportion of pts in endoscopic remission over time (up to 6 months) and by baseline LA grade. Time in symptomatic remission

Inclusion criteria: Verified erosive reflux oesophagitis (LA grades A–D), confirmed by endoscopy within 7 days prior to visit 1; at least 18 years old, able to understand and comply with study procedures, required to provide written informed consent; history of heartburn episodes over at least 6 months and at least 4 days with heartburn episodes during the week prior to visit 1. Pts. with coexisting endoscopic signs of Barrett's metaplasia (BM) were also eligible for study provided there was no indication or history of high-grade dysplasia. Women of child-bearing potential were required to maintain effective contraception during the study period. No PPI therapy was permitted within 14 days of visit 1. Pts eligible for maintenance phase had to be healed after either 4 or 8 weeks of PPI treatment and had experienced, at most, 1 day of no more than mild heartburn during 7 days prior to 4 or 8-week follow up visit.	**Exclusion criteria:** History of oesophageal, gastric or duodenal surgery (except for simple closure of an ulcer), or other gastrointestinal (GI) complications such as Zollinger-Ellison syndrome, gastric/duodenal ulcer (within last 3 months) or clinically significant oesophageal stricture requiring intervention; significant disease of any other system; any suspected or confirmed current malignancy;
Symptoms (describe): Frequency and severity of heartburn; severity of acid regurgitation, dysphagia and epigastric pain.	**Hiatal hernia (specify whether considered and size used for exclusion)**: Considered but not used for exclusion.
EGD (performed or not and results): Performed and graded according to Los Angeles classification. See inclusion criteria above.	**Esophagitis/stricture/Barrett's**: Barrett's metaplasia (BM) eligible for study provided no indication or history of high-grade dysplasia. Stricture assessed at baseline but not used for exclusion.
pH study (performed or not and results): Not performed.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** All eligible patients initially treated for 4–8 weeks, until healed, with the recommended healing dose of esomeprazole, 40 mg once daily. Pts who had undergone oesophageal, gastric or duodenal surgery (except for simple closure of an ulcer) were

	excluded. (per exclusion criteria)
Esophageal manometric studies (performed or not and results): Not performed	Other: No rescue medication, other PPIs or H2RAs were provided in conjunction with treatment. H. pylori positive status assessed at baseline.

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B	
Blinding: Not described	Allocation concealment: Not described
Intention-to-treat: Yes	Method of Randomization: Yes, computer-randomized (in blocks of four)
Other comments:	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: esomeprazole once daily: 55 (22-87); esomeprazole on-demand: 54 (20-82)	N enrolled: 477 (qualified for randomization)
%Male: esomeprazole once daily: 65%; esomeprazole on-demand: 56%	N completed: 370
Race: Not described	Dropouts/reasons: 107 (Adverse events, relapse, not willing to continue, major protocol deviation, other)
BMI: Not described—Weight (kg): once daily: 82.6; esomeprazole on-demand: 82	Follow-up period: 6 months
Comments: Intake of at least 85% during the healing phase was a randomization criterion.	

Results

Primary outcome(s): Severity of individual GERD symptoms @ 6 months—No significant difference btw Tx groups in terms of overall symptomatic relapse (5.0% once daily; 5.7% on-demand, p=.77).

For individual symptoms:

	Once daily (n=204)					On-demand (n=164)			
	Normal	Mild	Moderate	Severe	p	Normal	Mild	Moderate	Severe
Heartburn	184	16	2	2	<.0001	110	41	11	2
Acid regurgitation	194	9	0	1	.0025	143	15	8	0
Dysphagia	202	2	0	0	.023	158	5	2	1
Epigastric pain	188	13	2	1	.020	140	23	2	1

Secondary outcome(s): Proportion of pts in endoscopic remission over time- @ 6 months, cumulative proportion of pts in remission on once daily Tx was 81% compared vs 58% in on-demand group. Once daily Tx was associated with significantly longer time in remission than on-demand Tx (p=<.0001).

Endoscopic relapses in pts taking on-demand therapy were related to baseline severity of erosive esophagitis with

more relapses occurring in pts with more severe oesophagitis at entry (relapse diagnosed at 3 and 6 months).

Significantly higher proportion of pts with baseline LA grades A, B and C remained in remission during once daily treatment vs. on-demand therapy.

Baseline grade LA grade was found to have a significant effect on overall relapse rates (p=00.17—more severe grades relapsing more frequently).

6 month freedom from remission rates by LA grade

	Once daily	On demand	p-value
A	93%	78%	.03
B	90%	65%	<.0001
C	90%	51%	.0002
D	80%	44%	.09

Comments: Approximate heartburn symptoms estimated from graph (figure 4).

Compliance:
39 patients taking once daily treatment discontinued the study, 12 for reasons of relapse, 8 because of AEs. Compared with 68 patients taking on-demand treatment, where 49 relapsed and three had AEs.

Adverse Events:
Once daily,
n (%; n = 243)
Nasopharyngitis 3 (1.2)
Abdominal pain 3 (1.2)
Gastroenteritis 5 (2.0)
Headache 2 (0.8)
Pneumonia 3 (1.2)
Vertigo 2 (0.8)
Diarrhoea 7 (2.9)
On-demand,
n (%; n = 234)
Nasopharyngitis 3 (1.3)
Abdominal pain 4 (1.7)
Gastroenteritis 1 (0.4)
Headache 3 (1.3)
Pneumonia 2 (0.9)
Vertigo 3 (1.3)
Diarrhoea 1 (0.4)

<u>Esomeprazole 20mg daily</u>
- Serious AE: 10/243 (4.1%), including death
- Death: 1/243 (0.4%)

<u>Esomeprazole 20mg on demand</u>
- Serious AE: 7/234 (3.0%)
- Death: 0/234 (0%)

Applicability: (narrow/wide): Narrow	Comments: Tx population consists of responders to initial PPI Tx.

GERD data extraction form

Author: Spence	**Yr: 2006**	**UI: 16713542**	**Questions addressed: 1**	**Extractor: DM**

Objective/Topic: Comparison of clinical outcomes in anterior 90° fundoplication versus Nissen fundoplication without division of the short gastric vessels

Study design:	**Country/Setting:**	**Funding:**
RCT	Australia/Hospital	National Heath and Medical Research Council of Australia (Governmental body)

Interventions(s):	**Comparator(s):**
anterior 90° partial fundoplication	Nissen fundoplication without division of the short gastric vessels

Primary outcome(s):	**Other outcome(s):**
Symptom assessment: 1) **Heartburn** – yes/no as well as visual analogue scale (0 =no heartburn, 10= severe heartburn) 2) **Dysphagia** - yes/no as well as previously validated score (0= no dysphagia, 45 = severe dysphagia) that combines information about difficulty swallowing nine types of liquids and solids was used as well. 3) **Dysphagia for solids** - yes/no as well as visual analogue scales (0=no dysphagia, 10=total dysphagia) 4) **Dysphagia for liquids** - yes/no as well as visual analogue scales (0=no dysphagia, 10=total dysphagia) 5) epigastric pain 6) regurgitation 7) odynophagia 8) early satiety 9) epigastric bloating 10) anorexia 11) nausea 12) vomiting 13) wheezing 14) coughing 15) increased flatulence Ability to relieve bloating Whether a normal diet was being consumed	**Modified Visick grading** 1=No symptoms 2 = Mild symptoms easily controlled by simple care such as avoiding certain foods or eating small meals, etc. 3= Moderate symptoms not controlled by simple care but not interfering with social or economic life 4= Moderate symptoms interfering with social or economic life 5= Symptoms as bad worse than preoperatively **Subjective patient grading of operational outcome** Excellent = Complete recovery Good = Major improvement with minor problems Fair = Major improvement with still significant problems or adverse effects Poor = Minor or no improvement or deterioration **Patient satisfaction with the operative outcome** – visual analogue scale (0= dissatisfied, 10=satisfied). **Early hospital outcomes** Postoperative stay (days) Days to taking oral fluids Days to taking solid foods **Postoperative EGD, pH and manometry tests** **Reoperative rate**

Inclusion criteria:	**Exclusion criteria:**
All patients with reflux who presented for laparoscopic antireflux surgery	Severe esophageal motility disorder that precluded the performance of a Nissen fundoplication, if patients required a contemporaneous abdominal procedure (e.g., cholecystectomy), or patients had previously undergone any type of gastric surgery.
Symptoms (describe):	**Hiatal hernia (specify whether considered and size used**

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Percent of patients with the listed symptoms in each group

Symptom	Anterior %	Nissen %
Heartburn	100	97
Dysphagia for solids	32	21
Dysphagia for liquids	6	8
Dysphagia VAS – solids		
Dysphagia VAS-liquids		
Dysphagia overall score		
Dysphagia Scored “0” on overallscore (%)		
Epigastric pain	56	71
Regurgitation	79	89
Odynophagia	15	24
Early satiety	35	53
Epigastric bloating	50	61
Anorexia	9	16
Nausea	29	50
Vomiting	35	34
Cough	35	34
Wheeze	24	26
Can relieve bloat	55	53
Eats normal diet	70	70
Increased flatus	NA	NA

for exclusion):

EGD (performed or not and results):
Yes, no data

Esophagitis/stricture/Barrett’s:
nd

PH study (performed or not and results):
Done only to confirm reflux in patients who did not have unequivocal reflux disease demonstrated by endoscopy

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):

Esophageal manometric studies (performed or not and results):
yes

Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous;	
Blinding: no	**Allocation concealment: nd**
Intention-to-treat: no	**Method of Randomization: sealed envelope technique**
Other comments: One patient who was randomized to undergo a Nissen fundoplication underwent an anterior 90° fundoplication due to surgical difficulty.	

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Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
x		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 46.5%	**N enrolled: 80**
%Male: 54.4%	**N completed: 79**
Race:	**Dropouts/reasons: Change of operation allocation – from Nissen fundoplication to anterior 90° fundoplication**
BMI: 29.4 *(In both groups,calculated as mean wt/(mean height)^2*	**Follow-up period:** 1 year
Comments:	

Results

Primary outcome(s):
Symptom Assessment

	Preoperative		I month		3-6 months		1 year	
	Anterior %	Nissen %	Anterior %	Nissen %	Anterior %	Nissen %	Anterior %	Nissen %
Heartburn	100	97	11	14	22	3	16	12
Epigastric pain	56	71	49	39	36	33	29	46
Regurgitation	79	89	11*	39*	15	26	3*	27*
Odynophagia	15	24	20	33	18	15	7	18
Early satiety	35	53	60	61	49	59	26*	67*
Epigastric bloating	50	61	37	47	55	56	32	39
Anorexia	9	16	26	31	9	10	3	12
Nausea	29	50	23	19	27	26	7*	30*
Vomiting	35	34	3	17	9	8	7	6
Cough	35	34	20	25	21	13	26	15
Wheeze	24	26	9	11	3	13	0	0
Increased flatus	NA	NA	54	44	46	67	42*	79*

**P<0.05 (Nissen vs. anterior fundoplication, Fisher exact test).*

Heartburn Visual Analog Scale: Median (Interquartile range)

	Anterior %	Nissen %
Preoperative	7 [2.8–9.1]	5 [3–8]
I month postop	0 [0–0]	0 [0–0]
3-6 months postop	0 [0–0.5]	0 [0–0]
1 year postop	0 [0–2]	0 [0–0]

Assessment of ability to relieve bloat, and eating normal diet

	Preoperative		I month		3-6 months		1 year	
	Anterior %	Nissen %	Anterior %	Nissen %	Anterior %	Nissen %	Anterior %	Nissen %

Can relieve bloat	55	53	38	56	50	61	69	50
Eats normal diet	70	70	47	27	89	74	90	83

Dysphagia assessment

Measure	Anterior	Nissen	Anterior	Nissen	Anterior	Nissen	Anterior	Nissen
Dysphagia for solids (%)	32	21	63	69	30	49	13*	49*
Dysphagia for liquids (%)	6	8	3	14	0*	21*	0	3
Dysphagia for solids VAS median (IQR)	0 [0–3.3]	0 [0–5]	3 [0–6.8]*	5 [3.3–7.8]*	0 [0–2.5]*	2.5 [0–6.3]*	0 [0–2]*	2 [0–6]*
Dysphagia for liquids VAS median (IQR)	0 [0–0]	0 [0–2.5]	0 [0–0]*	0 [0–4.3]	0 [0–0]	0 [0–1]	0 [0–0]*	0 [0–3]*
Overall Dysphagia score median (IQR)	1.7 [0–19.5]	8.2 [0–15.9]	16 [0–25.5]*	24 [17.7–29.9]*	0 [0–12]*	9.5 [0–23.5]*	0 [0–8.7]*	12 [3.5–19.5]*
Scored “0” on Overall Dysphagia score (%)	50	44	27	11	66*	33*	56*	18*

Secondary outcome(s):

Outcomes	3-6 months		1 year	
	Anterior	Nissen	Anterior	Nissen
Modified Visick grade				
1	25%	21%	32%	16%
2	47%	54%	48%	52%
3	6%	3%	8%	13%
4	8%	18%	0	19%
5	14%	5%	12%	0
Patient Assessment of Outcome				
Excellent	43%	28%	40%	21%
Good	30%	41%	33%	50%
Fair	11%	23%	13%	29%
Poor	16%	8%	13%	0%
Patient Satisfaction score	9 (7.5-10)	9 (7-10)	9 (6.1-10)	9 (6-10)
‘‘Made correct decision"	86%	77%	87%	76%

Early hospital outcomes

Variable	Anterior	Nissen	p-value
Postoperative stay (days)	2 [2–3]	2 [2–3]	0.42
Days to taking oral fluids	1 (1-1)	1 (1-1)	0.52
Days to taking solid foods	1.5 (1-2)*	2 (1.5-2)*	0.03

Postoperative EGD, pH and manometry tests

1) Postoperative Savary-Miller grading of esophagitis: 1/8 scored as Savary-Miller grade 1 after anterior 90° fundoplication, and 1/16 grade 3 esophagitis after Nissen fundoplication.
2) Twenty-four-hour pH monitoring demonstrated normalization of acid exposure times in all but one of the 23 patients studied

(This patient underwent a Nissen fundoplication)
3) The percentage time with pH less than 4 over the 24-hour study period was significantly less in the Nissen fundoplication group (0% [0%–0.6%] vs. 0.7% [0.3%–2.5%]; P = 0.02).
4) The postoperative lower esophageal sphincter resting pressure measured at esophageal manometry was similar for the two groups (anterior 14mmHg[10–24] vs. Nissen 18 [14–29]; P=0.22).
5) Lower esophageal sphincter residual relaxation pressure was, however, significantly higher after Nissen fundoplication (7 mm Hg [3–13] vs. 3 [0–5]; P = 0.02).

Reoperative rate
6) A reoperative procedure was performed between 4 and 10 months after surgery in five patients, two after anterior 90° fundoplication, and three after Nissen fundoplication.

Comments:

Compliance:

Adverse Events:

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Strate	**Yr: 2008**	**UI: 18027055**	**Questions addressed: 2; 3**	**Extractor: DM**

Objective/Topic:
Evaluate the effect of laparoscopic Nissen and Tupet fundoplication on reflux control and complication rate (dysphagia) after 2 years in two different groups of patients - with and without esophageal dysmotility

Study design:	**Country/Setting:**	**Funding:**
RCT	Germany / Hospital	nd

Interventions(s):	**Comparator(s):**
Nissen fundoplication (360°)	Toupet partial fundoplication (270°)

Primary outcome(s):
Symptoms of recurrent reflux, dysphagia, gas bloat and belching as measured by questionnaire.

Dysphagia and heartburn scale: mild (1–4 points), moderate (5–8 points), and severe (9–12 points) complaints.
Scale score: multiplication of the frequency and intensity. ***Frequency*** *of reflux symptoms was scored from 0 to 4 (0=no symptoms; 1=monthly; 2=weekly; 3= more than once a week; 4=daily);* ***Severity*** *was scored from 1 to 3 (1= easily controlled by dietary measures and occasional intake of antacids; 2= requiring continuous medical therapy; 3= symptoms despite effective medical treatment, i.e., proton pump inhibitors [PPI] that caused considerable discomfort to the patient).*

Other outcome(s):
1) Endoscopy
2) esophageal manometry tests - lower esophageal sphincter (LES) pressure, intraabdominal and overall length of the LES, relaxation of the LES, and motility of the esophageal body (Esophageal motility disorders were defined as mean contraction amplitude less than 40 mmHg and/or failed primary peristalsis of 10 wet swallows in more than 40%.)
3) 24-hour pH monitoring – DeMeester score as measured by a) cumulative total percentage time pH < 4, b) cumulative percentage time pH < 4 while upright, c) cumulative percentage time pH < 4 while supine, d) number of reflux episodes (pH < 4), e) number of reflux episodes lasting > 5 min, and f) longest reflux episode. The normal value < 14.7
4) modified Visick grading (score 1–4)
5) Subjective assessment: very satisfied, satisfied, unsatisfied or very unsatisfied.

Inclusion criteria:
1) Typical history
2) Report at least one endoscopic examination.
3) Pathological 24-hour pH-monitoring and/or endoscopically proven esophagitis

Exclusion criteria:
1) Previous antireflux surgery
2) Required a concurrent abdominal procedure
3) Pregnancy
4) age < 18 years.

Symptoms (describe):
Baseline symptoms [#]

Symptoms	Normal motility (n=100)				Esophageal Dysmotility (N=100)			
	Tot	Mild	Mod	Sev	Tot	Mild	Mod	Sev
Heartburn (n)	94	6	56	32	98	3	49	46[a]
Regurgitation (n)	78	25	32	21	81	16	31	34
Retrosternal pressure (n)	64	9	33	22	66	9	32	25
Chest pain (n)	51	5	27	19	56	2	24	30
Dysphagia (solid) (n)	25	11	12	2	38[a]	14	11	13[b]

Hiatal hernia (specify whether considered and size used for exclusion):

	Normal Motility			Esophageal Dysmotility		
	Tot (100)	Ns (50)	Tp (50)	Tot (100)	Ns (50)	Tp (50)
Hiatal hernia	81	38	43	85	44	41

Respiratory symptoms (n)	22	8	10	4	39[a]	13	12	14[b]

Tot=total, mod=moderate, sev=severe; [a] p<0.05 vs. normal motility; [b] p<0.005 vs. normal motility

[#] This was extracted from the original study publication (Fibbe C, Layer P, Keller J, Strate U, Emmermann A, Zornig C.Esophageal motility in reflux disease before and after fundoplication: a prospective, randomized, clinical, and manometric study.Gastroenterology. 2001 Jul;121(1):5-14) as this information was not presented, only cited.

	Normal Motility		Esophageal Dysmotility	
	Ns (50)	Tp (50)	Ns (50)	Tp (50)
Dysphagia	12	10	12	23

EGD (performed or not and results):
Yes

	Normal Motility			Esophageal Dysmotility		
	Tot (100)	Ns (50)	Tp (50)	Tot (100)	Ns (50)	Tp (50)
Esophagitis (Savary–Miller classification):						
0°	24	10	14	27	15	12
1°	41	20	21	37	17	20
2°	25	15	10	26	12	14
3°	8	4	4	7	5	2
4°	2	1	1	3	1	2
Barrett's esophagus						
Barrett's	6	3	3	14	9	5

Values in brackets indicate numbers; Tot= total, Ns = Nissen, Tp=Toupet

Esophagitis/stricture/Barrett's:
See EDG

PH study (performed or not and results):
Yes

Variable	Normal Motility		Esophageal Dysmotility	
	Ns (50)	Tp (50)	Ns (50)	Tp (50)
Median DeMeester Score	35.3	26.1	30.3	29.8

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):

Esophageal manometric studies (performed or not and results):
Yes

Manometry	Normal Motility		Esophageal Dysmotility	
	Ns (50)	Tp (50)	Ns (50)	Tp (50)
LES intra-abdominal length (cm)	0.4	0.5	0.3	0.6
LES pressure (mmHg)	11.3	13.6	8.9	10.1

Other:

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Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Y

Quality Assessment for RCTs: A/rigorous	
Blinding: Yes	**Allocation concealment: Yes**
Intention-to-treat: Yes	**Method of Randomization: sealed envelope technique**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients #	**Results: Disposition of Enrolled Subjects**
Age: 56 y (Median), range: 20-80y	**N enrolled: 200**
%Male: 61%	**N completed: 200**
Race: nd	**Dropouts/reasons: -**
BMI: nd	**Follow-up period: 2 years**
Comments: # This was extracted from the original study publication (*Fibbe C, Layer P, Keller J, Strate U, Emmermann A, Zornig C.Esophageal motility in reflux disease before and after fundoplication: a prospective, randomized, clinical, and manometric study.Gastroenterology. 2001 Jul;121(1):5-14)* as this information was not presented, only cited.	

Results

Primary outcome(s):

Treatment/Comparison:	**Nissen Fundoplication (n=100)**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Esophageal motility	Complained of dysphagia after 2 years: 6/50 without motility disorder, 13/50 with motility disorder – N.S. Gas bloat and belching: no effect	pH monitoring: No effect Manometry:Intra-abdominal length of the LES: no effect Manometry:Total LES pressure: no effect			No effect on satisfaction with operative result	

Secondary outcome(s):

GERD data extraction form

Treatment/Comparison:	**Toupet Fundoplication (n=100)**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Esophageal motility	Complained of dysphagia after 2 years: 3/50 without motility disorder, 5/50 with motility disorder – N.S. Gas bloat and belching: no effect	pH monitoring: No effect Manometry:Intra-abdominal length of the LES: no effect Manometry:Total LES pressure: no effect intra-abdominal length of the LES: no effect Total LES pressure: no effect				

Comments:

Compliance:

Adverse Events:
New onset dysphagia **one week after hospital discharge**

	Normal Motility		Esophageal Dysmotility	
	Ns (50)	Tp (50)	Ns (50)	Tp (50)
New onset dysphagia	14	5	9	5

Ns 23/100 (23%)
Tp 10/100 (10%)

Gas bloating: 106/200 (53%) – Nissen+Toupet
Inability to belch: Nissen 25/100 (25%), Toupet 13/100 (13%)
Conversion of a total fundoplication into a partial: 6 patients/100 (6%) -- Nissen

After 2 years
Nissen+Toupet: 27/200 patients (13.5%), moderate to severe dysphagia

Reoperation: Nineteen patients after 2 years (15/100 (15%) Nissen, 4/100 (4%) Toupets)

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Attwood	**Yr**: 2008	**UI**: 18709511	**Questions addressed**: 1, 2	**Extractor**: JC

Objective/Topic: compare treatment outcome in patients with and without BE submitted to standardized laparoscopic antireflux surgery (LARS) or esomeprazole treatment

Study design: RCT	**Country/Setting**: European/multi-center	**Funding**: AstraZeneca

Interventions(s): maintenance medical treatment with esomeprazole 20 mg od for their disease. Medical treatment was started at 20 mg od but could be dose adjusted, not to exceed 20 mg bid.	**Comparator(s)**: laparoscopic antireflux surgery (LARS)-- performed within 3 months of randomization, but patients could be treated with esomeprazole up to 40 mg od while awaiting surgery

Primary outcome(s): Therapeutic outcomes for symptoms related to GERD as measured by the Gastrointestinal Symptom Rating Scale (GSRS questionnaire) and by investigator assessments after LARS in BE compared to non-BE patients.	**Other outcome(s)**:

Inclusion criteria: adults aged 18–70 years with confirmed GERD, with or without BE. The patients had to have a history of chronic reflux esophagitis (>6 months) or chronic symptomatic GERD (>6 months) with pathological 24-h pH metry, according to local standards, and a requirement for long-term acid suppressive therapy. All patients were required to have had pH monitoring and manometry within 12 months prior to randomization and all had to be considered suitable for both surgical treatment and for long-term management with a PPI (esomeprazole).

Additionally, patients had to be capable of completing quality-of-life questionnaires.

Exclusion criteria: Any patient who had a primary need for surgery (e.g., for paraesophageal hernia or failure of medical therapy to control symptoms adequately) was not eligible to be recruited.

Patients who required PPI treatment for diseases other than GERD were excluded from the study, as were those who had a history of esophageal, gastric, or duodenal surgery or who had other diseases that might have a negative impact on their subsequent treatment within the study.

Symptoms (describe): Symptoms related to GERD as well as other gastrointestinal (GI) symptoms including epigastric pain, flatulence, bloating, diarrhea, ability to vomit, and ability to belch were scored by use of the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire and by investigator assessments (the latter for ability to vomit and ability to belch).

Hiatal hernia (specify whether considered and size used for exclusion): Considered-not used for exclusion

EGD (performed or not and results): Performed and graded according to Los Angeles classification.

	LARS		Esomeprazole	
Grade	Non-BE	BE	Non-BE	BE
None	120	14	109	20
A	72	7	54	1
B	55	9	68	4
C	9	1	7	3
D	0	1	0	0

Esophagitis/stricture/Barrett's: See inclusion criteria: adults aged 18–70 years with confirmed GERD, with or without BE. For the purposes of the trial, BE was defined as intestinal metaplasia on biopsy of endoscopically apparent columnarization.

GERD data extraction form

pH study (performed or not and results): All patients were required to have had pH monitoring within 12 months prior to randomization (see inclusion criteria)

	LARS		Esomeprazole	
	Non-BE	BE	Non-BE	BE
% time pH <4 Median (P10/P90)	7.9 (2.0-21.4)	13.2 (3.6-46.8)	8.8 (2.5-22.8)	7.4 (1.1-38.6)

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Before randomization, the protocol mandated a 12-week run-in period, which allowed baseline recordings to be made and medical treatment with esomeprazole 40 mg od to facilitate healing of the esophagitis.

