

Comparative Effectiveness of Management Strategies For Gastroesophageal Reflux Disease

Appendixes

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Search strategy

1. exp Gastroesophageal Reflux
2. gastro-esophageal reflux.tw.
3. gastro-esophageal reflux.tw.
4. gastro-oesophageal reflux.tw.
5. exp esophagitis
6. esophagitis.tw.
7. oesophagitis.tw.
8. (GERD or GORD).tw.
9. bile reflux
10. heartburn
11. heartburn.tw.
12. (acid adj5 reflux).tw.
13. exp dyspepsia
14. dyspep\$.tw.
15. or/1-14
16. limit 15 to human
17. limit 16 to english language
18. limit 17 to adult
19. 17 not 18
20. limit 19 to child
21. 17 not 20
22. follow-up studies
23. (follow-up or followup).tw.
24. exp cohort studies
25. cohort.tw.
26. exp Case-Control Studies
27. (case adj20 control).tw.
28. exp Longitudinal Studies
29. longitudinal.tw.
30. (random\$ or rct).tw.
31. exp Randomized Controlled Trials
32. exp random allocation
33. exp Double-Blind Method
34. exp Single-Blind Method
35. randomized controlled trial.pt.
36. clinical trial.pt.
37. controlled clinical trials
38. (clin\$ adj trial\$.tw.
39. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj (blind\$ or mask\$)).tw.
40. exp Research Design
41. exp Evaluation Studies
42. exp Prospective Studies
43. exp Comparative Study

Appendix A. Search strategy (continued)

44. or/22-41
45. 21 and 44
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)
47. 45 not 46
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)
49. 47 not 48
50. dt.fs.
51. su.fs.
52. 49 and (50 and 51)
53. 49 not 52
54. 53 and 51
55. 53 not 54
56. 55 and 50
57. 55 not 56
58. th.fs.
59. 57 and 58
60. 57 not 59
61. co.fs.
62. 60 and 61
63. 60 not 62
64. limit 63 to "all adult (19 plus years)"
65. exp Gastroesophageal Reflux
66. gastro-esophageal reflux.tw.
67. gastro-esophageal reflux.tw.
68. gastro-oesophageal reflux.tw.
69. exp esophagitis
70. esophagitis.tw.
71. oesophagitis.tw.
72. (GERD or GORD).tw.
73. bile reflux
74. heartburn
75. heartburn.tw.
76. (acid adj5 reflux).tw.
77. exp dyspepsia
78. dyspep\$.tw.
79. or/65-78
80. limit 79 to human
81. limit 80 to english language
82. limit 81 to "all adult (19 plus years)"
83. 81 not 82
84. limit 83 to "all child (0 to 18 years)"

Appendix A. Search strategy (continued)

85. 81 not 84
86. follow-up studies
87. (follow-up or followup).tw.
88. exp cohort studies
89. cohort.tw.
90. exp Case-Control Studies
91. (case adj20 control).tw.
92. exp Longitudinal Studies
93. longitudinal.tw.
94. (random\$ or rct).tw.
95. exp Randomized Controlled Trials
96. exp random allocation
97. exp Double-Blind Method
98. exp Single-Blind Method
99. randomized controlled trial.pt.
100. clinical trial.pt.
101. controlled clinical trials
102. (clin\$ adj trial\$).tw.
103. ((singl\$ or doubl\$ or treb1\$ or tripl\$) adj (blind\$ or mask\$)).tw.
104. exp Research Design
105. exp Evaluation Studies
106. exp Prospective Studies
107. exp Comparative Study
108. or/86-105
109. 85 and 108
110. limit 109 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)
111. 109 not 110
112. limit 111 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)
113. 111 not 112
114. dt.fs.
115. su.fs.
116. 113 and (114 and 115)
117. 113 not 116
118. 117 and 115
119. 117 not 118
120. 119 and 114
121. 119 not 120
122. th.fs.
123. 121 and 122
124. 121 not 123