Esophageal manometric studies (performed or not and results): All patients were required to have had manometry within 12 months prior to randomization (see inclusion criteria) Result not described in this paper.

Other: After 12-week run-in, an investigational week was scheduled without therapy to allow endoscopy, assessment of esophagitis according to the Los Angeles classification, biopsy sampling, laboratory screening, and 24-h pH metry with manometry and symptom association probability (SAP).

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B	
Blinding: Not described	Allocation concealment: Not described
Intention-to-treat: Yes	Method of Randomization: Yes, randomized blocks of four to two parallel study arms
Other comments:	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: Mean-LARS (Non-BE: 45; BE: 47) Esomeprazole (Non-BE: 45; BE: 50)	N enrolled: 554 patients with chronic GERD, 60 patients were found to fulfill the given criteria for BE, of whom 28 were randomized to medical treatment and 32 to antireflux surgery
%Male: LARS (Non-BE: 66.8 ; BE: 87.5) Esomeprazole (Non-BE: 74.8 ; BE: 75.0)	N completed: Not described in this paper
Race: Not described	Dropouts/reasons: Not described in this paper
BMI: Mean-LARS (Non-BE: 27; BE: 28) Esomeprazole (Non-BE: 27; BE: 27)	Follow-up period: 3 years
Comments:	

Results

Primary outcome(s):,

Ambulatory 24-h pH metry 6-months postop, Change in total acid exposure time from baseline (p=0.002)

LARS- 13.2%, to a median of 0.4%

Esomeprazole-7.4%, to a median of 4.9%

Therapeutic outcome as assessed by GSRS-Mean Scores demonstrating normal values and no significant differences between BE and non-BE patients or between LARS and ESO strategies

	LARS		Esomeprazole	
	Baseline	3 years	Baseline	3 years
Non BE				
Diarrhea	1.8	1.8	1.8	1.7
Indigestion	2.5	2.7	2.4	2.3
Constipation	1.7	1.6	1.6	1.6
Abdom pain	2.1	1.8	2.0	1.8
Reflux	1.9	1.2	1.7	1.7
BE				
Diarrhea	1.5	1.7	1.6	1.3
Indigestion	2.0	2.7	2.5	1.9
Constipation	1.6	1.8	1.6	1.4
Abdom pain	1.6	1.5	1.9	1.5
Reflux	1.5	1.3	1.7	1.3

Mean HRQL scores as assessed by QOLRAD

	LARS		Esomeprazole	
	Baseline	3 years	Baseline	3 years
Non BE				
Emotional	6.4	6.9	6.4	6.6
Sleep	6.4	6.9	6.3	6.5
Food/drink	6.1	6.9	6.2	6.4
Physical/social	6.5	6.9	6.5	6.8
Vitality	6.2	6.9	6.2	6.5
BE				
Emotional	6.5	7.0	6.5	6.8
Sleep	6.5	7.0	6.5	6.8
Food/drink	6.5	6.9	6.2	6.5
Physical/social	6.7	6.9	6.5	6.7
Vitality	6.7	6.9	6.2	6.6

Side effects of a total fundoplication were compared between BE and non-BE patients in the LARS group. BE as well as non-BE patients expressed similar profiles of obstructive and gas bloat-like complaints and, if anything, a trend was observed towards less complaints in the BE group.

% without complaints

	Dysphagia		Flatulence	
	Baseline	3 years	Baseline	3 years
Non BE	80	90	51	33
BE	93	88	57	32

Secondary outcome(s):

Comments: #'s for side-effects estimated from graph

Compliance: In the patients with BE, 100% of operations were completed as a 360° Nissen fundoplication, compared to 98% in the patients who did not have BE. There were no conversions to open surgery—all procedures were completed laparoscopically.

When the symptomatic and overall therapeutic outcomes were evaluated at 3 years, there was one treatment failure in BE patients submitted to LARS and three in those treated medically (ns).

Adverse Events: No apparent difference between the groups in postoperative complication rates for LARS (perioperative data described (include?) post op data not described) There were no conversions to open surgery—all procedures were completed laparoscopically. **Postoperative hospital stay** (p=0.11) BE patients- 63% staying 3 days or longer non-BE- 47% staying 3 days or longer

Applicability: (narrow/wide): Wide	Comments: large, multinational, European trial representing a chronic GERD population in which no selection criteria have been made except for those defined in the protocol to regulate the enrollment.

GERD data extraction form

Author: Grant	**Yr**: 2008	**UI**: 19074946	**Questions addressed**: 1	**Extractor**: JC

Objective/Topic: To determine the relative benefits and risks of laproscopic fundoplication surgery as an alternative to long term drug tx for chronic GORD.

Study design: RCT	**Country/Setting**: UK/21 hospitals	**Funding**: NIHR Health Technology Assessment Programme

Interventions(s): laproscopic fundoplication	**Comparator(s)**: Placebo bid for 8 weeks.

Primary outcome(s): REFLUX quality of life score	**Other outcome(s)**: SF 36, EQ 5D, and medication use, measured at time points equivalent to 3 and 12 mnts post surgery and surgical complications.

Inclusion criteria: Patients were eligible if they had more than 12 months' symptoms requiring maintenance treatment with a proton pump inhibitor (or alternative) for reasonable control; they had endoscopic or 24 hour pH monitoring evidence of GORD, or both; they were suitable for either policy (including American Society of Anesthesiologists (ASA) grade I or II); and the recruiting doctor was uncertain which management policy to follow.	**Exclusion criteria:** Exclusion criteria were morbid obesity (BMI >40); Barrett's oesophagus of more than 3 cm or with evidence of dysplasia; para-oesophageal hernia; and oesophageal stricture. See exclusion criteria.
Symptoms (describe): The primary outcome was the REFLUX questionnaire score, a validated "disease specific" measure incorporating assessment of reflux and other gastrointestinal symptoms and the side effects and complications of both treatments (score range 0 to 100, the higher the score the better the patients felt). The score was derived from the weighted average of six questions on quality of life (heartburn; acid reflux; eating and swallowing; bowel movements; sleep; and work, physical, and social activities). Five symptom scores were also developed as secondary measures (general discomfort; wind and frequency; nausea and vomiting; limitation in activity; constipation and swallowing).	**Hiatal hernia (specify whether considered and size used for exclusion)**: Considered para-oesophageal hernia--used for exclusion.
EGD (performed or not and results): Performed. See inclusion criteria.	**Esophagitis/stricture/Barrett's**: Pts. with Barrett's oesophagus of more than 3cm or evidence of dysplasia or oesophageal stricture excluded. See exclusion criteria.
pH study (performed or not and results): Performed. See inclusion criteria.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Patients were eligible if they had more than 12 months' symptoms requiring maintenance treatment with a proton pump inhibitor (or alternative) for reasonable control. See inclusion criteria
Esophageal manometric studies (performed or not and results): In the absence of erosive oesophagitis on	Other:

endoscopy, and when necessary to exclude achalasia, manometry or pH studies were performed before surgery.	

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B/C	
Blinding: No. Staff in the central trial office entered details of participants on the secure database, then notified participants and respective clinical sites of their allocation. There was no subsequent blinding.	Allocation concealment: No. Random allocation was organised centrally by a secure system. Staff in the central trial office entered details of participants on the secure database, then notified participants and respective clinical sites of their allocation.
Intention-to-treat: Yes	Method of Randomization: Yes, Random allocation was organised centrally by a secure system, using a computer generated sequence, strati-fied by clinical site, with balance in respect of age (18-49 or ≥50), sex (men or women), and BMI (≤28 or >29) secured by minimisation. Staff in the central trial office entered details of participants on the secure database, then notified participants and respective clinical sites of their allocation. There was no subsequent blinding.
Other comments:	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A=rigorous		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: Surgical: ITT-46.7, PP-46.3; Medical: ITT-45.9, PP-45.9	N enrolled: 357
%Male: Surgical: ITT-65, PP-61; Medical: ITT-67, PP-68	N completed: 299
Race: Not described	Dropouts/reasons: 58 (withdrawn, lost to follow up, death)---Access TABLE A at BMJ.com for more description?
BMI: Surgical: ITT-28.5, PP-28.7; Medical: ITT-28.4, PP-28.3	Follow-up period: 12 months
Comments: % Current smoker: Surgical: ITT-26, PP-26; Medical: ITT-40, PP-36	

Results

Primary outcome(s):

REFLUX QoL at baseline and 12 months – Mean (SD)

	Surgical		Medical	
	Randomized	Per protocol	Randomized	Per protocol
Baseline	63.6 (24.1)	61.9 (24.5)	66.8 (24.5)	68.2 (24.4)
12 months	84.6 (17.9)	88.3 (15.6)	73.4 (23.3)	73.1 (23.7)

Secondary outcome(s):
EQ-5D at baseline and 12 months – Mean (SD)

	Surgical		Medical	
	Randomized	Per protocol	Randomized	Per protocol
Baseline	.71 (.26)	.72 (.24)	.72 (.25)	.73 (.25)
12 months	.75 (.25)	.78 (.23)	.71 (.27)	71 (.27)

Comments: Enter SF36 data from BMJ.com???

Compliance:

Adverse Events:
Minimally described—includes both randomized and pt preference groups:
No differences were detected between the trial groups in their questionnaire responses at 12 months regarding "difficulty swallowing" and "bloatedness/trapped wind," but there was some evidence of more frequent "wind from the lower bowel" after surgery.

Applicability: (narrow/wide): Wide	Comments: non-restrictive inclusion/exclusion criteria

GERD data extraction form

Author: Lundell	**Yr:** 2007; 2009	**UI:** 17256807; 19490952	**Questions addressed: Q1**	**Extractor: MC**

Objective/Topic: 7-year (Lundell, 2007) and 12-year (Lundell, 2009) follow up of a comparative trial of omeprazole with open anti-reflux surgery in patients with chronic GERD – SOPRAN study

Study design: RCT, multicenter	**Country/Setting:** Nordic countries	**Funding:** AstraZeneca

Interventions(s): open anti-reflux surgery: Nissen (primarily), semi-fundo, and others	**Comparator(s):** Omeprazole 20 mg or 40 mg or 60 mg daily Dose adjustment to either 40 or 60 mg omeprazole in patients who had a relapse of symptoms with 20 mg daily

Primary outcome(s): not applicable because the 7-yr and 12-yr follow-up analyses were not originally planned	**Other outcome(s):** 7-year and 12-year follow up with treatment failure as the primary outcome variable. Treatment failure, was defined as the presence of at least one of the following criteria: moderate or severe heartburn or acid regurgitation during the previous 7 days before a hospital visit; oesophagitis of at least grade 2; moderate or severe dysphagia or symptoms of odynophagia in combination with mild heartburn or acid regurgitation; requirement for omeprazole treatment for more than 8 weeks after antireflux surgery to control reflux symptoms, or need for reoperation; after randomization to omeprazole, being considered by the physician to require antireflux surgery to control symptoms; and patient opting for antireflux surgery during the course of the study for any reason, despite randomization to omeprazole. Quality of life assessments: Assessed once a year using Psychological and Gerneral Well-Being index and the disease-specific instrument Gastrointestinal Symptom Rating Scale (GSRS)

Inclusion criteria: chronic GERD symptoms with concomitant esophagitis by endoscopy	**Exclusion criteria**: no esophagitis
Symptoms (describe): Results were not described in 2007 or 2009 paper	**Hiatal hernia (specify whether considered and size used for exclusion):** No exclusion
EGD (performed or not and results):yes Results were not described in 2007 or 2009 paper	**Esophagitis/stricture/Barrett's:** At 7 years, Barrett's - PPI 18%; surgery 14% at baseline At 12 years, Barrett's - PPI 18%; surgery 17% at baseline
PH study (performed or not and results): yes Results were not described in 2007 or 2009 paper	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No data
EMS (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) **No, more lost to follow up in surgery group.**

Quality Assessment for RCTs: C due to large lost to follow up	
Blinding: yes, "particular care was taken that the operating surgeon took no part in the postoperative evaluation of that particular patient,"	**Allocation concealment:** yes
Intention-to-treat: yes	**Method of Randomization:** randomization carried out by a blinded computer based system
Other comments: patients were stratified for each center in blocks of ten subjects. Large dropout at both 7-yr and 12-yr follow up. It seems that the long-term follow-up study (beyond 5 years) was not originally planned	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
	B	

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: • At 7-year follow-up, patients' baseline median age (range) Surgery (n=99): 51 (19-73) Omeprazole (n=119): 55 (22-76) • At 12-year follow-up, patients' baseline median age (range) Surgery (n=59) 50 (19-73) Omeprazole (n=78): 52 (28-76)	**N enrolled:** 344, only 310 were randomized; 155 randomized to surgery; 155 randomized to omeprazole; 144 had surgery
Gender: surgery Males 76% omeprazole Males 74%	**N completed:** • 99 in the surgery group and 119 in omeprazole group completed the 7-year follow-up • 59 in the surgery group and 78 in omeprazole group completed the 12-year follow-up
Race: no data	**Dropouts/reasons:** • At 5-year follow-up (reported in original article, Lundell 2001, in previous report)- 9 refused operation; 1 had no esophagitis; 1 had bronchial carcinoma (therefore the operation was cancelled); 1 died of MI 3 months post-op; 3 withdrawn due to unacceptable adverse events; 2 due to non-compliance, 1 to other reasons, 6 were lost to follow up, and 10 refused to comply with the follow-up procedures; In the medical arm, 1 patient never had omeprazole, 10 withdrawn due to unacceptable adverse events; 2 due to non-compliance, 1 to other reasons, 4 were lost to follow up, and 4 refused to comply with the follow-up procedures. • Between 5-year and 7-year follow-up – 6 patients were withdrawn from the omeprazole group and 1 from the antireflux surgery group • Beyond 5-yr follow-up – Primary due to logistic and other technical reasons at the time of prolongation of the study protocol.
BMI: no data	**Follow-up period:** from year 5 up to 12 years
Comments: 34/344 patients had incompleted response to omeprazole during the run-in period and were offered surgery, therefore, only 310 were randomized	

Results

Primary outcome(s):

Secondary outcome(s):

- Analysis of the cumulative rate of treatment failures revealed superiority for antireflux surgery over time (P=0.002, log rank test). Up to 12-yr follow-up (survival analysis), 53% remained in sustained remission in the surgical arm compared with 40% in the medical arm.

Reasons for treatment failure during 7-year follow-up:

	Omeprazole (n=154)	Surgery (n=144)
Symptoms with oesophagitis	4	4
Symptoms without oesophagitis	54	21
Endoscopic oesophagitis	16	17
Treatment failure for other reasons	7	8
Censored before 7 years	20	34
Completed 7 years without relapse	53	60

- In patients with symptomatic and/or endoscopic recurrence, an increase in omeprazole dose was allowed; this resulted in a smaller difference in treatment failure rates between the two groups, but antireflux surgery was still superior (P=0.045)

Obstructive symptoms such as dysphagia, flatulence and inability to belch were reported more frequently after antireflux surgery than for omeprazole therapy (P = 0·006, P = 0·001 and P = 0·001 respectively). The incidence of these complaints remained stable over the 7-year follow-up.

- Up to 12 years follow-up, the main reflux symptoms of heartburn and regurgitation were significantly more comment in PPI than surgery group (HR=1.73, 95%CI 1.6-1.9 and HR=2.38, 95% CI 2.1-2.7, respectively).
- During the 12 years of follow-up, 21 of the 155 patients initially randomized to PPI were referred for fundoplication (14%). In total, 52 of the 144 surgical patients (36%) were treated with PPI for more than 8 weeks, with a slow but steady increase over time.
- The GSRS mean scores for the 2 treatment arms were very similar and at a level is considered to be normal.

Comments:

These two articles are 7-yr and 12-yr follow-up of a RCT by Lundell 2001 (in previous report)

Adverse Events: see 1998 paper for acute AEs.

Long-term safety (up to 12 years follow-up):

- There were no surgery-related deaths. In the surgical arm, more AEs were listed as procedural complications (including hernia, postoperative infections, etc.). One patient randomized to surgical arm was found to have esophageal cancer 12 years after fundoplication, compared with none in those treated with PPI. This patient had a Barrett's diagnosed at initial endoscopy for inclusion in the study. The presence of BE (with intestinal metaplasia but with the absence of dysplasia) had been documented 3 years before the endoscopic diagnosis of esophageal cancer.
- Fatal outcome and heart-related cause of AEs were more common in the PPI group than in the surgical group. 8 patients in the PPI group died of heart-related causes, and 9 experienced non-fatal heart attacks. 2 surgical patients died of heart-related causes, and 2 experienced non-fatal MI. These data were from FDA database, and claimed that FDA concluded that baseline differences and other confounding factors (eg, withdrawal from the surgical group and/or receiving both therapess) could have biased the safety data.

Applicability: (1/2/3): Wide	**Comments:**

GERD data extraction form

Author: Lundell	Yr: 2008	UI: 18469091	Questions addressed: 1, 3	Extractor: WY

Objective/Topic:
Compare laparoscopic antireflux surgery (LARS) and esomeprazole in managing gastro-esophageal reflux disease

Study design: RCT	Country/Setting: Multicenter, in 11 European countries, centers were academic units or affiliated with a university	Funding: AstraZeneca

Interventions(s):	Comparator(s):
laparoscopic antireflux surgery (LARS), within 3 months of randomization	esomeprazole 20mg q day, for 3 years if symptom was not controlled after 8 weeks, dose increased to 40mg q day for 8 weeks, then to 20mg bid day for 8 weeks or back to 20mg q day

Primary outcome(s):	Other outcome(s):
Time to treatment failure	GERD symptom control Quality of life

Inclusion criteria:	Exclusion criteria:
Oesophagitis no more than LA grade B GERD symptoms no more than mild	Hx of oesophageal, gastric or duodenal surgery, hx or current Zollinger-Ellison syndrome, primary oesophageal disorders, inflammatory bowel disease, dysplastic changes in a columnar-lined oesophagus or abnormal GI absorption, significant concomitant disease, potential for poor compliance
Symptoms (describe): Heartburn None 35.02% Mild 23.99% Moderate 24.35% severe 16.60% Acid regurgitation None 46.38% Mild 20.54% Moderate 24.54% severe 8.44%	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): Yes grade A 24.18% grade B 24.55% grade C 3.64% grade D 0.16% No oesophagitis 47.46%	Esophagitis/stricture/Barrett's: Barrettt's: 9.92%
PH study (performed or not and results): yes	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): yes
Esophageal manometric studies (performed or not and results):	Other: H pylori status assessed, not reported

no	Hx of GERD <1yr	29.63%
	Hx of GERD 1-5yr	50.75%
	Hx of GERD >5yr	19.11%

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: C/Poor (please select one and delete others)	
Blinding: no	Allocation concealment: no
Intention-to-treat: yes, per-protocol for efficacy data	Method of Randomization: unclear, in blocks of 4
Other comments: dropout >20%; pt blinding not possible	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 45.09	N randomized: 554
%Male: 71.84	N completed: 412
Race: not reported	Dropouts/reasons: adverse events (1 in LARS before surgery, 2 in LARS after surgery, 10 in esomeprazole), ineligible (1 in LARS before surgery, 2 in esomeprazole), "study-specific discontinuation" (1 in LARS before surgery, 10 in LARS after surgery, 1 in esomeprazole), lost to follow-up (2 in LARS before surgery, 6 in LARS after surgery, 7 in esomeprazole), lack of therapeutic response (16 in LARS after surgery, 15 in esomeprazole), other (35 in LARS before surgery, 10 in LARS after surgery, 23 in esomeprazole),
BMI:27.25	Follow-up period: 3 years
Comments: There was a 3-month run-in period when all pts took esomeprazole 40mg q day. Out of the 288 pts randomized to undergo LARS, only 248 were operated. Unsure why there were "ineligible" pts after randomization.	

Results
Primary outcome(s): Time to treatment failure Percentage of pts in remission after 3 years, ITT LARS: 90% Emesoprazole: 93% P=0.25 Percentage of pts in remission after 3 years, per-protocol LARS: 90% Emesoprazole: 95% P=0.045
Secondary outcome(s): Among the emesoprazole group, at 3 years, 23% of pts were on an increased dose of esomeprazole; 8% on the maximum allowed dose schedule. Heartburn: throughout the study, there was a decrease in LARS group, and similar level in esomeprazole group. Overall, there was more heartburn in esomeprazole group (p<0.001)(Figure 4A) Acid regurgitation: throughout the study, there was a decrease in LARS group, and similar level in esomeprazole group. (Figure 4B)

Dysphagia: mostly mild, more common in LARS group post-op (p<0.001) (Figure 4C)
Flatulence: more common in LARS group ost-op (p<0.001) (Figure 4D)

Quality of life scores

	LARS (mean ± SD)	Esomeprazole (mean ± SD)	P between groups***
Quality of life in reflux and dyspepsia*, vitality score	Baseline: 6.28 ± 1.08 3 years: 6.90 ± 0.31	Baseline: 6.21 ± 1.22 3 years: 6.53 ± 0.85	P<0.001
Quality of life in reflux and dyspepsia*, food and drink	Baseline: 6.16 ± 1.16 3 years: 6.85 ± 0.4	Baseline: 6.19 ± 1.12 3 years: 6.38 ± 0.91	P<0.001
Gastrointestinal symptom rating scale**, reflux	Baseline: 1.81 ± 1.07 3 years: 1.18 ± 0.42	Baseline: 1.73 ± 1.03 3 years: 1.63 ± 0.88	P<0.001

* 7= no problem, 6= minimal problems
** 1= no discomfort, 2= minimal discomfort
*** ANOVA

Comments:

Compliance:
NA

Adverse Events:
0.8% of LARS pts and 3.8% of esomeprazole discontinued study due to adverse events.
There was no perioperative mortality, 3% morbidity within hospital stay or within 30 days post-op.
One pt died from pneumonia in the esomeprazole group.

	Refused LARS (n=40) n (%)	LARS (n=248) n (%)	Esomeprazole (n=266) n (%)
Injury, poisoning, procedural	1 (2.5)	15 (6.0)	2 (0.8)
Gastrointestinal disorders	0	12 (4.8)	5 (1.9)
Musculoskeletal/connective tissue	0	2 (0.8)	8 (3.0)
Infections and infestations	1 (2.5)	3 (1.2)	6 (2.3)
General disorders	0	5 (2.0)	4 (1.5)
Cardiac disorders	1 (2.5)	4 (1.6)	3 (1.1)
Neoplasms, benign/malignant	0	2 (0.8)	6 (2.3)
Reproductive system including breast	0	1 (0.4)	4 (1.5)
Respiratory, thoracic, mediastinal	0	5 (2.0)	1 (0.4)
Vascular disorders	0	3 (1.2)	3 (1.1)
Hepatobiliary disorders	1 (2.5)	3 (1.2)	0
Any serious adverse events	4 (10)	55 (21)	42 (14.3)

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Mehta	**Yr: 2006**	**UI: 17114017**	**Questions addressed: Q1; Q3**	**Extractor: MC**

Objective/Topic:
This is 7-yr follow-up of a RCT by Mahon, 2005 (included in 2005 GERD report)

Study design:	**Country/Setting:**	**Funding:**
Non-RCT	UK	No data

Interventions(s): Original RCT was comparing Nissen with PPI for 12 months. After the first year, patients who had undergone surgery were kept under long-term review. Those in the PPI arm were offered the chance to undergo surgery or to remain on optimal PPI medication. Group 1: Laparoscopic Nissen fundoplication. Group 2: Patients received 1-year PPI in RCT phase, who later opted to received laparoscopic Nissen fundoplication	**Comparator(s):** Group 3: Patients received 1-year PPI in RCT phase, who remaining on PPI. The majority of patients were on regular omeprazole (53%) at a mean dosage of 20 mgs/day. 27% were on lansoprazole at a mean dosage of 28 mgs/day, 10% were on another type of PPI, and the other 10% were on a combination of two or more PPIs.

Primary outcome(s): DeMeester symptom score questionnaire	**Other outcome(s):**

Inclusion criteria: 16-70 yrs; reflux based on EGD and/or 24-h pH study with good symptom correlation (>50% heartburn associated with acid reflux). This long-term follow-up non-RCT only included 183 (out of 217) patients in Norwich.	**Exclusion criteria:** significant esophageal dysmotility, BMI>35
Symptoms (describe): Symptoms of GERD for at least 6 mos and on PPI for at least 3 mos	**Hiatal hernia (specify whether considered and size used for exclusion):** LNF: 94%; PPI: 93%
EGD (performed or not and results): Performed (Reported in Mahon, 2005 article)	**Esophagitis/stricture/Barrett's:** No data
PH study (performed or not and results): Mean DeMeester LNF (n=91): 3.5 PPI then surgery (n=54): 3.3 PPI alone (n=38): 2.4	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** No data
Esophageal manometric studies (performed or not and results): Performed (Reported in Mahon, 2005 article)	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
No. Patients opted to receive surgery after 1-year PPI treatment had significantly higher DeMeester symptom scores at 12 months (end of RCT) than patients received surgery or PPI alone.

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

GERD data extraction form

Quality Assessment Non-RCTs: C
Comments: Questionnaire response rate was 79%. Patients opted to receive surgery after 1-year PPI treatment had significantly higher DeMeester symptom scores at 12 months (end of RCT) than patients received surgery or PPI alone.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 47 (range 24-69)	**N enrolled: 183**
%Male: 69	**N completed: 145 (calculated based on the 79% response rate)**
Race: no data	**Dropouts/reasons: no response to the follow-up symptom questionnaire.**
BMI: mean weight=80 (range 61-126) kg	**Follow-up period: median 6.9 years (range, 4.3-8.3)**
Comments:	

Results

Primary outcome(s):

Mean (SD) DeMeester symptom scores

	12 mo	Median 6.9 yr*
LNF (n=91)	0.9 (1.4)	1.1 (1.9)
PPI then surgery (n=54)	2.3 (2.3)	0.8 (1.4)**
PPI alone (n=38)	1.1 (1.5)	0.9 (1.0)

*response rate=79%

**significant change in score from 12 mo (Mann-Whitney test, $P < 0.01$)

Secondary outcome(s):

Comments:

Compliance:

Adverse Events:

Nissen fundoplication -

- 2 patients suffered splenic bleeding and 2 had inadvertent esophageal injury. These were dealt with laparoscopically and there were no postoperative sequelae.
- In the early postoperative period, 2 patients suffered wrap migration requiring laparoscopic correction and 4 patients had dysphagia within the first 3 months, requiring endoscopic esophageal dilation.

PPI -

- A proportion of patients (10%) suffered side effects of headache, diarrhea, vomiting, or abdominal pain, requiring alteration of the PPI type.
- A further 18% required dosage escalation during the trial period to relieve GERD symptoms.

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Olberg	**Yr: 2005**	**UI: 15932167**	**Questions addressed: 1,3**	**Extractor: JHL**

Objective/Topic: Long-term outcome of surgically and medically treated patients with GERD

Study design: A matched-pair follow-up study	**Country/Setting: Norway**	**Funding: AstraZeneca AS, Norway**

Interventions(s):	**Comparator(s):**
• Open or laparoscopic fundoplication	• Controls treated medically

Primary outcome(s):	**Other outcome(s):**
• GERD symptoms	• Health-related quality of life

Inclusion criteria:	**Exclusion criteria:**
Patients • Patients operated on with fundoplication because of GERD at St. Olav's Hospital (SOHO) and at Levanger Hospital (LH) in the period 1992-99 • SOHO 215 patients 209 patients (a 360° fundoplication ad modum Nissen-Rosetti) + 6 patients (hemifundoplication ad modum Toupet) Matching controls • "… Comparability with regard to hospital, sex, age (±/5 years for those 50 years or above and ± 10 years for those </50 years), follow-up time (gastroscopy in the same year as operated on or ±/1 year if none was found), highest grade of esophagitis recorded at the time of operation or earlier, graded according to Savary & Miller (regarding Barrett's esophagus as a separate grade), and presence of hiatus hernia or Barrett's esophagus."	**Matching controls** • "Serious disease representing a contraindication against operation, alcoholism, reduced mental function incompatible with completing questionnaires and later operation with fundoplication. It was not possible to find a suitable control for 90 operated patients (43 from SOHO and 47 from LH)."
Symptoms (describe): ND	**Hiatal hernia (specify whether considered and size used for exclusion):** SOHO 87.3%, LH 100%
EGD (performed or not and results): ND	**Esophagitis/stricture/Barrett's:** Esophagitis Grade 0/I/II/III/IV (%) • SOHO 8.8/28.4/51.0/8.8/2.9 • LH 6.5/3.9/36.4/35.1/18.2 Barrett's esophagus • SOHO 2.9%, LH 6.5%
PH study (performed or not and results): ND	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): ND	**Other:** Matching controls: medical treatments vary based on the severity of GERD and the general practitioner. "Patients with no or only mild esophagitis were first given a 1-3 months' treatment course with an H2RA and advised of subsequent on-demand use if satisfactory relief was obtained. If no satisfactory relief was achieved the next step would be continuous, intermittent or on-demand treatment with a PPI. In the majority of patients with mild reflux disease, however, follow-up and further treatment were the responsibility of the submitting general practitioner."

GERD data extraction form

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
No (matched pair, surgically vs. medically treated patients)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: • No information on diagnostic tests for GERD • 179 pairs, 102 from SOHO + 77 from LH; "…no significant differences between operated patients and controls with regard to the matching criteria, smoking status, and the presence of concurrent disease. Disease history in both hospitals, however, was significantly longer in operated patients than in controls ($p < 0.05$ – p </0.001)."

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
C/Poor (No data)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: SOHO 54y, LH 54.5y	**N enrolled:** • SOHO 215 operated patients • LH 158 operated patients
%Male: SOHO 63.7%, LH 81%	**N completed: SOHO 102 pairs, LH 77 pairs**

Race: ND	**Dropouts/reasons:**
	St Olavs Hospital
	215 operated patients (OPR): 162 OPR with matched control + 43 OPR without matched control + 10 OPR excluded; Died 2 and 3 years after the operation for reasons unrelated to the operation or GERD (n=2), mentally retarded (n=1), had eosophagectomy as a result of Barrett's esophagus and severe dysplasia (n=1), demanded that the fundoplication be reversed (n=1), not possible to classify their preoperative degree of esophagitis (n=3), alcoholism (n=1), an erroneously indicated age of 8 years in the archive (n=1)
	• OPR (Total n=162): 135 responders + 27 non-responders
	  o 135 responders: 125 completed data + 10 (excluded)
	  o 125 complete data: 102 with paired control + 23 without paired control
	• Controls (Total n=162): 126 responders + 36 non-responders
	  o 126 responders: 123 completed data + 3 (excluded)
	  o 123 complete data: 102 with paired OPR + 21 without paired OPR
	Levanger Hospital
	158 operated patients (OPR): 158 OPR with matched control + 47 OPR without matched control + 3 OPR excluded; died 5 years after the operation for a reason unrelated to the operation or GERD (n=1), not possible to classify their preoperative degree of esophagitis (n=2)
	• OPR (Total n=108): 102 responders + 6 non-responders
	  o 102 responders: 102 completed data + 0 (excluded)
	  o 102 complete data: 77 with paired control + 25 without paired control
	• Controls (Total n=108): 82 responders + 26 non-responders
	  o 82 responders: 80 completed data + 2 (excluded)
	  o 80 complete data: 77 with paired OPR + 3 without paired OPR

BMI: ND	**Follow-up period: SOHO 71.5 months (mean), LH 79 months (mean)**

GERD data extraction form

Comments:

Results

Primary outcome(s):

- **Drug use for patients operated on with fundoplication and their paired controls from St. Olav's Hospital (SOHO) and Levanger Hospital (LH). Difference tested with the χ^2 test.**

	SOHO (n=102 pairs)			**LH (n=77 pairs)**		
	Operated	Controls	Diff	Operated	Controls	Diff
Antireflux drugs the previous week (%)	19.8	76.5	p < 0.001	18.2	77.9	p < 0.001
Anti-reflux drugs the previous year (%)	27.7	88	p < 0.001	29.9	84.4	p < 0.001
Continuous use the previous week	11.9	52.9	p < 0.001	5.2	57.1	p < 0.001
PPI the previous week (%)	11	45.9	p < 0.001	6.5	54.5	p < 0.001
PPI the previous year (%)	17	56.1	p < 0.001	7.8	61	p < 0.001
The previous week H2RA (%)	1	20.4	p < 0.001	1.3	11.7	p < 0.001
H2RA the previous year (%)	2	21.4	p < 0.001	1.3	14.3	p < 0.001
Other anti-reflux drugs the previous week (%)	7	9.2	ns	7.8	11.7	ns
Other anti-reflux drugs the previous year (%)	8	10.2	ns	15.6	9.1	ns

- **Gastrointestinal Symptom Rating Scale (GSRS) and Psychological General Well-Being Index (PGWB) scores in patients operated with fundoplication and their paired controls, difference tested with the Wilcoxon signed-rank test.**

	SOHO (n=102 pairs)			**LH (n=77 pairs)**		
	Operated	Controls	Diff	Operated	Controls	Diff
GSRS						
Abdominal pain	2.0 (1.8 - 2.1)	2.3 (2.1-2.5)	p < 0.05	2.1 (1.9-2.2)	2.2 (2.0-2.4)	ns
Reflux	1.3 (1.2-1.4)	2.5 (2.3-2.7)	p < 0.001	1.4 (1.2-1.6)	2.5 (2.3-2.8)	p < 0.001
Diarrhea	2.1 (1.9-2.4)	2.0 (1.8-2.2)	ns	1.9 (1.6-2.1)	1.9 (1.6-2.1)	ns
Indigestion	2.8 (2.5-3.0)	2.4 (2.2-2.6)	p < 0.05	2.7 (2.5-2.9)	2.5 (2.3-2.8)	ns
Constipation	1.8 (1.6-2.0)	1.8 (1.6-2.0)	ns	1.8 (1.5-2.0)	1.8 (1.6-2.1)	ns
Total GSRS	2.2 (1.9-2.2)	2.2 (2.0-2.3)	ns	2.0 (1.9-2.2)	2.2 (2.0-2.4)	ns
PGWB						
Anxiety	24 (23-25)	23 (22-24)	ns	24 (23-25)	24 (23-24)	ns
Depression	15 (15-16)	15 (15-16)	ns	16 (15-16)	15 (15-16)	ns
Pos. well-being	15 (15-16)	15 (14-16)	ns	16 (15-16)	15 (15-16)	ns
Self-control	15 (15-16)	15 (14-16)	p < 0.05	16 (15-16)	15 (14-15)	ns
General health	14 (13-14)	13 (12-13)	ns	14 (13-14)	13 (12-14)	ns

Vitality	16 (16-17)	16 (15-17)	ns	16 (15-17)	16 (15-17)	ns
Total PGWB	100 (97-104)	97 (93-100)	ns	101 (98-104)	98 (94-102)	ns

- **GSRS and PGWB scores for patients operated on with fundoplication and their paired controls, belonging to paires without concurrent disease, difference tested with the Wilcoxon signed-rank test.**

	SOHO (n=24 pairs)			**LH (n=19 pairs)**		
	Operated	Controls	Diff	Operated	Controls	Diff
GSRS						
Abdominal pain	1.7 (1.4-2.1)	2.2 (1.7-2.6)	ns	2.2 (1.7-2.6)	2.2 (1.9-2.6)	ns
Reflux	1.1 (1.0-1.3)	2.6 (2.1-3.2)	$p < 0.001$	1.6 (1.1-2.1)	2.6 (2.0-3.2)	$p < 0.01$
Diarrhea	2.3 (1.8-2.8)	2.0 (1.5-2.4)	ns	2.0 (1.5-2.4)	2.0 (1.5-2.6)	ns
Indigestion	2.7 (2.2-3.1)	2.2 (1.8-2.6)	ns	2.5 (2.0-2.9)	2.4 (2.0-2.8)	ns
Constipation	1.5 (1.3-1.7)	1.4 (1.2-1.7)	ns	1.8 (1.3-2.3)	1.8 (1.3-1.7)	ns
Total GSRS	2.0 (1.7-2.2)	2.2 (1.7-2.4)	ns	2.1 (1.7-2.4)	2.2 (1.9-2.5)	ns
PGWB						
Anxiety	26 (25-27)	23 (21-25)	$p < 0.05$	24 (22-26)	22 (20-25)	ns
Depression	16 (16-17)	16 (15-17)	ns	15 (14-17)	16 (14-17)	ns
Pos. well-being	17 (16-19)	15 (14-16)	$p < 0.05$	16 (14-17)	15 (13-17)	ns
Self-control	17 (16-17)	15 (13-16)	$p < 0.01$	16 (14-17)	15 (14-16)	ns
General health	16 (15-17)	14 (12-15)	$p < 0.01$	14 (13-15)	14 (13-15)	ns
Vitality	19 (19-20)	16 (14-18)	$p < 0.01$	16 (14-18)	16 (14-17)	ns
Total PGWB	112 (107-117)	99 (91-106)	$p < 0.01$	101 (93-108)	97 (89-105)	ns

Secondary outcome(s):

Comments:

Compliance: NA

Adverse Events:

	Laparoscopy n=215 (%)	**Open n=158 (%)**
Peroperative		
- pneomothorax	6	
- intraabd. Bleeding		2
SUM	6 (2.8)	2 (1.3)
Early postoperative		
- gastric perforation	1	
- bleeding, transfusion	2	
- crural rupture		1
- pulmonary embolism	1	
- lung infection	8	4
- wound infection		2
- acute paraesoph. Herniation	3	
SUM	15 (7.0)	7 (4.4)
Late postoperative		
- ventral hernia		2
- port site hernia	13	
- diaphragmatic hernia		1
- paraesophageal herniation	9	
- slipped Nissen	6	1
- disrupted Nissen or Toupet	3	

SUM	31 (14.4)	4 (2.5)
Complications total	52 (24.2)	13 (8.3)
Reoperations	17 (7.0)	5 (3.2)

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Szucs	**Yr: 2009**	**UI: 18783388**	**Questions addressed: KQ1,3**	**Extractor: MC**

Objective/Topic:
To assess the difference in direct medical costs between on-demand (OD) treatment with esomeprazole (E) 20 mg and continuous (C) treatment with E 20 mg qd.

Study design:	**Country/Setting:**	**Funding:**
open-label, randomized, multicenter study	Switzerland	AstraZeneca AG

Interventions(s):	**Comparator(s):**
Esomeprazole 20 mg Continuous daily for 26 weeks; one tablet once daily	Esomeprazole 20 mg On-demand; take one tablet daily if needed for the relief of heartburn and to stop when the heartburn is adequately controlled

Primary outcome(s):	**Other outcome(s):**
GERD symptoms: At each visit, the presence of heartburn and regurgitation during the past 7 days before the visit was assessed retrospectively. These symptoms were classified as: - none, mild (awareness of symptoms, but easily tolerated) - moderate (discomfort sufficient to cause interference with normal activities) - severe (incapacitating, with inability to perform normal activities).	Patient satisfaction: Patient satisfaction was measured using a 7-point Likert scale (completely satisfied, very satisfied, quite satisfied, satisfied, dissatisfied, very dissatisfied, and completely dissatisfied). Adverse events. In this trial, only serious adverse events (SAEs) and adverse events (AEs) leading to the discontinuation of the study drug or other important AEs according to the investigator occurring from the first administration of the study drug until the end of the study were recorded.

Inclusion criteria:	**Exclusion criteria:**
Endoscopically uninvestigated adult patients seeking primary care in Switzerland for symptoms suggestive of GERD (heartburn as the predominant symptom with or without acid regurgitation; for 3 days or more during the last 7 days) who demonstrated complete relief of symptoms (defined as patients with complete resolution of symptoms of not more than 1 day, with mild symptoms during the last 7 days before the visit) after an initial treatment of 4 weeks with esomeprazole 40 mg.	- existence of any significant “alarm symptoms,” such as unintentional weight loss, gastrointestinal bleeding, dysphagia, jaundice, or any other sign indicating serious or malignant disease - known history of complications of GERD, such as Barrett’s esophagus, esophageal stricture, ulcer, or significant dysplastic changes in the esophagus and or a history of esophageal, gastric, or duodenal surgery - current or historical evidence of irritable bowel syndrome, Zollinger-Ellison syndrome, primary esophageal motility disorder(s), gastric or duodenal ulcers within the last 3 months, malabsorption, unstable diabetes mellitus, or cerebrovascular disease - in need for continuous concurrent therapy of diazepam, phenytoin, or warfarin - pregnancy and lactation
Symptoms (describe): Heartburn (97%), regurgitation (85%), and epigastric pain (85%)	**Hiatal hernia (specify whether considered and size used for exclusion):** No data
EGD (performed or not and results): Performed (data not reported)	**Esophagitis/stricture/Barrett’s:** none
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras,**

No data	**Lifestyle modifications or other):** All patients responded to 4 weeks esomeprazole 40 mg treatment prior randomization
Esophageal manometric studies (performed or not and results): No data	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: B	
Blinding: no blinding	**Allocation concealment: not applicable**
Intention-to-treat: yes	**Method of Randomization: no data**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
	x	

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 55 (range 18-99) y	**N enrolled: 1935**
%Male: no data	**N completed: 1904**
Race: no data	**Dropouts/reasons: 31 patients excluded form the analysis due to persisting symptoms at visit 2 (n=16), unknown quantity of study drug used (n=14), and other reason (n=1)**
BMI: no data	**Follow-up period: 6 months**
Comments: Primary purpose of this study was to conduct a cost-effectiveness analysis (data not extracted or included in our report) so the reporting of baseline patients characteristics was limited	

Results

Primary outcome(s):
Mean number of tablets used in the on-demand group versus continuous: 116 (SD 63.1; median: 100) tablets versus 174 (SD 46.9; median: 188) tablets. This indicates that the on-demand group took their medication 4 to 5 days out of a 7-day week, whereas patients on continuous treatment took their tablets almost daily.

Summary of GERD symptoms at the end of the 6-month maintenance phase (last observation carried forward)

Symptoms	Esomeprazole 20 mg	
	On-demand (n=991)	Continuous (n=913)
Percentage of patients with heartburn by severity of symptom		
None*	80%	86%
Mild	12%	11%
Moderate	6%	2%
Severe	1%	1%
Percentage of patients with regurgitation by severity of symptom		
None	86%	89%
Mild	9%	8%
Moderate	4%	3%
Severe	1%	1%
Percentage of patients with epigastric pain by severity of symptom		
None	89%	89%

Mild	7%	9%
Moderate	3%	2%
Severe	1%	0%
Mean number of reflux days (SD)	0.43 (1.2	0.37 (1.2)

*P<0.001

Secondary outcome(s):

Comments:

Compliance:

Adverse Events:
"Esomeprazole was generally well tolerated. There were no tolerability concerns arising from this study, and there were no clinically relevant differences between the treatment groups regarding the profile or incidence of adverse events." [Note: specific adverse events were not reported]

Applicability: (narrow/wide): wide	**Comments:**

First author: Tedesco	**Year:** 2006	**UI: 16549695**

Modifying Factor(s): age

Study design: Retrospective review of findings from a prospective acquired database	**Country:** USA **Multicenter:** no	**Funding:** unspecified

Interventions(s): all patients underwent 360 degree fundiplication. post-operative symptoms scores were compared between older (B group) and younger (A) group . presence , duration, and severity of GERD symptoms were evaluated, presence of a hiatal hernia or esophageal stricture evaluated incidence of complications and length of hospital measured

Primary outcome(s): Duration of operation was similar in both groups, incidence of intraoperative /postoperative complications was low and similar in both groups, heartburn resolved in approx 90% in each group.	**Other outcome(s):** elderly patients more often had regurgitation and respiratory symptoms in addition to heartburn

Baseline characteristics: Group A (<65) vs. group B (>65)
GERD definition for the population included:
Age: , Group A:media age 46, Group B median age (69 years)

Gender: %Male (133/241 group A) <65
(35/63 group B) >65

Race: n/a
BMI: n/a
Severity of symptoms: : table 1 compared % of patients in each group wth heartburn, dysphagia, regurg,chest pain, cough , response to PPI
Duration of symptoms: symptomatic for an average of 60 months
Frequency of symptoms: n/a
Type of medications: use of acid-suppressing meds was discontinued 3 to 14 days before the study.
Acid reflux (by pH study): yes data incorporated into DeMeester DeMeester score and a score greater than 14.7 was considered to be abnormal.
Abnormal manometry study: yes; mean LES pressure of each group is presented and compared
Esophagitis by endoscopy: degree of esophagitis was graded according to Savary-Miller classification

Significant baseline differences between GroupA (<65) and Group B >65)

Preop Symptoms:	Group A	Group B
Heartburn	86%	47%
Dysphagia	38%	35%
Regurgitation	47%	71%
Chest pain	39%	28%

EGD: not reported
EMS: see below
PH study: time at pH <4% reported
Hiatal hernia: not compared
Meds used in the groups: n/a

Pre-op testing:	Group A <65	Group B >65
LES pressure (mean)	11+-6	12+-6
UES pressure	79+-32	77+-31
DeMeester Score	63+-44	54+-33

N enrolled per group: N enrolled: 551 consecutive patients	GroupA n/a	GroupB: n/a	
N com pleted per group: 304 included in study	GroupA 241	GroupB: 63	
Follow-up	15±21 months (range, 1-48months)	26±25 months (range, 1-60 months)	

Outcomes (as reported in the Results)	**Results**		
	GroupA: *<65*	GroupB: *>65*	GroupC: n/a
Symptom improvement Post-op symptoms score mean +-SD 0=no symptoms 4= disabling symptoms			
Heartburn p= 0.37	0.3 +-0.8	0.2 +- 0.8	
Dysphagia p=0.37	0.3 +- 0.8	0.2 +-0.8	
Regurgitation p>.99 Heartburn resolved Regurgitation resolved De nova dysphagia p=0.80	0.2 +-0.6 89% 94% 6%	0.2 +- 0.7 90% 97% 12%	

Adverse Events: ND (if reported, please add proportion of patients per adverse event; also separate to minor or major adverse events)

Quality Assessment:
Description of the biological plausibility for the hypothesis to be tested: yes
Description of inclusion /exclusion criteria and rationale: yes/no
Documentation of how data were collected and analyzed (eg, blinding): yes/no
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): no
Participant drop-out percentage (>20%?): yes
Description of statistical methods in sufficient detail to be replicated: yes
Overall grade: C

Comments: did have significant dropout from 551 to 304. groups were separated by age, the authors compared pre-op characteristics however did not really do a case-control match; group sizes were unbalanced and no adjustment was shown

ND: no data

GERD data extraction form

Author: Teixeira	Yr: 2009	UI:19453033	Questions addressed: 1,2,3	Extractor: SI

Objective/Topic: to examine QoL after LARS and modifying factors

Study design: retrospective	Country/Setting: Portugal	Funding: nd

Interventions(s): Nissen laparoscopic fundoplication	Comparator(s):

Primary outcome(s): QoL	Other outcome(s):

Inclusion criteria: Pts with GERD	Exclusion criteria: nd
Symptoms (describe): nd	Hiatal hernia (specify whether considered and size used for exclusion): 43% had a diaphragmatic hernia (62/143)
EGD (performed or not and results): yes, data not presented	Esophagitis/stricture/Barrett's: 24% erosive esophagitis (34/143); 4% Barrett's (6/143)
pH study (performed or not and results): yes, data not presented	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): nd
Esophageal manometric studies (performed or not and results): yes, data not presented	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
y

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: retrospective, no adjustment; QoL scale not externally validated; no power calculation

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 49.9 ± 4.55	N enrolled: 168
%Male: 42	N completed: 143
Race: nd	Dropouts/reasons: 6 refused to cooperate; 2 had incapacitating illnesses (Alzheimer and CVA); 5 died (unknown causes); 12 short follow up
BMI: nd	Follow-up period: 5.42 yr

GERD data extraction form

Comments:

Results
Primary outcome(s): QoL (scale included GI and non-GI symptoms, medication, physical , emotional and psychosocial; maximum score of 96, the higher the score, the better) Preop 56.25 ± 13.30 SD Postop @ 5 yr 74.00 ± 13.78 SD Net difference 17.50 ± 11.37 (P<0.001) Digestive symptoms. Average of the difference of the several items. Before vs. Present (Score 0-3) Heartburn +2.203* Medication +2.13* Regurgitation +1.95* Necessity to eat slowly +1.50* Gastralgia +1.23* Diet +1.18* Dysphagia +0.88* Incapacity to belch +0.74* Vomiting +0.69* Fullness +0.629* Nausea +0.61* Bad breath +0.42* Odynophagia +0.41* Gas bloating +0.40* Obstipation +0.16* Diarrhoea +0.10 (NS) *p<0.001
Secondary outcome(s): net difference in subgroups esophagitis severe vs. non-severe +18.4 ± 8.14 vs. +17.6 ± 12.23 hernia present vs. absent +16.1 ± 10.56 vs. +19.0 ± 11.80 sex male vs. female +17.6 ± 10.49 vs. +17.9 ± 6.57 age >45 vs. ≤45 +16.6 ± 10.37 vs. +19.7 ± 12.71 No significant differences in any of these comparisons

Treatment/Comparison:	Laparoscopic Nissen Fundoplilcation					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
Age (>45 vs. ≤45)					no difference	
Sex					no difference	
Esophagitis (severe vs. non-severe)					no difference	
Hiatal hernia					no difference	
Comments:						

GERD data extraction form

Compliance: nd

Adverse Events:
no operation mortality: 0/143 (0%) respiratory complications: 6/143 (4.2%) serious dysphagia: 6/143 (4.2%) conversion rate: 4/143 (2.7%)

Applicability: (narrow/wide): narrow	Comments: difficult to judge with lack of details on the population

GERD data extraction form

Author: Tepes	Yr: 2009	UI: 19453031	Questions addressed: 1,3	Extractor: WY

Objective/Topic:
Compare on-demand therapy with omeprazole 20mg and continuous therapy with omeprazole 10mg q day for 12 months for GERD maintenance

Study design:	Country/Setting:	Funding:
Controlled trial, some of the pts were randomized (see Quality Assessment section for details)	Slovenia, 24 out-pt clinics and hospitals	Not reported

Interventions(s):	Comparator(s):
Omeprazole 20mg on demand, but max of 3 consecutive days, for 12 months Can use antacid as needed	(1) omeprazole 10mg q day for 12 months; can use antacid as needed (2) omeprazole 20mg q day for 12 months; can use antacid as needed

Primary outcome(s):	Other outcome(s):
Percentage of pts in remission	Percentage of pts relapse Quality of life Adverse events

Inclusion criteria:	Exclusion criteria:
At least 18 years old, not pregnant, use adequate contraceptive (women at child-bearing age), heartburn and regurgitation resolved after omeprazole therapy for 8-16 weeks, no heartburn and regurgitation in the 7 days prior to study enrollment	Esophageal or gastric malignancy, terminal state of any diagnosis, renal impairment w/creatinine >300umol/L, Barrett's esophagus with dysplasia, active gastric or duodenal ulcer, GERD symptoms unresolved with 6 month of PPI Tx, use of continuous Tx with PPI w/i 30days prior to study, hypersensitivity to omeprazole, use of drugs that affect outcomes of Tx
Symptoms (describe): no	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): Grading before healing from omeprazole Tx before enrollment: No esophagitis: 25.9%, 56 pts Grade A: 38.9%, 84 pts Grade B: 25.9%, 56 pts Grade C or D: 9.3%, 20 pts	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): All esophagitis healed per endoscopy after omeprazole 20mg or 40mg q day for 8-16 weeks
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

GERD data extraction form

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding: no	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B/acceptable
Comments: Some of the pts were randomized but some were not. Pts with non-erosive disease and pts with erosive with LA grade A and B were randomized to either omeprazole 20mg on demand or 10mg q day continuously. Pts with healed ERD grade C and D were assigned omeprazole 20mg q day. Both ITT and PP analyses were performed. Blinding was not possible in this treatment design. There was no allocation concealment.