Appendix A. Search strategy (continued)

125. co.fs.
126. 124 and 125
127. 124 not 126
128. from 127 keep 1

Appendix B. List of Excluded Studies

List of Excluded Studies

Abbas AE;Deschamps C;Cassivi SD;Allen MS;Nichols FC;Miller DL;Pairolero PC;Barrett's esophagus: the role of laparoscopic fundoplication 2004 Feb Annals of Thoracic Surgery 77(2):393-6,
Outcome not of interest

Ackroyd R;Watson DI;Majeed AW;Troy G;Treacy PJ;Stoddard CJ;Randomized clinical trial of laparoscopic versus open fundoplication for gastro-oesophageal reflux disease.[see comment] 2004 Aug British Journal of Surgery 91(8):975-82,
Does not meet inclusion criteria

Alexander HC;Hendler RS;Seymour NE;Shires GT;Laparoscopic treatment of gastroesophageal reflux disease 1997 May American Surgeon 63(5):434-40,
Does not meet inclusion criteria

Alexiou C;Beggs D;Salama FD;Beggs L;Knowles KR;A tailored surgical approach for gastro-oesophageal reflux disease: the Nottingham experience 2000 Apr European Journal of Cardio-Thoracic Surgery 17(4):389-95,
Does not meet inclusion criteria

Alexiou C;Salama FD;Beggs D;Brackenbury ET;Knowles KR;Comparison of long-term results of total fundoplication gastropasty and Belsey Mark IV antireflux operations in relation to the severity of oesophagitis 1999 Mar European Journal of Cardio-Thoracic Surgery 15(3):320-6,
Technique not of interest

Allen CJ;Anvari M;Gastro-oesophageal reflux related cough and its response to laparoscopic fundoplication 1998 Nov Thorax 53(11):963-8,
Does not meet inclusion criteria

Allescher HD;Bockenhoff A;Knapp G;Wienbeck M;Hartung J;Treatment of non-ulcer dyspepsia: a meta-analysis of placebo-controlled prospective studies.[see comment] 2001 Sep Scandinavian Journal of Gastroenterology 36(9):934-41,
Population not of interest

Allgood PC;Bachmann M;Medical or surgical treatment for chronic gastroesophageal reflux? A systematic review of published evidence of effectiveness 2000 Sep European Journal of Surgery 166(9):713-21,
Poor quality

Althar RA;Laparoscopic anti-reflux surgery in the community hospital setting: evaluation of 100 consecutive patients 1999 Apr Journal of the Society of Laparoendoscopic Surgeons 3(2):107-12,
Does not meet inclusion criteria

Anderson JA;Myers JC;Watson DI;Gabb M;Mathew G;Jamieson GG;Concurrent fluoroscopy and manometry reveal differences in laparoscopic Nissen and anterior fundoplication 1998 Apr Digestive Diseases & Sciences 43(4):847-53,
Does not meet inclusion criteria

Anvari M;Allen C;Borm A;Laparoscopic Nissen fundoplication is a satisfactory alternative to long-term omeprazole therapy 1995 Jul British Journal of Surgery 82(7):938-42,
Does not meet inclusion criteria

Anvari M;Allen C;Moran LA;Immediate and delayed effects of laparoscopic Nissen fundoplication on pulmonary function 1996

Appendix B. List of Excluded Studies (continued)

Dec Surgical Endoscopy 10(12):1171-5,

Does not meet inclusion criteria

Arca MJ;Gagner M;GarciaRuiz A;Todd HB;The significance of pH and manometric testing after laparoscopic fundoplication.[see comment] 2002 Mar Surgical Endoscopy 16(3):395-400,

Outcome not of interest

Attwood SE;Barlow AP;Norris TL;Watson A;Barrett's oesophagus: effect of antireflux surgery on symptom control and development of complications 1992 Oct British Journal of Surgery 79(10):1050-3,