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: not reported	N enrolled: 216
%Male: not reported	N completed: 186
Race: not reported	Dropouts/reasons: non-compliance (6 in on-demand Tx group, 7 in 10mg continuous Tx group, 2 in 20mg continuous Tx group), new diagnosis occurrence or pregnancy (2 in on-demand Tx group, 2 in 10mg continuous Tx group), withdrew consent (1 in on-demand Tx group, 4 in 10mg continuous Tx group), unknown (2 in on-demand Tx group, 4 in 10mg continuous Tx group)
BMI: not reported	Follow-up period: 12 months
Comments: little demographic information was provided	

Results

Primary outcome(s):
Number and percentage of pts in remission

	Baseline LA grade	# of pts total	# of pts in remission at 12 months	% of pts in remission at 12 months (ITT) (%, 95%CI)	% of pts in remission at 12 months (PP)
Omeprazole 20mg on demand	No esophagitis	31	15	48.4% (30.8%, 66.0%)	57.7% (38.7%, 76.75%)
	Grade A	47	28	59.6% (45.6%, 73.6%)	65.1% (50.95%, 79.4%)
	Grade B	16	11	68.8% (46.0%, 91.5%)	78.6%
Omeprazole 10mg q day	No esophagitis	25	19	76.0% (59.2%, 92.7%)	90.5% (77.9%, 100%)
	Grade A	37	28	75.7% (61.9%, 89.5%)	90.3% (79.9%, 100%)
	Grade B	40	25	62.5% (47.5%, 77.5%)	75.8%
Omeprazole 20mg q day	Grade C or D	20	12	60% (38.5%, 81.5%)	66.7%

There was significant difference between omeprazole 20mg on demand group and omeprazole 10mg continuous group among pts with no esophagitis in both ITT and PP analyses ($p<0.05$).

There was no statistically significant different between omeprazole 20mg on demand group and omeprazole 10mg continuous group among pts with Grade A prior to healing in ITT analysis ($p=0.12$), but significant in PP analysis

(p<0.01).

There was no significant difference between omeprazole 20mg on demand group and omeprazole 10mg continuous group among pts and those with Grade B prior to healing in ITT analysis (p>0.05) and PP analysis (p=0.3).

Secondary outcome(s):
Number of pts relapse

	Baseline LA grade	# of pts total	# of pts relapse at 12 months
Omeprazole 20mg on demand	No esophagitis	31	11
	Grade A	47	15
	Grade B	16	4
Omeprazole 10mg q day	No esophagitis	25	2
	Grade A	37	4
	Grade B	40	8
Omeprazole 20mg q day	Grade C or D	20	8

Mean health-related quality of life score at 12 months (ranges from 1 to 10; 10 is best quality of life)
Omeprazole 20mg on demand: 9.4
Omeprazole 10mg q day: 9.7
Omeprazole 20mg q day: 9.8
p>0.05

Comments:
Primary outcome was not specified.

Compliance:
NA

Adverse Events:
Total of 37 adverse events from 16 pts (14 from omeprazole 10mg continuous group, 2 from omeprazole 20mg continuous group).
Adverse events at 3 months: headache (2.5%), fatigue (1.6%), constipation (1.6%), diarrhea (0.8%), skin rash (0.8%)
Adverse events at 12 months: headache (1%), vertigo (1%), diarrhea (1%).

Applicability: (narrow/wide): narrow	Comments: little demographic information was provided

GERD data extraction form

Author: Testoni	Yr: 2010	UI: 20091308	Questions addressed:1	Extractor: WY

Objective/Topic:
To evaluate the effectiveness of transoral incisionless fundoplication using EsophyX on GERD symptoms, PPI use, and pH-impedance

Study design:	Country/Setting:	Funding:
cohort	Italy	nd

Interventions(s):	Comparator(s):
EsophyX	NA

Primary outcome(s):	Other outcome(s):
GERD symptoms, PPI use, pH-impedance	

Inclusion criteria:	Exclusion criteria:
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: small sample size, short followup

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:45 ±14	N enrolled: 20
%Male: 60%	N completed:18
Race: nd	Dropouts/reasons: 2 had 24-hr pH-impedance within normal range so they were excluded from the followup analysis.

GERD data extraction form

BMI: 24 ± 3	Follow-up period: 6 months
Comments:	

Results				
Primary outcome(s):				
GERD-HRQL when off PPI (45 ± 20 vs. 16 ± 14, P < 0.001)	GERD-QUAL when off PPI (114 ± 29 vs. 74 ± 21, P < 0.001)	Grade 0 (17% vs. 22%, NS)	Off PPI (0% vs. 55.6%)	DeMeester score (20 ± 13 vs. 18 ± 17, NS) LES pressure (8 ± 5 vs. 10 ± 3, NS)
Secondary outcome(s):				
Comments:				

Compliance:

Adverse Events: nd

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Thibault	**Yr: 2006**	**UI: 16907894**	**Questions addressed: 1,2, 3**	**Extractor: DM**

Objective/Topic: To compare the long-term outcomes after Anti-Reflux Surgery (ARS) in two groups of patients with either non-erosive reflux disease (NERD) or Erosive oesophagitis (EO)

Study design: non-randomized comparative study of effects of ARS in 2 subgroups of GERD patients	**Country/Setting:** France/ Community Hospital	**Funding:** No external funding

Interventions(s): ARS in NERD patients	**Comparator(s):** ARS in EO patients

Primary outcome(s):	**Other outcome(s):**
Quality of life (This questionnaire consists of 37-items divided into seven dimensions (daily life, social life, well-being, mental health, fears, sleeping and feeding). Every item is graded according to a 5- grade Likert scale, consisting in five possible answers, each scored from 1 (‘very much’ or ‘permanently’) to 5 (‘never’ or ‘not at all’). Then these scores are linearly transformed from 1, 2, 3, 4, 5 to 0, 25, 50, 75, 100 respectively (0 representing the worst QOL and 100 the best QOL). The score of each dimension is determined as the mean of the scores of all the items constituting the dimension. The global REFLUX-QUAL score is determined as the mean of the scores of the seven dimensions, and is also graded from 0 to 100)	Post-operative use of antireflux drugs Post-operative symptoms

Inclusion criteria:

1) an antecedent history of GERD symptoms for more than 6 months
2) clear evidence that acid reflux was responsible for symptoms; in practice all patients had 24-h pH monitoring analysis and only those with a symptom index (SI) $\geq$50% and a symptom-association probability (SAP) equal to or higher than 95% were recruited. Patients with normal oesophageal acid exposure fitting these criteria were also included as recent studies have shown that acid exposure is normal in 30–50% of NERD patients
3) an upper gastrointestinal (GI) endoscopy performed within 6 months preceding ARS. Adequate information regarding the presence or the absence of mucosal breaks was required to be present in the patient record.

Exclusion criteria:

1) oesophageal stricture
2) a previous history of upper GI surgery
3) primary oesophageal motility disorder such as achalasia (which was the main reason for the systematic use of manometry prior to ARS).

Symptoms (describe):
All values are represented as n(%)

Variable	NERD (n=60)	EO (n=61)
Heartburn	54(90)	55(90)
Regurgitation	52(87)	50(82)
Epigastric burning	39(65)	43(70)
Dysphagia	12(20)	14(23)
Extradigestive	38(63)	38(62)

Hiatal hernia (specify whether considered and size used for exclusion): Not used for exclusion

Variable	NERD (n=60)	EO (n=61)
Hiatal hernia	29(48)	37(60)

Dyspepsia	48(80)	44(72)

EGD (performed or not and results):
Yes

Variable	NERD (n=60)	EO (n=61)
Mild/moderate oesophagitis (Los Angeles (LA) grades A and B)	0	55(90)
Severe oesophagitis (Los Angeles (LA) grades C and D)	0	6(10)
Barrett's oesophagus	4(7)	2(3)

Esophagitis/stricture/Barrett's: see EGD results

PH study (performed or not and results):
Values in mean + s.d unless indicated otherwise

Variable	NERD (n=60)	EO (n=61)
Total time pH<4 expressed as percentage	10.1 ± 5.1	10.0 ± 5.3
Oesophageal acid exposure abnormal (% of subjects)	83.3	83.6
Symptom index represented as percentage	77 ± 16	78 ± 16
Symptom association probability represented as percentage	99.9 ± 0.007	99.9 ± 0.009

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):

Variable	NERD (n=60)	EO (n=61)
PPIs	50(83)	49(80)
H2-blockers	4(7)	2(3)
Prokinetics	1(2)	1(2)
Unknown	5(8)	9(15)

Esophageal manometric studies (performed or not and results):

Variable	NERD (n=60)	EO (n=61)
Lower oesophageal sphincter pressure (mmHg)	16.6 ± 9.2	12.9 ± 6.7

Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
YES

Quality Assessment for RCTs:	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: No steps were taken to prevent selection bias in recruitment. The group of patients excluded after recruitment reported more daily symptoms and more dysphagia, but less regurgitation, and dyspepsia. They were not different in proportion of NERD and EO, as well as pH monitoring and motility parameters.

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 47 yrs	**N enrolled:** 194 recruited
%Male: 59.5 yrs	**N completed:** 121 included in analysis

Race: nd	**Dropouts/reasons:** 26 lack of QOL questionnaire, 20 lost to follow up, 19 opted for medical treatment, 7 did not have endoscopic data, 1 opted for radiofrequency treatment
BMI: nd	**Follow-up period:** 43 ± 19 months (12-82 mths), no differences between 2 groups. As per (inclusion criteria), the response rate to REFLUX-QUAL questionnaires was 100% while information on post-operative symptoms and drug use was available in 82% and 100% of cases respectively
Comments: Age was significantly different between the two groups (p=0.001)	

Results

Primary outcome(s):
Quality of life

Variable	NERD (n=60)	EO (n=61)
Global score	75 + 26	84 + 19
Daily life	82 + 25	89 + 21
Social life	72 + 31 *	86 + 25 *
Well-being	74 + 28	82 + 24
Psychism	70 + 34	80 + 27
Fears	76 + 29	86 + 22
Sleep	81 + 26	86 + 19
Feeding	72 + 31	78 + 24

* $p < 0.05$

Overall, 58% of patients reported excellent postoperative QOL (REFLUX-QOL > 80) after ARS (52% in NERD and 64% in the EO group, N.S.). The HRQOL was more severely impaired in female than in male patients, especially in the NERD group. An excellent post-operative HRQOL was reported by 72% of males and 37% of females (P = 0.0002).

Secondary outcome(s):
Postoperative drug use

	NERD(n=60)	**EO (n=61)**	**p-value**
Antireflux drug therapy N (%)	23(39)	15(25)	0.08
Drug needs N (%)			
Daily	19(32)	11(19)	N.S.
Weekly	1(2)	2(3)	N.S.
Monthly	3(5)	2(3)	N.S.
Type of drugs N (%)			
PPIs	19(32)	6(10)	0.005
H2-blockers	1(2)	1(2)	N.S.
Antiacids	1(2)	6(10)	0.05
Prokinetics	2(3)	2(3)	N.S.

Post-operative use of antireflux drugs was reported by 31% of patients. The proportion of patients continuing to take antireflux drugs was higher in the NERD cohort compared with EO group. Patients with NERD reported a significantly greater post-operative use of PPIs when compared to patients with EO. The most frequent dosing regimen reported corresponded to a daily use therapy.

Post-Operative symptoms
Daily symptoms were significantly more frequently reported by patients with NERD when compared to patients with EO. Patients with NERD reported more reflux-related symptoms (heartburn, regurgitation, epigastric burning)

GERD data extraction form

	NERD(n=60)	EO (n=61)	p-value
Frequency, N (%)			
Daily	30 (50)	18 (29)	0.03
Weekly	8 (13)	15 (24)	N.S.
Monthly	6 (10)	11 (18)	N.S.
Typical GERD symptoms, N (%)			
Heartburn	12 (20)	7 (11)	N.S.
Regurgitation	13 (22)	5 (8)	0.04
Epigastric burning	14 (23)	6 (10)	0.04
Atypical GERD symptoms, N (%)			
Chest pain	14 (23)	10 (16)	N.S.
Abdominal pain	15 (25)	11 (18)	N.S.
Respiratory symptoms	5 (8)	9 (15)	N.S.
ENT symptoms	16 (27)	11 (18)	N.S.
Dyspepsia symptoms, N (%)			
Epigastric weigh	20 (33)	18 (29)	N.S.
Epigastric pain	18 (30)	12 (20)	N.S.
Early satiety	14 (23)	13 (21)	N.S.
Bloating	26 (43)	24 (39)	N.S.
Indigestion	19 (32)	11 (18)	0.08
Nausea	7 (12)	6 (10)	N.S.
Vomiting	2 (3)	2 (3)	N.S.
Anorexia	5 (8)	3 (5)	N.S.

Comments:

Compliance:
NA

Adverse Events:

Side-effects of ARS, N (%)

	NERD (n=60)	EO (n=61)	Total (n=121)	p-value
Inability to belch	15 (25)	13 (21)	28 (23.1%)	N.S.
Inability to vomit	15 (25)	17 (28)	32 (26.4%)	N.S.
Dysphagia	13 (22)	20 (33)	33 (27.3%)	N.S.
Flatulence	26 (43)	23 (38)	49 (40.5%)	N.S.
Diarrhoea	9 (15)	10 (16)	19 (15.7%)	N.S.

Applicability: (narrow/wide): narrow	**Comments:**

GERD data extraction form

Author: Trullenque, R	**Yr:** 2005	**UI: 16004525**	**Questions addressed:** KQ1; 3	**Extractor:** Peter Bonis

Objective/Topic: Compare a 360 degree short and floppy laparoscopic Nissen fundoplication to an open procedure.

Study design: Prospective observational.	**Country/Setting:** General Hospital, Valencia, Spain	**Funding:** ND

Interventions(s): Laparoscopic Nissen fundoplication	**Comparator(s):** Open Nissen fundoplication

Primary outcome(s): Perioperative morbidity and mortality and effect on GERD symptoms	**Other outcome(s):** Results of ambulatory pH studies, upper endoscopy.

Inclusion criteria: 1) Absent or partial response to 8-12 weeks of medical treatment (not specified which kind), 2) those who responded to treatment but relapsed when it was discontinued or desired to be off medications 3) GERD complications (Grade II-IV esophagitis, stricture, ulcer, bleeding or atypical manifestations)	**Exclusion criteria:** ND
Symptoms (describe): No reporting of baseline characteristics of enrolled patients	**Hiatal hernia (specify whether considered and size used for exclusion):**
EGD (performed or not and results):	**Esophagitis/stricture/Barrett's:**
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results):	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs:
Comments: C/Poor. Dropouts not described (although follow-up reported as greater than 85%), average length of f/u not described, baseline characteristics of patients not described, proportion of group eligible for assessment at various time points not described.

GERD data extraction form

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

Characteristics of enrolled patients ND	Results: Disposition of Enrolled Subjects
Age:	**N enrolled:** 75 laparoscopic group, 28 open group
%Male:	**N completed:** Follow-up in more than 85% but data details not provided
Race:	**Dropouts/reasons:**
BMI:	**Follow-up period:**
Comments:	

Results
Primary outcome(s): Higher perioperative morbidity in open group (14.2 versus 6.6%); faster recovery and less pain in laparoscopic group; zero mortality in either group, return to work earlier in laparoscopic group; good result (Visick I and II) ranged from 94.6 to 100% in laparoscopic group compared with 66.6 to 100% in open group; satisfaction (would be willing to undergo procedure again) similar (92 versus 82.2%); recurrent symptoms requiring PPIs in 3 patients in laparoscopic group while two in the open group required reoperation for recurrent symptoms; late dysphagia occurred in 5 to 9% of laparoscopic group compared with 3.6-7.1% of open group.
Secondary outcome(s):
Comments: Authors report multiple outcomes at different time points but unclear how many patients were eligible to be assessed at each time point. Derivation of ranges for proportions described above unclear.

Compliance:

Adverse Events:

	Laparoscopic surgery	Open surgery
In the immediate postoperative period		
Conversion	1/75	0/28
Mortality	0/75	0/28
Others	Abdominal hematoma 1, wound complication 2, solid-induced dysphagia 2, subcutaneous emphysemas 3	Abdominal hemorrhage 1, hemothorax 1, surgical wound complication 3, solid-induced dysphagia 2
Revision (1 year minimum and 8 years maximum)		
Re-operation	0	3
Dysphagia	1	0
Early satiety	1	0
Meteorism	4	0
Gas bloat	1	0
Hindered vomiting and burping	15	1
Diarrhea	2	0
Hiccup	1	0

Applicability: (narrow/wide): narrow	Comments: Older study, poorly reported and analyzed, unclear if used contemporary surgical techniques for laparoscopic approach, nonrandomized design

GERD data extraction form

Author: Tsereteli	Yr: 2009	UI: 19172353	Questions addressed: 1	Extractor: WY

Objective/Topic:

Study design:	Country/Setting:	Funding:

Interventions(s):	Comparator(s):

Primary outcome(s):	Other outcome(s):

Inclusion criteria: At least 18 years old Had GERD Had laparoscopic Nissen fundoplication at the University of Missouri—Columbia medical center between 1999 and 2006 Had preoperative esophageal manometric assessment	Exclusion criteria:
Symptoms (describe):	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results):	Esophagitis/stricture/Barrett's:
PH study (performed or not and results):	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results):	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age:	N enrolled:
%Male:	N completed:
Race:	Dropouts/reasons:
BMI:	Follow-up period:
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Compliance:

Adverse Events:

Applicability: (narrow/wide):	Comments:

GERD data extraction form

Author: Vasiliadis	**Yr**: 2010	**UI**: 19809412	**Questions addressed**: 1, 3	**Extractor**: JC

Objective/Topic: Investigate efficacy of 3 different dosages of esomeprazole in pts receiving maintenance therapy for GERD, using the Bravo pH system.

Study design: RCT	**Country/Setting**: Not described	**Funding**: None

Interventions(s): group A: esomeprazole 40 mg twice daily; group B: esomeprazole 40 mg once daily; group C: esomeprazole 40 mg once every other day	**Comparator(s)**:

Primary outcome(s): % of total time with pH<4 using 48h Bravo wireless capsule pH system and DeMeester score.	**Other outcome(s)**:

Inclusion criteria: Non-erosive reflux disease (NERD or Endoscopy-negative reflux disease ENRD) or those with reflux esophagitis grade A or B, healed at time of enrollment, requiring long-term PPI therapy. NERD/ENRD defined as presence of typical reflux symptoms with normal endoscopy and positive 24h esophageal pH study while pts were not receiving antisecretory agents. Esophagitis defined according to the Los Angeles classification.	**Exclusion criteria:** Age < 18 or >70-years old; pregnancy or lactation; Barrett ' s esophagus; Zollinger-Ellison syndrome; scleroderma; achalasia; hemorrhagic diathesis (PLT < 30,000 or INR >1,5); history of esophagitis C or D (LA classification); stenosis of the gastrointestinal (GI) tract; serious co-morbidity (ASA class >III); esophageal varices; cardiac pacemaker; previous esophageal, gastric or duodenal surgery; recent GI bleeding; severe liver disease (Child Pugh class B or C) including cirrhosis and acute or chronic hepatitis; active inflammatory bowel disease; impaired renal function; unstable diabetes mellitus; recent (< 10 days) use of antisecretory medications; requirement — during the study period — for anticoagulants, anticholinergics, prostaglandin analogs, antineoplastic agents, steroids, H 2 receptor antagonists, sucralfate, bismuth compounds, promotility drugs, macrolide antibiotics, barbiturates, anticonvulsants, narcotics; inability / refuse to consent.
Symptoms (describe): Abnormal intraesophageal pH was defined as 24h time with pH <4.0 being 4% or DeMeester score higher than 14.7.	**Hiatal hernia (specify whether considered and size used for exclusion)**: determined during initial endoscopy, not used for exclusion.
EGD (performed or not and results): Performed and graded according to Los Angeles classification. See inclusion and exclusion criteria.	**Esophagitis/stricture/Barrett's**: BE used for exclusion.
pH study (performed or not and results): Intraesophageal pH monitored for 2 consecutive days using Bravo system 30 days after randomization. See results.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** See inclusion and exclusion criteria.
Esophageal manometric studies (performed or	Other: Helicobacter pylori status was determined using

not and results): Not described.	rapid urease testing while off PPI.

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: B	
Blinding: no	Allocation concealment: sealed envelope
Intention-to-treat: Yes	Method of Randomization: Not described
Other comments:	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
X		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: mean (s.d) A: 40.96 (11.98); B: 44.17 (11.18); C: 42.68 (11.34)	N enrolled: 75
%Male: 72.6%	N completed: 73
Race: all Caucasian	Dropouts/reasons: 2, early detachment of Bravo capsule, Loss of communication b/w capsule and receiver
BMI: mean (s.d) A: 26.6 (.97); B: 27.2 (.87); C: 26.8 (1.17)	Follow-up period: 30 days
Comments:	

Results

Primary outcome(s):

Mean (± s.d.) percent of total time pH < 4 & De Meester score on the first day of the study for the 3 groups

	Group A	**Group B**	**Group C**
Percent time pH < 4	0.9 ± 1.2	1.5 ± 1.6	1.3 ± 1.0
De Meester	4.1 ± 4.0	7.0 ± 6.9	6.0 ± 3.3

Mean (± s.d.) percent of total time pH < 4 & De Meester score on the second day of the study for the 3 groups

	Group A	**Group B**	**Group C**
Percent time pH < 4	0.7 ± 1.0	1.5 ± 1.8	7.0 ± 4.4
De Meester	3.9 ± 5.9	6.4 ± 6.6	29.4 ± 19.4

Secondary outcome(s):

Comments:

Compliance:

Adverse Events: none AEs reported as a result of Tx

Applicability: (narrow/wide): narrow	Comments: 91% NERD, all Caucasian, small sample size

GERD data extraction form

Author: Vcev	Yr: 2006	UI: 17058517	Questions addressed: 1,2,3	Extractor: JHL

Objective/Topic: Esomeprazole versus Pantoprazole for Healing Erosive Oesophagitis

Study design: Randomized, single blind, multi-centre study	Country/Setting: Croatia	Funding: ND

Interventions(s):	Comparator(s):
• **Esomeprazole 40 mg once daily for 4 weeks** Those who had unhealed esophagitis or GERD symptom continued treatments for another 4 weeks.	• **Pantoprazole 40 mg once daily for 4 weeks**

Primary outcome(s): Healing and symptom relief ("healing" was not defined)	Other outcome(s):

Inclusion criteria: History of GERD symptoms for at least 6 months immediately prior to enrollment, confirmed by endoscopy and graded using the LA grading system	**Exclusion criteria:** Other significant upper gastrointestinal disorders (including Zollinger-Ellision syndrome, gastric or duodenal ulcer, oesophageal stricture, history of dysplasia in Barrett's oesophagus); intake of medication liable to affect the outcome of the study (including non-steroidal anti-inflammatory drugs); pregnancy, childbearing potential (unless taking suitable precautions) or lactation; alcohol and/or drug abuse; PPI use within 4 weeks prior to the first endoscopy
Symptoms (describe): Number of days with symptoms of heartburn over the previous 7 days	**Hiatal hernia (specify whether considered and size used for exclusion): ND**
EGD (performed or not and results): performed	**Esophagitis/stricture/Barrett's:** LA grade oesophagitis A/B/C • Esomeprazole 40 mg (Total n=90), 37/40/13 • Pantoprazole 40 mg (Total n=90), 35/39/16 Barrett's oesophagus • Esomeprazole 40 mg, n=6/90 (6.7%) • Pantoprazole 40 mg, n=5/90 (5.6%)
PH study (performed or not and results): Not performed	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: C	
Blinding: Yes	**Allocation concealment: No**
Intention-to-treat: Yes	**Method of Randomization: ND**
Other comments: Outcomes were not defined clearly. Multicenter study but the statistical analyses did not consider the potential differences by center. Inconsistent reporting of sample size between test and table. Only 135 patients had healing rate by LA grade data.	

GERD data extraction form

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		
A (confirmed by endoscopy and graded using the LA grading system		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 50.3 y	**N enrolled: 180**
%Male: 64.4%	**N completed: 176**
Race: ND	**Dropouts/reasons:** • 2 patients (intake unknown study drug) • 2 patients (study protocol violation)
BMI: ND	**Follow-up period: 8 weeks**
Comments:	

Results

Primary outcome(s):

- Proportion of heartburn-free days (esomeprazole 40mg: 70.2%, pantoprazole 40mg: 69.8%)
- Time to sustained heartburn resolution (the first day of seven consecutive days with no heartburn) - equally short for the both groups (median days; 6)
- Healing rates of erosive oesophagitis (EE) after 4 weeks treatment by LA grade severity

LA grade	Esomeprazole 40mg n (%)	Pantoprazole 40mg n (%)
A	31 (83.8%)	29 (82.8%)
B*	31 (77.5%)	28 (71.8%)
C**	8 (61.5%)	8 (50.0%)
All patients*	70 (77.8%)	65 (72.2%)

*p<0.05, ** p<0.01

- Healing rates of erosive oesophagitis (EE) after 8 weeks treatment by LA grade severity

LA grade	Esomeprazole 40mg n (%)	Pantoprazole 40mg n (%)
A	35 (94.6%)	33 (94.3%)
B	38 (95.0%)	37 (94.9%)
C	10 (76.9%)	12 (75.0%)
All patients	83 (92.2%)	82 (91.1%)

Secondary outcome(s):

Comments:

Compliance:

- Assessed by counting unused capsules at the end of the study, patients taking 75-110% of prescribed doses
- Compliance rates (esomeprazole 40mg: 87.6%, pantoprazole 40mg: 88.2%)

Adverse Events:

- esomeprazole 40mg: 12%, pantoprazole 40mg: 11%
- the most common adverse events
  - esomeprazole 40mg: nausea, dizziness and headache
  - pantoprazole 40mg: headache, diarrhea and nausea
- “All these adverse events were considered mild or moderate in intensity and none were considered treatment-related.”

GERD data extraction form

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Wada	**Yr:** 2005	**UI:** 15943840	**Questions addressed: 1**	**Extractor: JHL**

Objective/Topic: The efficacy of famotidine and omeprazole in the treatment of GERD, especially non-erosive GERD

Study design: Open label, RCT	**Country/Setting:** Japan	**Funding:** ND

Interventions(s): Famotidine 20mg twice daily	**Comparator(s):** Omeprazole 20mg once daily

Primary outcome(s): Symptoms of GERD	**Other outcome(s):** Health-related quality of life

Inclusion criteria:
Out-patients coming to Nagoya City University Hospital between September 2003 and October 2004

Exclusion criteria:
Having gastric or duodenal ulcer, cancer, other digestive diseases, a past history of upper gastrointestinal surgery, or treatment with PPI for the past 1 month

Symptoms (describe):

	Famotidine (n=25)	Omeprazole (n=26)
Frequency of heartburn (times/week)	3.7±2.3	2.9±2.0

Hiatal hernia (specify whether considered and size used for exclusion): Not considered

	Famotidine (n=25)	Omeprazole (n=26)
Presence of hiatal hernia	14 (56%)	16 (61.5%)

EGD (performed or not and results):
Not performed

Esophagitis/stricture/Barrett's: ND

	Famotidine (n=25)	Omeprazole (n=26)
Grade of esophagitis (N/A/B/C/D)	21/2/1/0/1	18/4/3/1/0

PH study (performed or not and results):
Not performed

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND

Esophageal manometric studies (performed or not and results):
Not performed

Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B/acceptable

Blinding: No, open-label study	**Allocation concealment:** Not reported
Intention-to-treat: Not clear (maybe no, patients excluded because of interruption of treatment)	**Method of Randomization:** Not reported

Other comments:

- The questionnaire for the diagnosis of reflux disease (QUEST) score was significantly higher in the OPZ group than in FAM group (P <0.05).
- At baseline, mean gastrointestinal symptom scores for total and abdominal pain (using Gastrointestinal Symptom Rating Scale) were statistically different between FAM and OPZ groups (P <0.05).

Quality Assessment Non-RCTs:

Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**

	X	
B; GERD was diagnosed based on a score of higher than 4 on QUEST and heartburn at least 2 days a week.		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 60.6y	**N enrolled: 54** (76.5% were non-erosive GERD patients.)
%Male: 41.2%	**N completed: 51**
Race: Asian	**Dropouts/reasons: 3** (interruption of treatment or failure to complete the questionnaire)
BMI: 22.1	**Follow-up period: 8 weeks**
Comments: The results were reported for only 39 non-erosive GERD patients. (FAM=21, OPZ=18)	

Results

Primary outcome(s):

Mean gastrointestinal symptom scores as evaluated with Gastrointestinal Symptoms Rating Scale (GSRS) among non-erosive GERD patients before and after treatment with famotidine or omeprazole

	Famotidine (n=21)			Omeprazole (n=18)		
	Before	After	P-value	Before	After	P-value
Total	2.56 ± 0.78*	2.13 ± 1.05	<0.05	2.04 ± 0.65	1.80 ± 0.54	0.12
Reflux	3.41 ± 1.01	2.35 ± 1.54	<0.05	2.44 ± 1.24	1.90 ± 0.71	0.05
Abdominal pain	2.49 ± 0.96*	1.86 ± 0.81	<0.05	1.93 ± 0.73	1.82 ± 1.04	0.41
Indigestion	2.50 ± 1.00	2.00 ± 0.94	<0.05	1.97 ± 0.76	1.90 ± 0.60	0.33
Diarrhoea	2.03 ± 1.26	2.10 ± 1.77	0.84	1.63 ± 0.79	1.38 ± 0.70	0.09
Constipation	2.65 ± 1.35	2.33 ± 1.41	0.12	2.22 ± 1.14	2.02 ± 1.12	0.32

*P < 0.05 vs. omeprazole before treatment.

Total heart-burn free rate for daytime: "At 8 weeks, total symptom relief rate was 68.8% in the FAM group, which is not different from 66.7% in the OPZ group (P = 0.61, Fisher's exact probability test)."

Total heart-burn free rate for nighttime: "At 8 weeks, total symptom relief rate was 43.8% in the FAM group; however, this was marginally lower than 75.0% in the OPZ group (P = 0.10, Fisher's exact probability test)."

Secondary outcome(s):

Mean Short Form (SF)-36 score scales of patients among the non-erosive GERD group before and after treatment of famotidine or omeprazole

	Famotidine (n=21)			Omeprazole (n=18)		
	Before	After	*P*-value	Before	After	*P*-value
Physical function	85.2 ± 12.3	84.5 ± 16.0	0.56	83.2 ± 23.0	83.7 ± 24.0	0.29
Role physical	66.7 ± 45.6	79.4 ± 33.3	0.21	75.0 ± 40.2	76.7 ± 40.6	0.5
Body pain	65.0 ± 20.6	64.5 ± 29.5	0.63	64.5 ± 24.7	62.8 ± 27.7	0.79
General health	46.6 ± 17.4	47.6 ± 24.5	0.4	54.8 ± 17.4	56.7 ± 14.0	<0.05
Vitality	55.2 ± 18.9	57.5 ± 21.7	0.24	60.8 ± 27.2	67.3 ± 23.4	<0.05
Social functioning	75.6 ± 22.5	72.8 ± 23.9	0.5	81.9 ± 26.9	84.2 ± 30.8	0.22
Role emotional	58.7 ± 44.6	68.6 ± 39.9	0.13	72.2 ± 46.1	75.6 ± 40.8	0.42
Mental health	59.7 ± 21.1	66.5 ± 21.8	<0.05	70.2 ± 22.2	81.1 ± 16.2	<0.05

Comments:

Gastrointestinal Symptom Rating Scale (GSRS);

- At baseline, no significant difference between the FAM and the OPZ group except the mean total score and abdominal pain (P < 0.05)

Compliance: ND

Adverse Events: ND

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Wang	Yr: 2008	UI: 1836318	Questions addressed: 2	Extractor: WY

Objective/Topic:
Compare surgical outcome and quality of life after laparoscopic fundoplication between young and old patients

Study design:	Country/Setting:	Funding:
cohort	Taiwan	Not reported

Interventions(s):	Comparator(s):
Laparoscopic fundoplication	NA

Primary outcome(s):	Other outcome(s):
Quality of life	operation time, postoperative hospital stay, mortality, surgical complications

Inclusion criteria:	Exclusion criteria:
GERD pts who had laparoscopic (Nissen or Toupet) fundoplication in the authors' hospital between January 1999 and January 2006 failed medical treatment for 2 years	none
Symptoms (describe): yes	Hiatal hernia (specify whether considered and size used for exclusion):
EGD (performed or not and results): yes	Esophagitis/stricture/Barrett's:
PH study (performed or not and results): yes	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):
Esophageal manometric studies (performed or not and results): yes	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: incomplete outcome assessment in subgroup of patients. Only 82 (35.5%) pts had pre-op quality of life assessment and 89 pts had post-op quality of life assessment

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 73.0 ± 1.9 yr among the at least 70 yr old group, 46.7 ± 11.5 yr among the younger than 70 yr old group; overall mean 50.5 yr	N enrolled: 231

GERD data extraction form

%Male: 60.2%	N completed: 231, but only 82 pts had pre-op quality of life assessment and 89 pts had post-op quality of life assessment
Race: not reported	Dropouts/reasons:
BMI: 24.8 ± 3.7	Follow-up period: mean 30 months
Comments:	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Treatment/Comparison:	Laparoscopic fundoplication					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
Age (>=70 years old vs. <70 years old)	No effect				Quality of life questionnaire at 3 months post-surgery: no effect	Operative time, post-op hospital stay: no effect “recurrence”: 2 pts in young group, 0 pt in old group

Compliance:

Adverse Events:
2/33 (6.1%) post-op pneumonia (in old pt group), 1/33 (3.0%) post-op prolonged dysphagia and vomiting (in old pt group), 1/198 (0.5%) subcutaneous emphysema (in young pt group), 0/231 (0%) mortality.

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Wayman	Yr: 2007	UI: 17377929	Questions addressed: 2	Extractor: WY

Objective/Topic:
To compare surgical outcomes among upright, supine, and bipositional reflux patients

Study design:	Country/Setting:	Funding:
Retrospective cohort	Australia	Not reported

Interventions(s):	Comparator(s):
NA	NA

Primary outcome(s):	Other outcome(s):
Dysphagia	Heartburn Overall satisfaction Bloating

Inclusion criteria:	Exclusion criteria:
had 24-hr ambulatory pH monitoring and/or dual-isotope radionuclide gastric emptying studies had laparoscopic fundoplication	None
Symptoms (describe): Mean score, on a scale of 0-10 Heartburn score: 8 Solid dysphagia: 0 Liquid dysphagia: 0	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): Some pts had EGD; results were not reported	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): Yes Time pH < 4: 142min % time pH < 4: 10.6%	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: C
Comments: retrospective cohort without confounder adjustment

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		x

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 48.4	N enrolled: 372
%Male: 52.1%	N completed: 301 symptomatic assessment at 3 months, 148 symptomatic assessment at 5 years, 114 had postural pH analysis and assessment of gastric employing post-op
Race: not reported	Dropouts/reasons: no reason provided (because it's retrospective?), but authors commented that proportion of the number of pts without symptomatic assessment overtime were similar across reflux pattern groups

GERD data extraction form

BMI: 27.7	Follow-up period: 5 years
Comments:	

Results
Primary outcome(s): See key question 2 table
Secondary outcome(s):
Comments:

Treatment/Comparison:	laparoscopic fundoplication					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
Upright vs. supine vs. bipositional reflux	Time of oesophageal, solid or liquid gastric emptying, number of pts with delayed solid emptying, heartburn score, composite dysphagia score, postprandial bloating, ability to belch: no effect				Patient satisfaction score at 5 years: no effect Patient satisfaction at 3 months: greater in the bipositional reflux group than in the upright reflux group (P = 0.034)	

Compliance: NA

Adverse Events: Not reported

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Wijnhoven	Yr: 2008	UI: 18071830	Questions addressed: 1,2,3	Extractor: JHL

Objective/Topic: Use of Antireflux Medication After Antireflux surgery

Study design: Surgical cohort	**Country/Setting:** Australia	**Funding: ND**

Interventions(s): Fundoplication (62%, 360º Nissen fundoplication; 21%, 180º anterior fundoplication; 15% 90° anterior fundoplication; 2%, 270° posterior partial fundoplication)	**Comparator(s):**

Primary outcome(s): • Use of Antireflux medication	**Other outcome(s):**

Inclusion criteria: • "Patients were selected from a prospective database of individuals who underwent laparoscopic antireflux procedures between March 1992 and August 1 2006 by surgeons from Flinders University Department of Surgery, Flinders Medical Centre, Bedford Park, Australia and University of Adelaide Discipline of Surgery, Royal Adelaide Hospital, Adelaide, Australia. All patients were operated in a similar fashion and according to our standard operative techniques for laparoscopic fundoplication."	**Exclusion criteria:**
Symptoms (describe): ND	**Hiatal hernia (specify whether considered and size used for exclusion): 62.0%**
EGD (performed or not and results): ND	**Esophagitis/stricture/Barrett's: ND**
PH study (performed or not and results): ND	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): ND	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: "... medication usage is measured indirectly by prescription dispensed to a patient, and it is not known whether the patients actually took the medication. Furthermore, medications purchased "over-the-counter" are not detected by these databases (13% patients reported self medication in our study)..."

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
C/Poor (No data)		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 58.2y	**N enrolled:** 1008

GERD data extraction form

%Male: 51%	**N completed:** 844
Race: ND	**Dropouts/reasons:** 164
BMI: ND	**Follow-up period:** 5.9±3.9 years
Comments:	

Results

Primary outcome(s):

- Use of antireflux medication

	Medication (n=312)	**No medication (n=532)**	***p* value**
Type of Wrap (%)			0.017
360° Nissen	172 (55)	353 (67)	
180° Anterior	74 (24)	102 (19)	
90° Anterior	59 (19)	65 (12)	
270° Posterior	7 (2)	12 (2)	

- Postoperative symptoms

"...heartburn, chest pain, and regurgitation are experienced by 322 (38%), 332 (39%), and 325 (38%) of the overall group of patients, respectively"

- Factors predicting postoperative medication use: All patients who had undergone a different Laparoscopic antireflux surgery (360° Nissen, 180° Anterior, 90° Anterior, and 270° Posterior) were combined. Note: Need to flip all ORs in the table to get the OR of off all meds.

Treatment/Comparison:	**Laparoscopic antireflux surgery**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Age (yrs)				*p* <0.001 (OR=1.036)		
Sex				No effect		
Heartburn Yes				*p* <0.001 (OR=6.541)		
Chest pain Yes				*p* =0.005 (OR=1.664)		
Regurgitation Yes				*p* =0.006 (OR=1.666)		

Secondary outcome(s):

Comments:

Compliance: ND

Adverse Events:

- "Reoperations for recurrent reflux symptoms or paraesophageal herniation were undertaken in 70/844 patients (8%) after a median period of 14.3 months."
- Chest pain 332/833 (39.9%)

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Wijnhoven	**Yr: 2008**	**UI: 18070731**	**Questions addressed: Q1**	**Extractor: MC**

Objective/Topic: RCT that compared anterior versus posterior hiatal closure in patients who underwent laparoscopic Nissen fundoplication

Study design:	**Country/Setting:**	**Funding:**
This is a long-term follow-up article of a RCT (Watson et al. Arch Surg 2001;136:746-51)	Australia	Government and private funding

Interventions(s):	**Comparator(s):**
Nissen fundoplication – anterior repair of the diaphragmatic esophageal hiatus. 13 re-operations for dysphagia or paraesophageal herniation were undertaken in 10 patients (9.8%): 2 of 47 (4.3%) of these patients were in the anterior hiatal repair group, and 8 of 55 (14.5%) were in the posterior hiatal repair group (P= 0.094). No patient underwent re-operation for recurrent gastroesophageal reflux.	Nissen fundoplication – posterior repair of the diaphragmatic esophageal hiatus

Primary outcome(s):	**Other outcome(s):**
Symptomatic outcome – structured questionnaire • whether heartburn or dysphagia were present or absent • symptoms of dysphagia for solids and liquids were assessed using a 0 to 10 visual analog scale (0=no symptoms, 10=severe symptoms) • a previously validated and described dysphagia score (0=no dysphagia; 45=severe dysphagia) Overall satisfaction with the outcome of the procedure also was determined using a 0 to 10 visual analog scale (0=totally dissatisfied; 10= totally satisfied).	Esophageal manometry, 24-hr pH monitoring, endoscopy, and radionucleotide esophageal emptying studies were performed as part of the study protocol 3-4 months after the surgery. However, these measures were performed only in patients if clinically indicated during later follow-up period.

Inclusion criteria:	**Exclusion criteria:**
Patients who underwent a laparoscopic Nissen fundoplication for GERD (details in Watson et al. Arch Surg 2001;136:746-51).	• esophageal motility disorder • concurrent abdominal procedure • previous antireflux surgery • large hiatus hernia that was thought to preclude anterior hiatal repair
Symptoms (describe): Mean preoperative heartburn visual score (95% CI)-anterior repair group (n=47): 4.8 (4.0, 5.7); posterior repair (n=55): 4.9 (4.0, 5.7) Some patients had epigastric pain, regurgitation, odynophagia, early satiety, epigastric bloat, anorexia, nausea, nomiting, nocturnal cough, nocturnal wheeze	**Hiatal hernia (specify whether considered and size used for exclusion):** • Large hiatus hernia (ie, containing more than 50% of the stomach or >10 cm in length) was excluded. • A hiatus hernia was seen preoperatively in 49% of the anterior repair group vs 40% of the posterior repair group (P=.40)
EGD (performed or not and results): Performed - "Endoscopic grading of esophagitis before surgery was similar"	**Esophagitis/stricture/Barrett's:** 7 (15%) of the anterior repair group and 3 (5%) of the posterior repair group having complicated reflux disease, ie, either Barrett esophagus or stricture formation (*P*=.18).
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras,**

• Partially performed – 24-hr ambulatory pH monitoring was performed in 20 of the patients who underwent anterior hiatal repair and 28 of those undergoing posterior repair. • The mean percentage exposure time to an acid pH of less than 4 was 10.0% (6.8%-13.2%) for the anterior repair group and 8.7% (6.5%-10.8%) for the posterior repair group.	**Lifestyle modifications or other):** No data
Esophageal manometric studies (performed or not and results): • Preoperative esophageal manometry outcomes were • Similar between groups. • Resting LES pressure <10 mm Hg in 60% and 62% patients in anterior and posterior hiatal repair groups, respectively	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: B	
Blinding: Whether the hiatus was repaired in front or behind the esophagus was concealed from all patients, and all remained unaware of the exact procedure for the duration	**Allocation concealment:** sealed envelopes prepared by an independent research officer before the study
Intention-to-treat: no	**Method of Randomization:** envelopes were randomly selected by a departmental secretary at a surgeon's request
Other comments: Three patients did not receive the allocated treatment. In the anterior repair arm, 1 patient underwent posterior repair of the hiatal defect because an adequate repair could not be achieved by the placement of anterior sutures alone. More re-operations (although not for GERD) in posterior hiatal repair group than anterior repair group (11 vs. 2, respectively). Demographic characteristics of they study population were not reported.	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: no data	**N enrolled: 102**
%Male: no data	**N completed: 94**
Race: no data	**Dropouts/reasons:** death from MI, respiratory failure, metastatic colon carcinoma, and mixed drugs-alcohol intoxication (n=4); lost to follow-up (n=4)
BMI: no data	**Follow-up period:** median 5 years (range, 5-7 years)
Comments: I also checked the 2001 publication but still no demographic characteristics of these patients	

Results

Primary outcome(s):

	Anterior repair (n=45)	Posterior repair (n=49)	P value
No heartburn present (%)	34 (76)	29 (59)	0.092
Analog heartburn score, mean (SE)	0.71 (0.22)	1.73 (0.38)	0.052

Composite dysphagia score, mean (SE)	8.69 (1.36)	11.2 (1.55)	0.335

No significant difference in the satisfaction scores between groups. Eighty-four percent of the patients randomized to anterior hiatal repair and 83% of the posterior group indicated that they thought they had made the correct decision to have their original surgery.

Secondary outcome(s):
Between the 6-month and 5-year follow-up evaluations, esophageal manometry, 24-hour pH study, or an upper-gastrointestinal endoscopy were performed in 16 patients when clinically indicated. The indications for these tests were reflux symptoms, dysphagia, chest pain, or surveillance of Barrett's esophagus.

- Normal esophageal motility was found in 10 patients, and abnormal lower esophageal sphincter pressures in 4 patients without further consequences.
- Uppergastrointestinal endoscopy was performed in 10 patients and showed a small paraesophageal hernia in 2 patients (1 in each group); 1 patient also had symptoms of reflux, the other was asymptomatic. In 1 patient from the posterior hiatal repair group, endoscopic esophageal dilation was performed with relief of dysphagia after this intervention.
- All 24-hour pH studies (11 patients) showed a normal esophageal acid exposure.

Comments:
After enrollment in the trial, 5 patients have undergone additional surgical procedures that were not related directly to the original antireflux procedure (appendicectomy, 1; repair of umbilical hernia, 2; gastric bypass for morbid obesity, 1; and repair of a gastric perforation, 1). More re-operations (although not for GERD) in posterior hiatal repair group than anterior repair group (11 vs. 2, respectively).

Compliance:
No data

Adverse Events:
No data

Applicability: (narrow/wide): narrow	**Comments:** no demographic characteristics of these patients

First author: Wilkerson	**Year: 2005**	**UI: 16025197**

Modifying Factor(s): poor response to PPIs

Study design: prospective cohort **Follow up duration:** 1 yr (6wk; 6mo)	**Country:** UK **Multicenter:** no	**Funding:** None reported

Interventions(s): laparoscopic Nissen fundoplication

Primary outcome(s): Symptom (Visick score)	**Other outcome(s):**

Baseline characteristics:
GERD definition for the population included: symptoms and positive pH test result; patients with reflux symptoms, normal endoscopies, and physiological acid exposure levels if their symptoms corresponded well (>50%) with acid reflux episodes on 24-h pH testing (‘‘Sensitive esophagus’’)
Age: 45 y (median)
Gender: 65% male
Race: ND
BMI: ND
Severity of symptoms: >50% symptom relief after PPI (GroupB:72%); <50% symptom relief (GroupA: 28%)
Duration of symptoms: ND
Frequency of symptoms: ND
Type of medications: PPIs
Acid reflux (by pH study): yes /Describe definition of abnormal: pH <4more than 6% of the time during the day; pH <4more than 2% of the time during the night; pH <4more than 4% of the total time; DeMeester score >14.2
Abnormal manometry study: yes /Describe definition of abnormal: ND
Esophagitis by endoscopy: yes

Significant baseline differences between GroupA and GroupB (and GroupC… etc)

Symptoms: there were significantly more poor responders with atypical chest pain
EGD: No difference (non-ersosive reflux disease; sensitive esophagus); significantly more good responders with Barrett’s esophagus
EMS: No difference
PH study: No difference
Hiatal hernia: ND
Meds used in the groups: No difference

Other: Poor responders (GrouA) had a significantly lower median weight than good responders (GroupB) (73 vs. 80.2 kg, $P<0.05$)
Motility tests: No difference

N enrolled per group:	GroupA: 91	GroupB: 233	GroupC: NA
N completed per group:	GroupA: 91	GroupB: 233	GroupC: NA

Outcomes (as reported in the Results)	**Results**	
	GroupA: *poor responders to PPI*	GroupB: *good responders to PPI*
Number of patients with “excellent/ good” outcome (Visick score: I/II) (NS, P=0.08)	79	218

Adverse Events: ND

Quality Assessment: Description of the biological plausibility for the hypothesis to be tested: yes/no Description of inclusion /exclusion criteria and rationale: yes/no Documentation of how data were collected and analyzed (eg, blinding): yes/no Assessment of confounding (eg, comparability of cases and controls in studies where appropriate): yes/no Participant drop-out percentage (>20%?): yes/no Description of statistical methods in sufficient detail to be replicated: yes/no **Overall grade: B**
Comments:

ND: no data; NA: non-applicable; NS: non-significant

GERD data extraction form

Author: Xirouchakis	Yr: 2009	UI: 18600453	Questions addressed: 2	Extractor: WY

Objective/Topic:
Compare effectiveness of rabeprazole 20mg to 40mg among patients with 4 different baseline esophagitis (per Hill) categories

Study design:	Country/Setting:	Funding:
cohort	Greece	Did not receive any funding

Interventions(s):	Comparator(s):
rabeprazole on demand 20mg (max of 40mg daily) for 3 months	none

Primary outcome(s):	Other outcome(s):
GERD symptom score	Use of rabeprazole

Inclusion criteria:	Exclusion criteria:
At least 18 years old, had GERD symptoms, confirmed GERD per endoscopy, grade A or B esophagitis or non-erosive esophagitis, at least 1 episode of heartburn per week, in 6 months prior to the study, had rabeprazole 20mg daily for 8 weeks prior to study	use of any PPI or H_2 antagonist in the last 6 months, grade C or D esophagitis per endoscopy, any severe disease and/or neoplasia, use of drugs that cause esophageal injury (tetracyclines, bisphosphonates, ferrum tablets), motility disorders and previous esophageal or gastric surgery
Symptoms (describe): Heartburn severity: 26 pts mild, 20 pts moderate, 1 pt severe, 2 pts very severe Heartburn frequency: 9 pts 1-2 days/week, 16 pts 3-4 days/week, 11 pts 5-6 days/week, 13 pts 7 days/week Mean symptom score: 4.14 (don't know what scale it is)	Hiatal hernia (specify whether considered and size used for exclusion): 17 pts
EGD (performed or not and results): Yes, no results reported	Esophagitis/stricture/Barrett's: Erosive esophagitis: 24 pts
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): 95.5% (43 pts) had symptom control after 8 weeks of rabeprazole 20mg daily
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	Allocation concealment:
Intention-to-treat:	Method of Randomization:
Other comments:	

Quality Assessment Non-RCTs: B
Comments: cohort study, no covariate adjustment, sample size not large

GERD data extraction form

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 49 years (range 21-76)	N enrolled: 49
%Male: 46.9%	N completed: 45
Race: not reported	Dropouts/reasons:4 lost to follow up
BMI: 28.5	Follow-up period: 3 months
Comments: all pts had rabeprazole 20mg daily for 8 weeks prior to study	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Treatment/Comparison:	Rabeprazole on demand 20mg, up to 40mg daily					
Potential modifying factor (references)	Outcomes					
	Symptoms	pH	Medications		Quality of life/ Satisfaction	Global Success/ Failure
			Off PPIs	Off all meds		
Esophagitis (per Hill's grading II, III, or IV)	No effect (total symptom score at 8 weeks)		Use of rabeprazole was more among Hill IV group than Hill III or Hill II groups (Hill II vs. IV, p=0.02) (Hill III vs. IV, p=0.001)			

Compliance: Not reported

Adverse Events: Not reported

Applicability: (narrow/wide): wide	Comments:

GERD data extraction form

Author: Yang	Yr: 2008	UI: 18156921	Questions addressed: 1	Extractor: si

data supplemented from Watson 1997 and O' Boyle 2002 Annals of Surgery 235: 165-170

Objective/Topic:
division vs. non-division of short gastric vessels during laparoscopic Nissen fundoplication

Study design:	Country/Setting:	Funding:
RCT	Australia	government

Interventions(s):	Comparator(s):
division of short gastric vessel	no division

Primary outcome(s):	Other outcome(s):
GERD symptoms	dysphagia

Inclusion criteria:	Exclusion criteria:
GERD with either ulcerative esophagitis or abnormal pH monitoring	esophageal motility monitoring
Symptoms (describe): preop heartburn: 88% in divided; 94% in non-divided preop regurgitation: 88% in divided; 90% in non-divided	**Hiatal hernia (specify whether considered and size used for exclusion):** 54% in divided; 48% in non-divided not a factor in exclusion
EGD (performed or not and results): yes	**Esophagitis/stricture/Barrett's:** Barrett's or stricture: 19% in divided; 24% in non-divided
pH study (performed or not and results): 24 in divided and 22 in non-divided had pH study mean % exposure to pH <4: 10% vs. 10.3%	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): LES resting pressure: 8.3 vs. 6.3 mm Hg	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding: single blind	Allocation concealment: nd
Intention-to-treat: yes	Method of Randomization: not stated
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
A		

Characteristics of enrolled patients (divided vs. non-divided)	Results: Disposition of Enrolled Subjects (divided vs. non-divided)
Age: 45.3 vs. 46.7 (overall: 46)	N enrolled: 52 vs. 50
%Male: 59.6% vs. 62% (overall: 61%)	N completed: 44 vs. 44 (total 88 (86%))

GERD data extraction form

Race: nd	**Dropouts/reasons: 3 lost to follow up; 2 refused; 6 died during follow up for reasons unrelated to the procedure; 3 unable to provide information (2 pts with dementia; 1 with cerebrovascular accident)**
BMI: wt (84.5 vs. 83.5 Kg) overall 84 Kg	**Follow-up period: 10 years**
Comments:	

Results
Primary outcome(s): in 44 (divided) vs. 44 pts (non-divided) (unclear what the denominators were in the ITT) **1. heartburn 11% vs. 18%** **2. regurgitation 24% vs. 22%** **3. epigastric bloating 66% vs. 64%** **4. unable to belch 41% vs. 32%** all NS
Secondary outcome(s): **1. second operation for either recurrent reflux or a problem attributed to the original procedure** **8 vs. 5** **2. PPI intake at 10 year follow up** **4 vs. 9 (NS)** **3. dysphagia (dichotomous outcome: score of zero (no dysphagia))** **preop: 57% (divided) vs. 48% (non-divided);** **postop: 20% (divided) vs. 34% (non-divided)** all NS
Comments:

Compliance:

Adverse Events: **second operation for either recurrent reflux or a problem attributed to the original procedure** **8 (divided: 5 dysphagia; 1 bleeding from SGV; 1 paraesophageal hiatal hernia; 1 recurrent reflux due to slipped fundoplication) vs. 5 (non-divided: 2 dysphagia; 2 paraesophageal hiatal hernia; 1 postprandial pain due to bilobed stomach)**

Applicability: (narrow/wide): wide	**Comments:**

GERD data extraction form

Author: Yano	Yr: 2009	UI: 19207552	Questions addressed: 2	Extractor: MC

Objective/Topic: to assess the effect of pre-existing depression as a factor in patient satisfaction and GI quality of life index (GIQLI) outcomes after antireflux surgery

Study design:	Country/Setting:	Funding:
Retrospective cohort	US	nd

Interventions(s):	Comparator(s):
Primary or redo antireflux surgery	Depression (documented in preoperative history and were taking >=1 antidepressants) vs. no depression

Primary outcome(s):	Other outcome(s):
GI quality of life	Reflux symptoms and satisfaction questionnaire

Inclusion criteria:	Exclusion criteria:
Patients underwent primary or redo antireflux surgery from September 2003 through December 2005 who ad filled a preoperative and a postoperative questionnaires.	nd
Symptoms (describe): Heartburn, dysphagia, regurgitation, chest pain	**Hiatal hernia (specify whether considered and size used for exclusion):** nd
EGD (performed or not and results): nd	**Esophagitis/stricture/Barrett's:** nd
PH study (performed or not and results): mean DeMeester score of 25.8 mean percent total time pH < 4 was 8.9	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** nd
Esophageal manometric studies (performed or not and results): nd	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
unclear

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: C
Comments: retrospective chart review; very selected patients; small sample size

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		X

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 28-81	**N enrolled: n/a**
%Male: 41	**N completed: 32**
Race: nd	**Dropouts/reasons: n/a**
BMI: nd	**Follow-up period: n/a**
Comments: retrospective chart review	

Results
Primary outcome(s):
Secondary outcome(s):
Comments:

Treatment/Comparison:	**Laparoscopic antireflux surgery**					
Potential modifying factor (references)	**Outcomes**					
	Symptoms	**pH**	**Medications**		**Quality of life/ Satisfaction**	**Global Success/ Failure**
			Off PPIs	**Off all meds**		
Psychosocial (depression)	No sig. diff. between groups		Use of PPI at follow-up: Group A 0/7 Group B 3/25 No sig. diff between groups		In group A (depression) patients, the GI QLI score increased significantly from 64.4 ± 17.3 to 88.6 ± 23.7 postoperatively (P = 0.02). In group B (no depression) patients, the GIQLI score was 89.6 ±18.6 preoperatively and 102.2 ±18.6 postoperatively (P<0.001). No sig. diff. in satisfaction score between groups	

Compliance: nd

Adverse Events: nd

Applicability: (narrow/wide): narrow	**Comments: highly selective patients**

GERD data extraction form

Author: Zacharoulis	**Yr: 2006**	**UI: 17024541**	**Questions addressed: 1,3**	**Extractor: JHL**

Objective/Topic: Laparoscopic fundoplication

Study design: Retrospective surgical cohort	**Country/Setting:** UK	**Funding: ND**

Interventions(s): Laparoscopic Nissen fundoplication (LNF)	**Comparator(s):**

Primary outcome(s): • Response of symptoms to LNF (heart burn, regurgitation, respiratory symptoms, abdominal, dysphagial) • Complications	**Other outcome(s):** • Overall rate of satisfaction • Antireflux medication

Inclusion criteria: • "From December 1991 to March 2003, a total of 808 consecutive patients underwent 838 LNF for GERD at Hull Royal Infirmary, United Kingdom."	**Exclusion criteria:**
Symptoms (describe): Heartburn (n = 645, 80%), regurgitation (n = 582, 72%), wind-related symptoms (n = 404, 50%), dysphagia (n = 145, 18%), and respiratory symptoms (n = 81, 10%)	**Hiatal hernia (specify whether considered and size used for exclusion):** ND
EGD (performed or not and results): Performed, ND	**Esophagitis/stricture/Barrett's:** 595 (73.6%), esophagitis grades 1 to 4; 62 (7.6%), Barrett's esophagus
PH study (performed or not and results): Performed, median preoperative Demeester score - 48 (range, 15–65)	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** ND
Esophageal manometric studies (performed or not and results): Performed, ND	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) NA

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A/rigorous (Upper gastrointestinal endoscopy, 24-h esophageal pH monitoring, and manometry)		

GERD data extraction form

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 49 years	**N enrolled:** 808 patients had LNF
%Male: 56%	**N completed:** 778 (in the analysis)
Race: ND	**Dropouts/reasons:** 130/880 (lost to follow-up)
BMI: ND	**Follow-up period:** Median 60 months (2months-10 years)
Comments:	

Results
Primary outcome(s): • "During a median follow-up period of 60 months, *heartburn* decreased to 3% of the patients (19/645) and *regurgitation* to 2% (11/582) ($p < 0.01$)." • "After 10 postoperative years, only 3% (30/484) were found to have *abdominal symptoms*, whereas the incidence of *dysphagia* declined to zero." • "Postoperatively, 69 (85%) of 81 patients with respiratory symptoms reported immediate improvement, which was sustained at subsequent long-term review, whereas 12 patients (15%) derived no benefit."
Secondary outcome(s): • "The overall rate of satisfaction with the procedure at 7 years and longer was 96% (250/260)." • "At 7 years and longer after the surgery, 12% (30/260) were taking antireflux medication."
Comments:

Compliance: NA

Adverse Events:
• "Intraoperative complications occurred in 11 (1.3%) of 808 patients undergoing primary surgery. All the complications occurred in the first 325 cases, and included esophageal perforation (n = 3), stomach perforation (n = 4), and hemorrhage (n = 4)." • "During the follow-up period, 12 (1.5%) of 808 patients underwent reoperative surgery for symptoms of recurrent reflux; 15 patients (1.8%) required intervention for symptoms of dysphagia (6 dilations and 9 laparoscopic reoperations), and 11 patients (1.4%) presented with symptoms of intrathoracic wrap migration (9 laparoscopic reoperations and 2 open repairs). 13 unrelated deaths (1.6%) occurred."

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Zehetner	**Yr: 2006**	**UI: 16391962**	**Questions addressed:**	**Extractor: JHL**

Objective/Topic: Five-year results of laparoscopic Toupet fundoplication

Study design: Surgical cohort	**Country/Setting: Switzerland**	**Funding: ND**

Interventions(s): Laparoscopic Toupet fundoplication	**Comparator(s): NA**

Primary outcome(s): • DeMeester score • Adverse effects • Patient satisfaction	**Other outcome(s):**

Inclusion criteria: • "Between September 1993 and June 1998, 100 consecutive patients were treated for symptomatic GERD by laparoscopic Toupet fundoplication" • One or more of the following criteria had to be fulfilled by all patients: 1. Unsatisfactory response of GERD to conservative medical antireflux treatment 2. Patient wish for operative treatment 3. Development of GERD complications (esophageal strictures, Barrett esophagus, esophagitis grade III/IV) 4. Atypical reflux-related symptoms such as cough, asthma, aspiration, hoarsenessGERD symptoms were evaluated pre- and postoperatively by the modified clinical DeMeester score. (Range 0–12 points).	**Exclusion criteria:**
Symptoms (describe): No description of baseline	**Hiatal hernia (specify whether considered and size used for exclusion):** hiatal hernias was 92%; axial hiatal hernias in 72%, paraesophageal hernias in 6%, and mixed hiatal hernias in 14%
EGD (performed or not and results): Performed, 95% of patients, an esophagitis grade I–IV according to the Savary-Miller classification	**Esophagitis/stricture/Barrett's:** 4%, Barrett's esophagus
PH study (performed or not and results): Performed, "Preoperative 24-h pH-metry showed a mean fraction time of pH < 4 of 17.8 ± 12.5% (normal value < 4%)."	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): Performed, 29% a pathologic esophageal motility • 18%, A minimal reduced motility (diminished contraction amplitude in normal amount of contractions) • 11%, a severe pathologic esophageal motility	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) NA

GERD data extraction form

Quality Assessment for RCTs: A/rigorous; B/acceptable; C/Poor (please select one and delete others)	
Blinding:	**Allocation concealment:**
Intention-to-treat:	**Method of Randomization:**
Other comments:	

Quality Assessment Non-RCTs: B
Comments: Only first 34 patients had a postoperative control endoscopy and 24-h pH-manometry at 8 weeks postoperatively (due to high costs and patient discomfort)

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
A/rigorous (endoscopy)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 50.4y	**N enrolled: 100**
%Male: 63%	**N completed: 87**
Race: ND	**Dropouts/reasons: 13%**
BMI: ND	**Follow-up period: 5 years**
Comments:	

Results
Primary outcome(s): • DeMeester score: "The mean preoperative clinical DeMeester score (range 0–12 points) was 4.27 ± 1.5 points. One month postoperatively the score had dropped to 0.86 ± 0.9 points ($p < 0.0005$). One year postoperatively the score was 0.25 ± 0.5 points. At 5 years follow-up the DeMeester score reached 0.47 ± 0.9 points" • 24-hr pH-manometry: "Preoperative 24-h pH-metry showed a mean fraction time of pH < 4 of 17.8 ± 12.5% (normal value < 4%). For the first 34 patients a control-24-h pH-manometry was performed 8 weeks postoperatively. The mean fraction time of pH < 4 was significantly decreased to 0.9 ± 1.2% ($p < 0.0005$)" • Dysphagia: "At 4 weeks after procedure, a transient dysphagia was found in 43% of patients. Eight weeks postoperatively, 15% of patients still complained of mild dysphagia. One and 5 years postoperatively, 3% and, respectively, 2% of patients declared occasional dysphagia." • Being reinstalled on a regular PPI treatment 3.5%, postoperative GERD
Secondary outcome(s):
Comments:

Compliance: NA

Adverse Events:

- Frequency of symptoms/side-effects 1 and 5 years after laparoscopic Toupet fundoplication

Symptoms	After 1 year (n=100)	After 5 years (n=87)
None	47%	46%
Early satiety	31%	41%
Burp impossibility	25%	33%
Flatulence	15%	10%
Mild dysphagia	3%	2%
Diarrhea	8%	11%
GERD recurrence/heartburn	3%	15%[a]

[a] 3 patients take PPI on a regular basis

- List of treatment failure or complications after laparoscopic Toupet fundoplication necessitating a reoperation during 5 years follow-up

Complications	Rate	Reoperations
GERD recurrence	15%	1
Wrap dislocation	3.4%	3
Gas-bloat syndrome	1.1%	1
Total morbidity rate	19.5%	
Reoperation rate		5%

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Zheng	**Yr: 2009**	**UI: 19248200**	**Questions addressed: 1**	**Extractor: DM**

Objective/Topic:
Symptom relief after 7 day- and healing of esophagitis as determined by endoscopy after 8 week - course of omeprazole, lansoprazole, pantoprazole, and esomeprazole in patients with reflux esophagitis.

Study design:	**Country/Setting:**	**Funding:**
4-arm RCT	China/Hospital	nd

Interventions(s):	**Comparator(s):**
20 mg omeprazole	40 mg pantoprazole, 30 mg lansoprazole, and 40 mg esomeprazole

Primary outcome(s):	**Other outcome(s):**
Severity of heartburn and acid reflux The severity of symptoms was graded on a six-point scale (0: none; 1: mild; 2: mild-moderate; 3: moderate; 4: moderate-severe; 5: severe and/or intolerable) Mild symptoms: heartburn/acid reflux that did not disturb the normal daily activity of the patients. Moderate symptoms: bothered the daily activity, while the patients continued to work productively Severe symptoms: high-grade symptoms that stopped the daily productive activity of the patients.	Endoscopic healing of reflux esophagitis: Based on the Los Angeles (LA) classification

Inclusion criteria:
endoscopically proven reflux esophagitis

Exclusion criteria:
Subjects with active peptic ulcer, upper gastrointestinal cancers, malignant diseases of
other organs, severe cardiac, hepatic, or renal diseases,
anemia (hemoglobin concentration < 10 g/dL), or
who were pregnant and/or lactating,

Symptoms (describe):

	Omeprazole (n = 68)	Lansoprazole (n = 69)	Pantoprazole (n = 69)	Esomeprazole (n = 68)
Heartburn N(%)	61 (89.7)	63 (91.3)	62 (89.9)	63 (92.6)
Acid reflux N (%)	33 (48.5)	35 (50.7)	34 (49.3)	35 (51.5)

Hiatal hernia (specify whether considered and size used for exclusion):

EGD (performed or not and results):

Endoscopic esophagitis (Los Angeles classification)

	Omeprazole (n = 68)	Lansoprazole (n = 69)	Pantoprazole (n = 69)	Esomeprazole (n = 68)
A	20	20	20	20
B	26	26	28	26
C	20	21	20	20
D	2	2	1	2

Esophagitis/stricture/Barrett's:
See EGD

GERD data extraction form

PH study (performed or not and results): no	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):**
Esophageal manometric studies (performed or not and results): **no**	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)

Quality Assessment for RCTs: A/rigorous	
Blinding: y	**Allocation concealment: Yes**
Intention-to-treat: y	**Method of Randomization: sealed envelope method**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 57 y	**N enrolled: 274**
%Male: 49.2	**N completed: 264**
Race: Asian (Chinese)	**Dropouts/reasons: 10 (3.6%); did not consent to endoscopy**
BMI: nd	**Follow-up period: 1 week for symptoms, 8 weeks for endoscopy**
Comments:	

Results
Primary outcome(s): 1 week results were not extracted as it is not an outcome of interest
Secondary outcome(s): Endoscopic healing rates

Omeprazole (n = 68)	**Lansoprazole (n = 69)**	**Pantoprazole (n = 69)**	**Esomeprazole (n = 68)**
87.7%	89.6%	91.1%	95.4%

Comments:

Compliance:

Adverse Events:

Applicability: (narrow/wide): narrow	**Comments:** The correlation of endoscopic healing with symptom control was not established at 8 weeks, so that narrows the applicability of this study

Evidence table of systematic review

Author Year	**Chang 2009** DOI: 10.1002/14651858
Design	RCTs on GERD treatment for chronic cough (non-specific dry cough ≥ 3 weeks duration unrelated to underlying respiratory disease (COPD, asthma or cystic fibrosis) or secondary to medication use).
Population	Adults and pediatric patients with chronic cough
Intervention (Exposure) and Comparator	Intervention 1- Anti reflux conservative measures 2- H2 receptor antagonists 3- Proton pump inhibitors 4- Surgical therapy Control- placebo
Results	18 articles, 13 on adults, 5 on pediatric population. 10 parallel studies, 3 crossover studies (with a washout periods of two weeks). Meta-analysis model and heterogeneity (if applicable) - PPI vs. placebo (Adults >18 years) for failure to cure based on clinical features (still coughing at end of trial or reporting period). o Random effects model, Pooled OR 0.46 (95 percent CI 0.19 to1.15) [Heterogeneity:- Tau^{2-}=0.00, Chi^2 = 1.14, df=3 (P=0.77); I^2=0 percent] - PPI vs. placebo (Adults >18 years) for mean cough scores at end of intervention. o Random effects model, Pooled OR -0.38 (95 percent CI -0.77 to 0.00) [Heterogeneity:- Chi^2 = 1.98, df=3 (P=0.58); I^2=0 percent] - PPI vs. placebo (Adults >18 years), for change in cough scores (end-beginning of intervention); data from parallel group / crossover studies: o SMD effect estimate -0.39 (95 percent CI -0.71 to -0.08) [Heterogeneity:- Chi^2 = 5.68, df=5 (P=0.34); I^2=12 percent] o Only Crossover studies; standardized scale; fixed effects model. SMD effect estimate -0.41 (95 percent CI -0.75 to -0.07). [Heterogeneity:- Chi^2 = 0.10, df=1 (P=0.76); I^2=0 percent] o Crossover studies; Absolute scores; fixed effects model. SD effect estimate -0.29 (95 percent CI -0.62 to -0.04). [Heterogeneity:- Chi^2 = 0.38, df=1 (P=0.54); I^2= 0 percent] Meta-analysis revealed no significant difference in cure of cough between PPIs and placebo. Meta-analysis revealed significant improvement on cough outcomes at end of trial and in change in cough scores (both in overall scores as well as in data from crossover trials).
Comments	1-Small number of studies and select availability of unpublished articles therefore potential for publication bias. 2-Lack of validated scales and objective data on cough. 3-lack of allocation concealment data due to clinical heterogeneity of participants and medications 4-Most studies did not use the GORD criteria specified by guidelines of American and European Gastroenterology Associations.

AMSTAR

A priori design?	Yes	**Study quality assessment performed?**	Yes
Two independent reviewers?	Yes	**Study quality appropriately used in analysis?**	Yes
Comprehensive literature search?	Yes	**Appropriate statistical synthesis?**	Yes
All publication types and languages included?	Yes	**Publication bias assessed?**	Yes
Included and excluded studies listed?	Yes	**Conflicts of interest stated?**	Yes
Study characteristics provided?	Yes		

Evidence table of systematic review

Author Year [PMID]	Coughlan 2001 [11182012]
Design	SR of RCTs of reflux esophagitis with reported asthma outcomes; from Cochrane trials register & Cochrane Airways Groups
Population	adults with asthma diagnoses
Intervention (Exposure) and Comparator	PPI, H2RA blockers
Results	259 abstracts, 21 full text, 12 RCTs (N=432) included in the analysis; Jadad score 6.2 (4-7) 1. Asthma outcomes reported inconsistently 2. No clear and consistent benefit of anti-reflux treatment on lung function 3. 3 of 12 trials reported significant improvement in symptoms 4. 4 studies identified participants in whom reflux appeared to trigger asthma; no consistent benefit of GERD Rx on asthma outcomes
Comments	This SR may be dated.

AMSTAR

A priori design?	y	**Study quality assessment performed?**	y
Two independent reviewers?	y	**Study quality appropriately used in analysis?**	y
Comprehensive literature search?	y	**Appropriate statistical synthesis?**	n/a
All publication types and languages included?	n	**Publication bias assessed?**	n
Included and excluded studies listed?	n	**Conflicts of interest stated?**	n
Study characteristics provided?	y		

Evidence table of systematic review

Author Year [PMID]	Gibson 2003
Design	A systematic review of GERD treatment for asthma in adults and children
Population	Patients with asthma – adults (1 study of H2RA vs placebo included children and adolescents between 10-20 years of age).
Intervention (Exposure) and Comparator	1. H2 antagonist - ranitidine and cimetidine 2. Proton Pump Inhibitor (Only Omeprazole in varying doses - 20 mg, 40 mg, 80 mg and 160 mg 3. Conservative anti-reflux therapy: raising the head of the bed, drinking warm water after meals, not eating for 3 hours prior to bed time, anti-reflux medication as required, avoid use of aspirin and anticholinergic preparations and avoidance of procedures increasing intra-abdominal pressure 4. Surgery
Results	• Database search yielded 262 abstracts, 22 full-text articles and 1 abstract were retrieved. Of these, 12 RCTs were included. • 9 cross-over trials and 3 parallel design, quality of studies (7 A studies, 4 B studies, and one C study), types of interventions: proton pump inhibitors (6 studies), histamine antagonists (5 studies), surgery (1 study), conservative management (1 study). With exception of 1 RCT comparing H2 antagonist with placebo who studied children and adolescents (aged 10-20 years old), all other RCTs investigated adults. • 9 of 12 studies failed to show a significant improvement in asthma symptoms. • Meta-analysis model and heterogeneity (if applicable): o H2 antagonist , Proton Pump inhibitor, conservative or surgical therapy vs. placebo on FEV1: No effect of treatment o H2 antagonist or Proton Pump inhibitor vs. placebo on morning peak expiratory flow, Fixed effect model, mean difference [95% CI]: 5.28 [-35.43, 44.72] Heterogeneity: Chi^2 = 0.3, df=2 (P=0.86); I^2=0.0% o H2 antagonist or Proton Pump inhibitor vs. placebo on evening peak expiratory flow, Fixed effect model, mean difference [95% CI]: 7.03 [-25.88, 39.95] Heterogeneity: Chi^2 = 0.02, df=2 (P=0.99); I^2=0.0% o H2 antagonist vs. placebo on nocturnal symptoms score (including a study on adolescents), Fixed effect model, mean difference [95% CI]: -0.16 [-0.42, 0.11] Heterogeneity: Chi^2 = 0.97, df=3, (P=0.81); I^2=0.0% o Proton Pump inhibitor vs. placebo, Outcome: puffs per day, Fixed effect model, mean difference [95% CI]: -0.52 [-1.7, 0.67] Heterogeneity: Chi^2 = 0.59, df=2, (P=0.74); I^2=0.0%
Comments	The duration of medical treatments was short in the most studies. Insufficient sample size in the pooled studies. One study included children and adolescents aged from 10 to 20 years.

AMSTAR

A priori design?	Y	**Study quality assessment performed?**	Y
Two independent reviewers?	Y	**Study quality appropriately used in analysis?**	N
Comprehensive literature search?	Y	**Appropriate statistical synthesis?**	Y
All publication types and languages included?	Y	**Publication bias assessed?**	N
Included and excluded studies listed?	Y	**Conflicts of interest stated?**	Y
Study characteristics provided?	Y		

Evidence table of systematic review

Author Year [PMID]	Hopkins 2009 [16437513]
Design	Randomised and quasi-randomised, controlled, double-blinded trials, controlled clinical trials (trials using a control group but no adequate randomisation procedure) and quasi-randomised trials of anti-reflux therapy for adult patients with hoarseness in the absence of other identifiable causes, irrespective of diagnosis of laryngopharyngeal reflux and GERD.
Population	All adult (aged 18 or over) patients with hoarseness (dysphonia), regardless of GERD diagnosis, and who have undergone laryngoscopy to exclude other identifiable causes of hoarseness including malignancy, vocal cord paralysis and vocal cord nodules.
Intervention (Exposure) and Comparator	Non-surgical: a) Lifestyle modification and patient education b) Drugs: Proton pump inhibitors (PPIs), Antacids, H2-receptor antagonists, Prokinetic agents, Erythromycin Surgical: a) Fundoplication repair - Nissen, Rossetti, Toupet partial fundoplication, Bore partial fundoplication, Collis gastroplasty followed by fundoplication b) Non-fundoplication repairs: Hill repair (gastropexy), Belsey Mark IV
Results	302 studies of hoarseness; 6 RCTs comparing gastric acid suppression with PPI vs placebo; no randomised trials of other methods of anti-reflux treatment. In all 6 RCT, 275 patients (sample size ranged from 15-145 participants) randomized to PPI or placebo. f/u ranged from 2 months - 3 months. Quality of outcome assessment (i.e. hoarseness) was not adequate as symptoms used for inclusion into the studies did not correlate with the results from the pH studies within these studies. The studies also used different and invalidated instruments to measure the outcome of interest, making inter-study comparisons invalid. 4 of 6 studies included in the review could not find a significant difference in resolution of symptoms/hoarseness between the PPI and placebo groups; Authors state that excluded studies indicate a placebo effect (data not shown).
Comments	The SR was limited by the quality of the studies available in the literature. The outcome of interest, hoarseness, could not be ascertained reliably in all the RCTs that were screened.

AMSTAR

A priori design?	Y	**Study quality assessment performed?**	Y
Two independent reviewers?	Y	**Study quality appropriately used in analysis?**	N/A
Comprehensive literature search?	Y	**Appropriate statistical synthesis?**	N/A
All publication types and languages included?	nd	**Publication bias assessed?**	nd
Included and excluded studies listed?	Y	**Conflicts of interest stated?**	Y
Study characteristics provided?	N		

Evidence table of systematic review

Author Year [PMID]	Iqbal 2008 [19105666]
Design	A systematic review of retrospective and prospective studies, including RCTs, of surgical fundoplication in the treatment of the symptoms of extra-esophageal reflux (EER).
Population	Adults
Intervention (Exposure) and Comparator	Surgery / fundoplication, versus placebo/medical therapy
Results	25 studies – 24 case series (10 prospective and 14 retrospective) and 1 RCT (in asthmatics, which compared medical and surgical therapy) **Asthma**: Seven studies, 350 patients – 1 RCT, four prospective studies, 2 retrospective studies; Most studies showed a benefit, with 49–84% of patients improving after surgery; RCT - 74% of patients showed sustained improvement after antireflux surgery, compared to 9.1% in patients treated medically and 4.2% in the control group but only 16 patients in surgery group. Surgery may have a role in carefully selected patients with reflux-related asthma; it decreases the need for medication in majority of patients. **Chronic Cough**: 13 studies suggested that 60–100% of patients improve after surgery. Surgery in cough was still less successful than surgery for classical GERD. **Laryngeal symptoms**: 8 studies reported that the range of proportion of patients with complete or partial relief of symptoms was 65–94%. A good operative response to antiacid medication and preoperative dual-probe pH testing were predictive of a good response to surgery
Comments	Included both prospective and retrospective studies; only 1 RCT for asthma; no quantitative analysis; quality of studies was not assessed

AMSTAR

A priori design?	N	**Study quality assessment performed?**	N
Two independent reviewers?	N	**Study quality appropriately used in analysis?**	n/a
Comprehensive literature search?	Y	**Appropriate statistical synthesis?**	n/a
All publication types and languages included?	N	**Publication bias assessed?**	N
Included and excluded studies listed?	N	**Conflicts of interest stated?**	Y
Study characteristics provided?	Y		

GERD data extraction form

Author: dos Santos	**Yr: 2007**	**UI:** 17724529	**Questions addressed: atypical GERD – asthma update**	**Extractor: JHL**

Objective/Topic: Evaluation of pantoprazole treatment response of patients with asthma and gastroesophageal reflux

Study design: A randomized prospective double-blind placebo-controlled study	**Country/Setting: Brazil**	**Funding: ND**

Interventions(s): Pantoprazole 40 mg/day	**Comparator(s): Placebo**

Primary outcome(s): • Quality of life • Respiratory and digestive symptoms	**Other outcome(s):**

Inclusion criteria:

- "…Patients being older than 18 years of age; having been clinically/functionally diagnosed with asthma; having concomitant GERD; presenting a clinical history consistent with asthma and symptoms stabilized for at least two months; spirometry results had to be characteristic: forced expiratory volume in one second/forced vital capacity ratio (FEV_1/FVC) < 90% of predicted, indicating airflow obstruction; obstruction reversibility represented by FEV_1 > 200 mL and 7% of predicted; presenting positivity for bronchial hyperresponsiveness on the methacholine broncho-provocation test regardless of the spirometry findings"

Exclusion criteria:

- "…Recent history of smoking (past eight weeks); abnormalities in sinus/chest X-rays; history of proton pump inhibitor use within four weeks preceding the study outset; history of H-2 receptor blocker use within two weeks preceding the study outset; systemic arterial hypertension when using angiotensin-converting enzyme inhibitors, β-adrenergic receptor blockers, or calcium channel blockers that could not be changed; presence of other severe systemic diseases; pregnancy; illiteracy of a complete lack of understanding of the forms that had to be completed."

Symptoms (describe): Used GERD symptoms developed by Harding et al.

	Placebo	**Medication**
GERD symptoms score	12.9 ± 9	11.4 ± 7

Hiatal hernia (specify whether considered and size used for exclusion): ND

EGD (performed or not and results): ND

Esophagitis/stricture/Barrett's: ND

PH study (performed or not and results): Performed

	Placebo	**Medication**
	n	**n**
DeMeester score (normal 14.7)	40.1 ± 28	29.7 ± 12
% total time (normal < 4.2%)	9.5 ± 7	7.5 ± 3
% time standing (normal 6.3%)	8.3 ± 7	7.2 ± 5
% time supine (normal < 1.2%)	11.7 ± 14	7.7 ± 8
Episodes > 5 min (normal < 3)	4.7 ± 4	3 ± 2
Normal of reflux episodes (normal < 50)	115.9 ± 59	94 ± 37

Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND

Esophageal manometric studies (performed or not and results): Performed

Other:

	Mean ± SD	Mean ± SD
LES tonus (normal 14-40mmHg)	15.5 ± 5	18.1 ± 5
LES extension	5 ± 1	5.5 ± 1
UES tonus	67.6 ± 32	63.4 ± 31

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B/acceptable	
Blinding: Yes	**Allocation concealment: ND**
Intention-to-treat: Yes	**Method of Randomization: ND**
Other comments: No information on allocation concealment, method of randomization was not described.	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		
A/rigorous (diagnosed by 24-h esophageal pH-metry)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 42.5	**N enrolled: 49**
%Male: 20.5%	**N completed: 44**
Race: ND	**Dropouts/reasons: 5** (2, worsening of symptoms and consequent hospitalization; 1, noncompliance with the protocol; 1, intolerance to the medication used in the study; and 1, having started smoking)
BMI: ND	**Follow-up period: 90 days**
Comments: Discrepancy with numbers in the baseline characteristics table	

Results

Primary outcome(s):

- Clinical control of asthma variables and quality of life

Variable	Placebo (n=22)			Medication (n=22)			P between groups
	Initial	Final	p	Initial	Final	p	
Diurnal SS*	68.8 ± 26	64.92 ± 4	0.29	69.2 ± 29	58.9 ± 23	0.01	0.11
Nocturnal SS	66 ± 25	63.42 ± 6	0.24	66.92 ± 7	57.9 ± 23	0.01	0.16
Total QoL*	63.8 ± 13	61.8 ± 13	0.25	61.61 ± 5	48.7 ± 12	0	0.001
Physical lim. QoL	60 ± 20	58.1 ± 18	0.31	63.7 ± 15	52.81 ± 7	0.02	0.67
Symptoms QoL	47.3 ± 23	53.4 ± 24	0.18	55.42 ± 6	40.8 ± 15	0.05	0.08
Compliance QoL	47.8 ± 26	42.22 ± 6	0.46	53.62 ± 4	37.42 ± 7	0.08	0.55
Socioecon. QoL	61.31 ± 9	59.72 ± 1	0.62	60.4 ± 20	56.31 ± 9	0.39	0.58
Psychosocial QoL	56 ± 13	51.61 ± 7	0.33	58 ± 22	43.62 ± 3	0.03	0.11

SS: symptoms score; QoL: quality of life, points; lim.: limitation; Socioecon.: Socioeconomic; and *mean ± standard deviation.

- Respiratory variables

Variable	Placebo (n=22)			Medication (n=22)			P between groups
	Initial	Final	p	Initial	Final	p	
FVC (% predicted)*	85.81 ± 5	85.9 ± 16	0.57	79.5 ± 17	81.3 ± 18	0.79	0.4
FEV1 (% predicted)*	60.4 ± 19	58.9 ± 13	0.55	61.6 ± 19	62 ± 21	0.46	0.65
FEV1/FVC (% predicted)	69.4 ± 13	70.2 ± 12	0.16	71.7 ± 11	73.8 ± 14	0.54	0.4
Diurnal PEF (L/min)*	264 ± 86	267 ± 81	0.59	317 ± 126	327 ± 77	0.23	0.74
Nocturnal PEF (L/min)	261 ± 83	269 ± 77	0.39	307 ± 121	323 ± 127	0.46	0.1

PEF: peak expiratory flow; FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; and *mean ± standard deviation.

Secondary outcome(s):

Comments:

Compliance: Assessed but no data are presented.

Adverse Events: Assessed but no data are presented.

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Jiang	**Yr:**2003	**UI:** 12717871	**Questions addressed:** Atypical GERD asthma	**Extractor:** JC

Objective/Topic: Determine effects of antireflux treatment on bronchial hyper-responsiveness and lung function in asthmatic patients with GERD.

Study design: RCT	**Country/Setting:** China/Single hospital	**Funding:** Not described

Interventions(s): GROUP B-asthma medication including inhaled salbutamol (SAL) 200 mg four X/day day and budesonide (BUD) 400 mg 2X/ day & antireflux therapy including oral omeprazole (OME) 20 mg 1X/day and domperidone (DOM) 10 mg 3x/ day for 6 weeks	**Comparator(s): GROUP A-**asthma medication including inhaled salbutamol (SAL) 200 mg 4x/ day and budesonide (BUD) 400 mg 2x/ for 6 weeks

Primary outcome(s): Pulmonary function tests, histamine broncho-provocation test pre and post study. Pulmonary function tests: vital capacity (VC), forced vital capacity (FVC), forced expiratory volume at the first second (FEV1), peak expiratory flow rate (PEF), percentage of the above parameters over the predicted values. Bronchial hyper-responsiveness: histamine broncho-provocation test (HIT).	**Other outcome(s):**

Inclusion criteria: Thirty asthmatic patients with GERD from Second Affiliated Hospital Sun Yat-Sen University Diagnosis of asthma according to the Global Initiative for Asthma issued by the National Heart, Lung, and Blood Institute. Presence of GERD according to following standards: typical clinical symptom of GERD such as postprandial chest pain and sour regurgitation, signs of erosive esophagitis shown by barium esophagogram and/or lower esophageal erosions shown by endoscopic examination and mucosal biopsy.	**Exclusion criteria:** Not described
Symptoms (describe): postprandial chest pain and sour regurgitation, signs of erosive esophagitis and/or lower esophageal erosions	**Hiatal hernia** (specify whether considered and size used for exclusion): Not considered
EGD (performed or not and results): Performed for some subjects: signs of erosive esophagitis shown by barium esophagogram and/or lower esophageal erosions shown by endoscopic examination and mucosal biopsy.	**Esophagitis/stricture/Barrett's:** Not considered
PH study (performed or not and results): Not	**Response to previous therapy (specify, PPIs, H2Ras,**

performed	**Lifestyle modifications or other):** Not described
Esophageal manometric studies (performed or not and results): Not performed	**Other:** signs of erosive esophagitis shown by barium esophagogram and/or lower esophageal erosions shown by endoscopic examination and mucosal biopsy

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: C	
Blinding: No	**Allocation concealment:** Not described
Intention-to-treat: Not described	**Method of Randomization:** Randomization not fully described: The patients were randomly divided into two groups. There was no significant difference in age, sex, and duration of asthma between these two groups.
Other comments:	

Quality Assessment Non-RCTs: N/A
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		
A=Rigorous		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: SAL + BUD A mean 34.9±19.2 years), SAL+BUD+OME+DOM mean 35.6±17.4 years),	**N enrolled:** 30 randomized
%Male: Group A: 47%; Group B: 40%	**N completed:** 30
Race: ND	**Dropouts/reasons:** None
BMI: ND	**Follow-up period:** 6 weeks
Comments:	

Results

Primary outcome(s):

No significant difference in baseline values of pulmonary function and histamine PC20-FEV1 between the two groups.

Mean values for VC, VC%, FVC, FVC%, FEV1, FEV1%, PEF, PEF%, PC20-FEV1 did not change significantly in group A.

In group B the mean values for VC, VC%, FVC, FVC%, FEV1, FEV1%, PEF, PEF%, PC20-FEV1 all significantly increased.

Mean values for above indices were all significantly higher in group B than in group A.

Changes in pulmonary function and bronchial responsiveness in asthmatic patients with GERD (mean values ±SD)

outcome	**SAL + BUD**		**SAL + BUD+OME+DOM**	
	Before therapy	**After therapy**	**Before therapy**	**After therapy**
VC(L)	2.9±0.4	2.7±0.9	2.8±0.7	3.7±0.7ab
VC%	86.3±14.6	85.9±1.9	84.9±18.9	111.2±13.6ab
FVC(L)	2.9±0.6	2.7±0.8	2.8±0.4	3.6±0.9ab

FVC%	88.4±19.2	85.1±23.6	86.3±21.7	102.6±16.1ab
FEV1(L)	2.3±0.9	2.4±0.6	2.2±0.8	2.8±0.5ab
FEV1 %	76.8±11.6	77.5±16.3	75.6±14.5	84.6±12.7ab
PEF (L/S)	4.4±1.5	4.8±1.7	4.6±1.2	5.9±1.6ab
PEF %	74.8±19.6	75.±16.3	70.5±20.4	85.1±23.1ab
PC20-FEV1 (g/L)	0.31±0.11	0.28±0.16	0.33±0.14	0.84±0.22ab

a=$P<0.05$ *vs*. group A after therapy, the *t* values were 2.34, 2.59, 2.31, 2.55, 2.49, 2.26, 2.63, 2.22, and 2.68, respectively.

b=$P<0.01$ *vs*. group B before therapy, the *t* values were 3.93, 4.16, 3.87, 4.04, 3.95, 3.62, 4.46, 3.98, and 4.33, respectively.

Secondary outcome(s):

Comments:

Compliance: ND

Adverse Events: ND

Applicability: (narrow/wide): narrow	**Comments:** 30 subjects from a single site in China

GERD data extraction form

Author: Kiljander	Yr: 2006	UI: 16357331	Questions addressed: atypical GERD asthma	Extractor: WY

Objective/Topic:
Compare the effect of esomeprazole 40mg bid with placebo in pulmonary functions

Study design:	Country/Setting: US? Finland?	Funding:
RCT	Multi-center	AstraZeneca

Interventions(s):	Comparator(s):
esomeprazole 40mg bid (30 min before breakfast and 30 min before dinner) for 16 weeks	placebo bid (30 min before breakfast and 30 min before dinner) for 16 weeks

Primary outcome(s):	Other outcome(s):
Mean change of the morning PEF (baseline was defined as the last 7 days of run-in, and final was defined as the last 28 days of the study)	Change in evening PEF Asthma symptoms Antacid use Adverse events

Inclusion criteria:	Exclusion criteria:
aged 18 to 70 yr stable asthma outpatients treated with inhaled glucocorticosteroids and/or leukotriene pathway modifiers for at least 3 months prior to the study no change in asthma medication change in the last 30 days FEV1 of 50 to 80% predicted with 12% or greater (and ≥ 0.20 L) reversibility mean morning peak expiratory flow <80% predicted	current smoking or history of 10 pack-years or more; use of oral, rectal, or parenteral glucocorticosteroids <30 days before study; previous esophageal or gastric surgery; erosive esophagitis in the 16 wk or fewer before enrollment; PPI use in the 14 d before enrollment; recurrent moderate or severe GERD symptoms in the previous year in subjects older than 40 yr
Symptoms (describe): No	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): no	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: C/Poor	
Blinding: no (but used placebo?)	Allocation concealment: no
Intention-to-treat: no	Method of Randomization: not reported
Other comments: randomized within strata (3) based on nocturnal respiratory symptoms and presence of GERD a bit strange to find subjects that did not meet eligibility criteria after randomization	

GERD data extraction form

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
		x

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 44.7	N enrolled: 770 (350 in those with Gastroesophageal Reflux Disease and Asthma)
%Male: 30.5%	N completed: 624
Race: 80% white	Dropouts/reasons: not treated (1 in esomeprazole, 2 in placebo), did not meet eligibility criteria (22 in esomeprazole, 24 in placebo), adverse events (24 in esomeprazole, 31 in placebo), withdrew consent (8 in esomeprazole, 4 in placebo), lost to f/u (5 in esomeprazole, 5 in placebo), other (5 in esomeprazole, 15 in placebo)
BMI: 28 (median)	Follow-up period: 16 weeks
Comments:	

Results

Primary outcome(s):
Adjusted mean improvement in the change in morning PEF

	Number of subjects	Mean, last 28 days of the treatment period (L/min)
Esomeprazole	386	22.3
placebo	374	16

Change in morning PEF

Pt strata	Based on information from:	Mean difference (L/min) (esomeprazole - placebo)	95% CI	P value
All pts	Last 28 days of the treatment period	6.3		0.061
	Whole treatment period	5.6		0.042
Without GERD With nocturnal respiratory symptoms (Eso n=101; placebo n=100)	Last 28 days of the treatment period	3.6	-8.7, 16.1	0.57
	Whole treatment period	2.6	-7.6, 12.8	0.62
With GERD Without nocturnal respiratory symptoms (Eso n=112; placebo n=107)	Last 28 days of the treatment period	8.3	-3.7, 20.3	0.17
	Whole treatment period	5.6	-4.3, 15.4	0.27
With GERD With nocturnal respiratory symptoms (Eso n=174; placebo n=176)	Last 28 days of the treatment period	7.0	-2.5, 16.5	0.15
	Whole treatment period	8.7	0.8, 16.5	0.03

Secondary outcome(s):
Change in evening PEF

GERD data extraction form

Pt strata	Based on information from:	Mean difference (L/min) (esomeprazole - placebo)	95% CI	P value
All pts	Last 28 days of the treatment period	5.9		0.078
	Whole treatment period	5.4		0.053
Without GERD With nocturnal respiratory symptoms	Last 28 days of the treatment period	-0.3	-12.7, 12.0	0.96
	Whole treatment period	1.3	-9.0, 11.6	0.81
With GERD Without nocturnal respiratory symptoms	Last 28 days of the treatment period	6.7	-5.1, 18.6	0.27
	Whole treatment period	4.7	-5.2, 14.6	0.35
With GERD With nocturnal respiratory symptoms	Last 28 days of the treatment period	11.2	1.8, 20.6	0.02
	Whole treatment period	10.2	2.3, 18.0	0.012

Asthma symptoms

	Number of asthma exacerbations throughout the study	Median times to exacerbation	P value
Esomeprazole	22	42 days	0.70
placebo	24	67 days	

Use of antacid (daily mean number of tablets)
Esomeprazole (n=387): 0.47
Placebo (n=383): 0.58

Comments:
Analysis on the change in morning and evening PEF in pts who took long acting beta2-agonists only is also available. Briefly, esomeprazole significantly improved both morning and evening PEF among pts with both GERD and nocturnal respiratory symptoms (see table 3 for detailed data).
There was no difference in asthma symptoms and quality of life between the 2 groups. Among pts with both GERD and nocturnal respiratory symptoms, there was a significantly smaller reduction in proportion of days with PEF variability (p=0.016) (see supplemental material).

Compliance:
Not reported

GERD data extraction form

Adverse Events:
Any
Esomeprazole (n=386): 306 events in166 pts
Placebo (n=381): 288 events in 171 pts

Asthma
Esomeprazole (n=386): 23 (6%)
Placebo (n=381): 24 (6%)
All (n=767): 47 (6%)

Nasopharyngitis
Esomeprazole (n=386): 23 (6%)
Placebo (n=381): 22 (6%)
All (n=767): 45 (6%)

Headache
Esomeprazole (n=386): 25 (6%)
Placebo (n=381): 17 (4%)
All (n=767): 42 (5%)

Nausea
Esomeprazole (n=386): 9 (2%)
Placebo (n=381): 7 (2%)
All (n=767): 16 (2%)

Back pain
Esomeprazole (n=386): 6 (2%)
Placebo (n=381): 8 (2%)
All (n=767): 14 (2%)

Rhinitis
Esomeprazole (n=386): 6 (2%)
Placebo (n=381): 8 (2%)
All (n=767): 14 (2%)

Influenza
Esomeprazole (n=386): 9 (2%)
Placebo (n=381): 4 (1%)
All (n=767): 13 (2%)

Applicability: (narrow/wide): narrow	Comments: Applicability may be wide, but there is no information on the centers

GERD data extraction form

Author: Littner	Yr: 2005	UI: 16162697	Questions addressed: atypical GERD asthma	Extractor: JHL

Objective/Topic: To investigate whether treatment with 30mg of lansoprazole improved the control of asthma in patients with moderate-to-severe persistent asthma and acid reflux symptoms

Study design: RCT	Country/Setting: US	Funding: TAP Pharmaceutical Products, Inc.

Interventions(s):	Comparator(s):
• Lansoprazole 30 mg bid	• Placebo 30 mg bid

Primary outcome(s):	Other outcome(s):
• Daily asthma symptoms	• Rescue albuterol use, daily morning and evening peak expiratory flow, FEV1, FVC, asthma quality of life with standardized activities (AQLQS) questionnaire score, investigator-assessed symptoms, exacerbations, and oral corticosteroid-treated exacerbations

Inclusion criteria:	Exclusion criteria:
(1) ≥ 18 years of age; (2) investigator-determined history of, or current, symptomatic acid reflux (the presence of acid reflux was based primarily on symptoms of heartburn without preset criteria and was subsequently confirmed by investigator assessment; consistent with clinical practice and current guidelines, investigators recruited patients who would typically be given empiric acid-suppressive therapy; however, 24-h esophageal pH monitoring was optional for the confirmation of acid reflux); (3) not taking daily or near-daily acid-suppressive treatment, apart from antacids; (4) moderate-to-severe persistent asthma; (5) FEV1 > 50% predicted and < 85% predicted; (6) ≥ 12% improvement in FEV1 (in liters) over baseline values after the inhalation of 180 µg of albuterol; (7) not smoking for ≥ 1 year with < 10 pack-years of cigarette-smoking history; (8) treatment with an inhaled corticosteroid (ICS); (9) not having marked seasonal variability in asthma or allergy symptoms; (10) reporting five or more nocturnal asthma awakenings during the 4 weeks before screening; and (11) receiving stable doses of asthma medications for at least 4 weeks before screening	(1) they were receiving ipratropium bromide or > 10 mg/d prednisone or equivalent, (2) they were receiving astemizole, (3) they were undergoing immunotherapy for < 6 months or were unable to continue receiving the current dose, (4) there was a history of upper respiratory tract infection or hospitalization for asthma within 30 days, hospitalization more than once within 6 months, or any uncontrolled clinically significant medical condition, or (5) they had been treated with a PPI within 14 days of study inclusion, or with an anticoagulant, _-blocker, tricyclic antidepressant, monoamine oxidase inhibitor, or cholinergic agents before screening.
Symptoms (describe): "97% of patients receiving lansoprazole and 95% receiving placebo had heartburn; 80% of patients in both groups had gastroesophageal regurgitation, and 32% of patients receiving lansoprazole and 47% of patients receiving placebo had dysphagia (p = 0.036)."	**Hiatal hernia (specify whether considered and size used for exclusion): ND**
EGD (performed or not and results): Not performed	**Esophagitis/stricture/Barrett's: ND**
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras,**

Not performed	**Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): ND	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: B/acceptable	
Blinding: ND	**Allocation concealment: No**
Intention-to-treat: Yes	**Method of Randomization: ND**
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		
A/rigorous, history + physical examination, laboratory tests, spirometry (i.e, for measurement of FEV_1, and FVC), and 12-lead ECG		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 45.96y	**N enrolled: 343 (screened), 207 (randomized)**
%Male: 33	**N completed: 173** • Lansoprazole, n=99 • Placebo, n=108
Race: ND	**Dropouts/reasons:** • Placebo (n=20); Adverse event (4), lost to follow-up (3), therapeutic failure (5), personal reasons (1), poor compliance (1), pregnancy (1), other (5) • Lansoprazole (n=14); Adverse event (6), lost to follow-up (3), personal reasons (2), poor compliance (1), other (2)
BMI: 30.97	**Follow-up period: 24 weeks**
Comments: Patients receiving usual asthma care including an inhaled corticosteroid	

Results

Primary outcome(s):

- **Baseline and 24-week Asthma Diary Symptoms and Selected Secondary Outcomes**

	Baseline		**24 Weeks**	
Measure	Placebo (n=108)	Lansoprazole (n=99)	Placebo (n=108)	Lansoprazole (n=99)
Asthma diary symptoms day†	1.50 (0.55)	1.51 (0.55)	1.18 (0.59)	1.20 (0.57)
Asthma diary symptoms at night†	1.32 (0.52)	1.38 (0.58)	0.99 (0.57)	1.03 (0.62)
Albuterol use,‡ No. of puffs	4.5 (3.1)	4.3 (2.6)	3.6 (3.0)	3.3 (2.6)
PEFR, L/min				
Morning	355 (88)	366 (77)	365 (95)	371 (84)
Evening	369 (91)	377 (80)	381 (97)	381 (82)
FEV_1 post-BD				
L	2.7 (0.7)	2.6 (0.6)	2.7 (0.8)	2.6 (0.7)
% predicted	83 (13)	82 (12)		
FVC post-BD				
L	3.8 (1.1)	3.6 (0.9)	3.7 (1.1)	3.6 (0.9)
% predicted	95 (16)	91 (14)		
AQLQS,§				
Overall	4.3 (0.11)	4.2 (0.12)	5.0 (0.13)	5.1 (0.14)
Emotion	4.3 (0.15)	4.1 (0.16)	4.9 (0.17)	5.1 (0.18)1
Overall asthma symptoms¶	1.56 (0.55)	1.57 (0.56)	1.35 (0.65)	1.21 (0.58)

Overall reflux symptoms¶	1.70 (0.65)	1.66 (0.69)	0.98 (0.85)	0.68 (0.65)#
Heartburn¶	1.72 (0.74)	1.75 (0.80)	1.03 (0.93)	0.49 (0.68)**
Regurgitation¶	1.27 (0.83)	1.31 (0.89)	0.75 (0.86)	0.51 (0.69)1
Dysphagia¶	0.70 (0.83)	0.46 (0.75)1	0.45 (0.77)	0.29 (0.58)

*Values are given as the mean (SD), unless otherwise indicated. post-BD = post-bronchodilator (*i.e*, after the inhalation of 180 µg of albuterol from a metered-dose-inhaler); PEFR = peak expiratory flow rate. Comparisons between treatments were not significant except as noted.
†Scale of 0 to 4, with 4 being the most severe.
‡Day and night values combined.
§Values given as the mean (SE).
‖$p < 0.05$.
¶An investigator-assessed scale was used, as follows: 0, none; 1, mild; 2, moderate; and 3, severe.
#$p < 0.01$.
**$p < 0.001$.
Abbreviations: AQLQS, asthma quality of life with standardized activities

Secondary outcome(s):

Asthma Exacerbations

- "Fewer patients receiving lansoprazole (8.1% vs 20.4%, respectively; p = 0.017) had exacerbations and oral corticosteroid-treated (*i.e*, moderate-to-severe) exacerbations (4% vs 13.9%, respectively; p = 0.016) of asthma."

Comments:

Compliance:

- The mean % of compliance; based on pill counts, lansoprazole (96.1±8.0%), placebo (97.3±5.2%)

Adverse Events:

- Any treatment-emergency adverse event: lansoprazole (74%), placebo (69%)
- "Significantly more patients receiving lansoprazole reported diarrhea (10% vs 3%, respectively) and infection (7% vs 0%, respectively). The percentages of severe adverse events were similar in the lansoprazole and placebo groups (8% vs 6%, respectively)."
- "Possibly, probably, or definitely treatment-related adverse events occurred in significantly more lansoprazole patients (13% vs 4%, respectively; p = 0.020)."

Applicability: (narrow/wide): Wide	**Comments:**

GERD data extraction form

Author: Peterson	Yr: 2009	UI: 18688720	Questions addressed: atypical GERD asthma	Extractor: JHL

Objective/Topic: The Role of Gastroesophageal Reflux in Exercise-Triggered Asthma

Study design: RCT	Country/Setting: US	Funding: PriCara, unit of Ortho-McNeil, Inc. and the AGA Foundation

Interventions(s):	Comparator(s):
• Rabeprazole (20 mg QD or 20mg per oral BID)	• Placebo 20mg BID

Primary outcome(s):	Other outcome(s):
• Respiratory symptoms • Quality of life	

Inclusion criteria:	Exclusion criteria:
• Recruited from a supra-esophageal GERD clinic at the University of Utah Hospital from 2002 to 2005 • Complained of respiratory symptoms (cough, shortness of breath, chest tightness) which occurred during (within 15 min) or directly after (10–15 min) moderate exercise, typical of asthma-related symptoms • Self-reported reflux symptoms less than twice weekly	• "…. excluded if they reported an average of greater than two episodes of heartburn weekly or concurrent use of acid suppression medication, were severe asthmatics with hospitalization within the preceding 6 months, suffered from pulmonary problems other than asthma, had a history of severe angina, cardiac arrhythmias, heart failure, myocardial infarction, or prior upper gastrointestinal surgery"
Symptoms (describe): Cough, shortness of breath, and chest tightness occurred during or directly after moderate exercise + Self-reported reflux symptoms	**Hiatal hernia (specify whether considered and size used for exclusion): ND**
EGD (performed or not and results): Not performed	**Esophagitis/stricture/Barrett's: ND**
PH study (performed or not and results):	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): ND**
Esophageal manometric studies (performed or not and results): Not performed	**Other:**

	Rabeprazole (n=23)	Placebo (n=8)
Abnormal pH	74%	63%

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
Yes

Quality Assessment for RCTs: C/Poor	
Blinding: Yes	**Allocation concealment: Yes**
Intention-to-treat: Yes	**Method of Randomization: ND**
Other comments: Subjective outcome measure: Dichotomous value for improvement in exercise symptoms ("yes" or "no")	

GERD data extraction form

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
		X
C/Poor (self-reported reflux symptoms)		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: 29.7y	**N enrolled: 37**
%Male: 51.6%	**N completed: 31**
Race: ND	**Dropouts/reasons: n=6** (due to intolerance of pH testing)
BMI: ND	**Follow-up period: 10 weeks**
Comments:	

Results
Primary outcome(s): All subjects • Symptoms improvement during exercise: rabeprazole (n=16/23, 70%) vs placebo (n=2/8, 25%), *P* = 0.03 Subgroup analysis • "the subjects with +GER also benefited from rabeprazole therapy [15/17 (88%) rabeprazole vs 1/5 (20%) placebo, *P* = 0.009]" • "those who refluxed during exercise, 15/19 demonstrated improvement in the rabeprazole group while 1/5 improved in the placebo group (*P* = 0.03). • "…no statistically significant improvement in symptoms when sub-grouped into chronic asthmatics (*P* = 0.13, RRR = 0.42) or no chronic asthmatics (*P* = 0.18)." • "…in chronic asthmatics with +GER, there was a significant improvement in symptoms in the rabeprazole group compared to placebo [10/11 (91%) vs 1/4 (25%), respectively, *P* = 0.03]" • "… no significant difference in response between the rabeprazole QD and BID groups [(12/16 (75%) vs 4/7 (57%), respectively, *P* = 0.33]" • "… no difference in PFTs (FEV1, FVC, FEV1/FVC) between the rabeprazole and placebo groups. By objective measures, rabeprazole did not provide any significant improvement in spirometry as compared to placebo (22% vs 50% respectively, *P* = 0.11)." • "Quality of life scores were also not improved after treatment in the rabeprazole groups compared to placebo in either the SF-36 (*P* = 0.97, 95% CI: -1.05 to 0.99) or mini-AQLQ (*P* = 0.21, 95% CI: -0.53 to 2.27)"
Secondary outcome(s):
Comments:

Compliance: ND

Adverse Events: No important adverse events

Applicability: (narrow/wide): Narrow (Exercise-Triggered Asthma)	**Comments:**

GERD data extraction form

Author: Sharma	Yr: 2007	UI: 17461474	Questions addressed: atypical GERD asthma	Extractor: WY

Objective/Topic:
Compare the effect of the combination of omeprazole 20 mg bid and domperidone 10 mg tid with placebo on GERD and asthma control

Study design:	Country/Setting:	Funding:
RCT	India	University of Delhi, Glaxo Smithkline Pharmaceuticals Limited, Dr. Reddy's Laboratories Ltd

Interventions(s):	Comparator(s):
omeprazole 20 mg bid (1 h before breakfast and 1 h before the dinner) and domperidone 10 mg tid (1 h before breakfast, lunch and dinner) for 16 weeks	Placebo for 16 weeks

Primary outcome(s):	Other outcome(s):
daytime and nighttime asthma symptom scores	reflux symptom scores albuterol use (number of puffs) daytime and nighttime peak expiratory flow rate (PEFR) post bronchodilator forced expiratory volume in 1 s (FEV_1) post bronchodilator forced vital capacity (FVC)

Inclusion criteria:	Exclusion criteria:
adult at least 18 years old attended the outpatient medicine and pulmonary clinics of Lok Nayak Hospital at least 12% improvement in FEV1 (in liters) after inhalation of 180 mg of albuterol mild-to-moderate persistent asthma no exacerbations or significant change in asthma medications during past weeks of screening confirmed GERD using 24-hour esophageal pH monitoring, with >4.5% total time for which pH was < 4	History of unstable chronic medical condition; current or post smokers; hex of other lung disease; use of antireflux medications including antacids, histamine-2-receptor antagonists, proton pump inhibitors or prokinetic agents
Symptoms (describe): no	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): no	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): All pts had >4.5% total time for which pH was < 4	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other:

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

GERD data extraction form

Quality Assessment for RCTs: B/acceptable	
Blinding: double blinded	Allocation concealment: no
Intention-to-treat: no	Method of Randomization: not reported
Other comments: dropout reasons were not described; method of randomization was not described.	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
x		

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 51.48 years old	N randomized: 204
%Male: 68.7%	N completed: 198
Race: not reported	Dropouts/reasons: 6 dropouts, reason not described
BMI: 27.35	Follow-up period: 16 weeks
Comments:	

Results

Primary outcome(s):
daytime asthma symptom scores

	Baseline	After 16 weeks	P (compared with baseline)	% mean change	P (btw groups)
omeprazole and domperidone	2.48 ± 0.80	2.04 ± 0.68	0.0002	17.4% decrease	0.0001
placebo	2.46 ± 0.79	2.24 ± 0.64	NS	8.94% decrease	

nighttime asthma symptom scores

	Baseline	After 16 weeks	P (compared with baseline)	% mean change	P (btw groups)
omeprazole and domperidone	2.60 ± 0.80	2.09 ± 0.67	0.0007	19.6% decrease	0.0001
placebo	2.59 ± 0.79	2.45 ± 0.71	NS	5.4% decrease	

Secondary outcome(s):
reflux symptom scores

	Baseline	After 16 weeks	P (compared with baseline)	% mean change	P (btw groups)
omeprazole and domperidone	2.48 ± 0.76	1.52 ± 0.52	0.00001	8.7% decrease	0.0003
placebo	2.49 ± 0.73	2.45 ± 0.64	NS	1.6% decrease	

albuterol use (number of puffs)

	Baseline	After 16 weeks	P (compared with baseline)	% mean change	P (btw groups)
omeprazole and domperidone	3.27 ± 1.04	2.51 ± 0.69	0.0001	23.2% decrease	0.0001
placebo	3.25 ± 1.02	3.15 ± 0.97	NS	3.08%	

morning peak expiratory flow rate (PEFR)

	Baseline	After 16 weeks	P (compared with baseline)	% mean change	P (btw groups)
omeprazole and	283.58 ± 43.27	306.36 ± 42.19	0.005	7.9%	0.004

domperidone				improvement	
placebo	285.45 ± 44.27	286.01 ± 43.89	NS	0.2% improvement	

evening peak expiratory flow rate (PEFR)

	Baseline	After 16 weeks	P (compared with baseline)	% mean change	P (btw groups)
omeprazole and domperidone	283.69 ± 54.49	311.45 ± 50.85	0.003	9.8% improvement	0.002
placebo	288.06 ± 57.38	286.63 ± 53.39	NS	0.5% improvement	

post bronchodilator forced expiratory volume in 1 s (FEV_1)

	Baseline (L)	After 16 weeks (L)	Baseline (% predicted)	After 16 weeks (% predicted)	P (compared with baseline)	% mean change	P (btw groups)
omeprazole and domperidone	1.89 ± 0.40	2.10 ± 0.34	68.58 ± 3.56	70.66 ± 3.02	0.001	11.1% improvement	0.0013
			68.89 (3.57)				
placebo	1.85 ± 0.40	1.92 ± 0.41	68.69 ± 3.59	68.89 ± 3.57	NS	3.78% improvement	

post bronchodilator forced vital capacity (FVC)

	Baseline (L)	After 16 weeks (L)	Baseline (% predicted)	After 16 weeks (% predicted)	P (compared with baseline)	% mean change	P (btw groups)
omeprazole and domperidone	1.94 ± 0.37	2.12 ± 0.31	69.24 ± 3.39	71.12 ± 2.88	0.002	9.3% improvement	0.0023
placebo	1.97 ± 0.35	1.94 ± 0.37	69.65 ± 3.45	69.28 ± 3.42	NS	1.52% improvement	

Comments:

Compliance:
By pill count:
omeprazole and domperidone group 95.2% ± 7.4%
placebo group 96.7% ±6.3%
p= 0.87

Adverse Events:
Any adverse events:
omeprazole and domperidone group 64%
placebo group 60%
p= 0.7
Severe adverse events:
omeprazole and domperidone group 10%
placebo group 8%
p= 0.4
Observed severe adverse events included myalgia (4%), aggression (3%), thrombocytopenia (1%), urticaria (1%) and Steven-Johnson syndrome (1%) in the omeprazole and domperidone group.

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

GERD data extraction form

Author: Shimizu	Yr: 2006	UI: 16778364	Questions addressed: atypical GERD asthma	Extractor: WY

Objective/Topic:
Compare the efficacy of Roxatidine, 150 mg/day and lansoprazole, 30 mg/day on asthma symptoms

Study design:	Country/Setting:	Funding:
RCT	Japan	"not supported by any grants"

Interventions(s):	Comparator(s):
Roxatidine 150 mg/day for 2 months	lansoprazole 30 mg/day for 2 months

Primary outcome(s):	Other outcome(s):
GERD symptoms per QUEST (questionnaire for the diagnosis of reflux disease) score	Morning peak expiratory flow (PEF) Forced expiratory volume in 1 second (FEV1) IgE Asthma symptoms per asthma control questionnaire (ACQ) score

Inclusion criteria:	Exclusion criteria:
16 years or older Diagnosed with both asthma and GERD GERD symptoms (QUEST ≥ 4) or endoscopic exam Grade ≥ M	Pregnant or lactating; smokers; mentally incompetent; history of liver, kidney or other severe diseases; history of esophageal, gastric or duodenal surgery; history of drug induced allergy; history of prior Tx with Ace inhibitor, muscarine receptor antagonist or acid suppressive drugs
Symptoms (describe): QUEST ≥ 4: 21 pts (70%) QUEST <3: 9 pts (30%)	Hiatal hernia (specify whether considered and size used for exclusion): no
EGD (performed or not and results): Yes LA Grade N: 5 pts LA Grade M: 9 pts LA Grade A: 13 pts LA Grade B: 2 pts LA Grade C: 1 pt LA Grade D: 0 pt	Esophagitis/stricture/Barrett's: no
PH study (performed or not and results): no	Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other): no
Esophageal manometric studies (performed or not and results): no	Other: no

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences)
yes

Quality Assessment for RCTs: B/acceptable	
Blinding: pt	Allocation concealment: not reported

GERD data extraction form

Intention-to-treat: N/A (no dropout)	Method of Randomization: not reported
Other comments:	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	B/acceptable	C/Poor
	x	

Characteristics of enrolled patients	Results: Disposition of Enrolled Subjects
Age: 57.5	N enrolled: 30
%Male: 43.3%	N completed: 30
Race: not reported	Dropouts/reasons: no dropout
BMI: not reported	Follow-up period: 2 months
Comments:	

Results

Primary outcome(s):
QUEST score

	Baseline (mean ± SD)	After 2 months (mean ± SD)	P (before vs after)
Roxatidine group (n=15)	8.1 ± 4.9	4 ± 3.6	0.002
Lansoprazole group (n=15)	8.3 ± 4.9	2.4 ± 2.8	0.0009

Secondary outcome(s):
Morning PEF

	Baseline (mean ± SD)	After 2 months (mean ± SD)	P (before vs after)
Roxatidine group (n=15)	321.5 ± 161.3	334.9 ± 141.2	0.08
Lansoprazole group (n=15)	323.1 ± 119.3	353.3 ± 119.4	0.002

$FEV_{1.0}$ (ml)

	Baseline (mean ± SD)	After 2 months (mean ± SD)	P (before vs after)
Roxatidine group (n=15)	1839.7 ± 880.7	2003.3 ± 883.4	NS
Lansoprazole group (n=15)	1993.3 ± 850.1	2057.4 ± 927.8	NS

IgE (IU/ml)

	Baseline (mean ± SD)	After 2 months (mean ± SD)	P (before vs after)
Roxatidine group (n=15)	239.0 ± 251.2	240.9 ± 248.1	NS
Lansoprazole group (n=15)	281.6 ± 289.3	286.0 ± 302.7	NS

ACQ

	Baseline (mean ± SD)	After 2 months (mean ± SD)	P (before vs after)
Roxatidine group (n=15)	12.3 ± 2.1	9.0 ± 3.1	NS
Lansoprazole group (n=15)	14.4 ± 4.2	9.4 ± 4.2	<0.05

WBC, RBC, AST, ALT, LDH, BUN, Cr, Na, K, and Cl did not change in both treatment groups.

Comments:

Compliance:
Not reported

Adverse Events: No adverse events found.

Applicability: (narrow/wide): narrow	Comments:

GERD data extraction form

Author: Sontag, SJ	**Yr:**2003	**UI:** 12809818	**Questions addressed:** Atypical GERD	**Extractor:** Peter Bonis

Objective/Topic: Compare two medical interventions with Nissen fundoplication in patients with GERD and asthma.

Study design: Parallel group RCT	**Country/Setting:** Multicenter US academic medical centers	**Funding:** VA merit Review Grant and Loyola University Stritchy School of Medicine

Interventions(s): Lifestyle modifications plus one of three intervention: 1) PRN antacids [control group] 2) Ranitidine 150 mg TID [medical group] 3) Nissen fundoplication [intervention group]	**Comparator(s):** Fundoplication compared with medical intervention and control group

Primary outcome(s): 1) Asthma symptom scores 2) Objective asthma parameters such as mean peak expiratory flow rate (PEFR), pulmonary function tests and need for pulmonary medications 3) overall predefined clinical status grade (defined as proportion achieving 40% improvement from baseline and mean percentage improvement from baseline as determined by the patient and study nurse. Categories included ("cure, markedly improved, improved, unimproved and worsened).	**Other outcome(s):** 1) Healing of esophagitis 2) GER symptom control 3) Esophageal manometry and pH testing results 4) Complications 5) Data reported for a subset of patients with up to 19.1 years f/u.

Inclusion criteria: Presence of both GER (defined as a positive 24-h ambulatory pH test and the presence of macroscopic or microscopic findings of GERD on endoscopy) and asthma (defined as a history of discrete attacks of wheezing, coughing or dyspnea and an increased in FEV1 of 20% from baseline with bronchodilator administration or a 20% decrease in FEV1 with up to 205.5 dose units of methacholine.	**Exclusion criteria:** 1)PaO2 <60 mm Hg, 2) PaCO2 >44 mm Hg, 3) FEV1 (after bronchodilator therapy) <50% predicted or less than 4L, 4) contraindications to antireflux surgery 5) mild asthma that causes no impairment in activities 6) occupational, extrinsic or seasonal asthma 7) previous GERD surgery or gastric outlet obstruction 8) age >80
Symptoms (describe): % in control, medical and surgical groups, respectively: heartburn (75, 66.7, 87.5); pharyngeal burning (41.7, 54.2, 37.5), reflux of food (50.0, 33.3, 37.5), sore throat (25.0, 37.5, 25.0), nighttime wheezing (58.3, 50.0, 43.8), nighttime cough (45.8, 59.1, 56.2), nighttime gasping (33.3, 41.7, 56.2), asthma score (5.9 +/- 1.4, 5.9 +/- 2.1, 5.1 +/- 2.1), reflux score (5.2 +/- 0-.6, 5.3 +/- 0.6, 4.8 +/- 0.5).	**Hiatal hernia** (specify whether considered and size used for exclusion): Did not specify if size was used for exclusion. % with hiatal hernia in control, medical and surgical groups, respectively: 79.2, 77.3, 68.8).
EGD (performed or not and results): Yes, in all patients. % with normal, erosions or ulcers in control, medical and surgical groups, respectively: 41.7, 45.8, 12.5; 40.9, 40.9, 18.2; 25.0, 56.2, 18.8)	**Esophagitis/stricture/Barrett's:** % with Barrett's with or without esophagitis in control, medical and surgical groups, respectively: 16.7, 27.2, 25.0)

GERD data extraction form

PH study (performed or not and results): yes, performed in all and classified as upright, supine % time pH<4 and number of reflux episodes/hr. Data in table 5 of manuscript. As noted in methods, was abnormal in all patients.	**Response to previous therapy (specify, PPIs, H2Ras, Lifestyle modifications or other):** Not described
Esophageal manometric studies (performed or not and results): Yes, performed in all patients. Mean LES pressure in control, medical and surgical groups: 15 +/- 8, 13+/- 9, 9 +/- 1.5)	**Other:**

Were Inclusion/Exclusion criteria the same for all arms? (Specify yes or no and describe differences) Yes

Quality Assessment for RCTs: C/Poor	
Blinding: No	**Allocation concealment:** Not described
Intention-to-treat: No	**Method of Randomization:** Not described
Other comments: Lack of blinding and subjective nature of symptom assessment for asthma outcomes were major shortcomings of the study, especially since the subjective outcomes did not correlate well with objective outcomes.	

Quality Assessment Non-RCTs:
Comments:

Diagnostic Quality: A/rigorous	**B/acceptable**	**C/Poor**
X		

Characteristics of enrolled patients	**Results: Disposition of Enrolled Subjects**
Age: Mean age in control, medical, surgical: 52, 52, 48	**N enrolled:** 75 randomized
%Male: 88, 95, 100	**N completed:** 62 analyzed : 24 control, 22 medical, 16 surgical
Race: ND	**Dropouts/reasons:** 13: 2 requested surgery, 2 lost to f/u, 9 refused surgery
BMI: ND	**Follow-up period:** 2 years
Comments:	

Results
Primary outcome(s): 1) No statistically significant difference in PEFR among the three groups, although trend toward improvement in surgical group compared to combined medical and control groups 2) No significant difference in requirement for pulmonary medications such as bronchodilators or corticosteroids 3) Overall clinical improvement significantly better in surgical group (p<0.001 compared with medical and control groups) Surgical group: 1 patient "cured," 6 "markedly improved, 5 "improved. Control group: "improvement" in 1 patient. Medical group: "improvement" in 2 patients. 4) Overall asthma symptom score (≥40% improvement from baseline) significantly better in the surgical versus medical/control groups (p<0.05)
Secondary outcome(s): 1) healing of esophagitis: 19, 42 and 100% in the control, medical and surgical groups, respectively (p<0.001 in surgical versus control and medical) 2) Authors report improvement in an additional 2 patients in the surgical group between 2 and 4 years after surgery, with near complete resolution of all pulmonary symptoms.
Comments:

GERD data extraction form

Compliance: ND

Adverse Events: 2 deaths in surgical group 8 and 6 months after the procedures. 1 patient in surgical group developed dysphagia for 31 days after the procedure, 3 had early gas bloat syndrome that resolved, one developed an incisional hernia that required repair

Applicability: (narrow/wide): narrow	**Comments:** Lack of blinding and subjective nature of symptom assessment for asthma outcomes were major shortcomings of the study, especially since the subjective outcomes did not correlate well with objective outcomes. The authors selected patients GERD by objective measures and thus results may not be applicable to all GERD patients. The medical group was treated with an H2RA and thus the results of this study are limited since such therapy is known to be inferior to PPI treatment for treatment of GERD. The authors did not include the 9 patients who refused surgery in the analysis. The group that was willing to have surgery may have had more severe symptoms making the benefit of surgery harder to detect. On the other hand, the trending benefit noted with surgery may have been confined to patients with relatively severe GERD