Does not meet inclusion criteria

Battle WS;Nyhus LM;Bombeck CT;Nissen fundoplication and esophagitis secondary to gastroesophageal reflux 1973 Apr Archives of Surgery 106(4):588-92,

Does not meet inclusion criteria

Bell RC;Hanna P;Powers B;Sabel J;Hruza D;Clinical and manometric results of laparoscopic partial (Toupet) and complete (Rosetti-Nissen) fundoplication 1996 Jul Surgical Endoscopy 10(7):724-8,

Does not meet inclusion criteria

Bensoussan AL;Yazbeck S;CarcellerBlanchard A;Results and complications of Toupet partial posterior wrap: 10 years' experience 1994 Sep Journal of Pediatric Surgery 29(9):1215-7,

Pediatrics

Bischof G;Feil W;Riegler M;Wenzl E;Schiessel R;Peptic esophageal stricture: is surgery still necessary? 1996Wiener Klinische Wochenschrift 108(9):267-71,

Population not of interest

Bisgaard T;Stockel M;Klarskov B;Kehlet H;Rosenberg J;Prospective analysis of convalescence and early pain after uncomplicated laparoscopic fundoplication 2004 Nov British Journal of Surgery 91(11):1473-8,

Outcome not of interest

Blomqvist A;Dalenback J;Hagedorn C;Lonroth H;Hyltander A;Lundell L;Impact of complete gastric fundus mobilization on outcome after laparoscopic total fundoplication 2000 Sep Journal of Gastrointestinal Surgery 4(5):493-500,

Does not meet inclusion criteria

Blomqvist A;Lonroth H;Dalenback J;Ruth M;Wiklund I;Lundell L;Quality of life assessment after laparoscopic and open fundoplications. Results of a prospective, clinical study 1996 Nov Scandinavian Journal of Gastroenterology 31(11):1052-8,

Does not meet inclusion criteria

Bloomston M;Niels W;Rosemurgy AS;Symptoms and antireflux medication use following laparoscopic Nissen fundoplication: outcome at 1 and 4 years.[erratum appears in JSLS. 2003 Oct-Dec;7(4):388] 2003 Jul Journal of the Society of Laparoendoscopic Surgeons 7(3):211-8,

Does not meet inclusion criteria

Bloomston M;Zervos E;Gonzalez R;Albrink M;Rosemurgy A;Quality of life and antireflux medication use following laparoscopic Nissen fundoplication 1998 Jun American Surgeon 64(6):509-13; discussion 513-4,

Does not meet inclusion criteria

Blum AL;Treatment of acid-related disorders with gastric acid inhibitors: the state of the art 1990Digestion 47 Suppl 1:3-10; discussion 49-52,

Data available in systematic review

Booth MI;Stratford J;Thompson E;Dehn TC;Laparoscopic antireflux surgery in the treatment of the acid-sensitive oesophagus 2001 Apr British Journal of Surgery 88(4):577-82,

Does not meet inclusion criteria

Boutelier P;Jonsell G;An alternative fundoplicative maneuver for gastroesophageal reflux 1982 Feb American

Appendix B. List of Excluded Studies (continued)

Journal of Surgery 143(2):260-4,
Does not meet inclusion criteria

Bowes KL;Sarna SK;Effect of fundoplication on the lower esophageal sphincter 1975 Jul Canadian Journal of Surgery 18(4):328-33,

Outcome not of interest

Bowes KL;Sarna SK;Effect of fundoplication on the lower esophageal sphincter 1975 Jul Canadian Journal of Surgery 18(4):328-33,

Outcome not of interest

Brand DL;Eastwood IR;Martin D;Carter WB;Pope CE;Esophageal symptoms, manometry, and histology before and after antireflux surgery: a long-term follow-up study 1979 Jun Gastroenterology 76(6):1393-401,

Does not meet inclusion criteria

Brouwer R;Kiroff GK;Improvement of respiratory symptoms following laparoscopic Nissen fundoplication 2003 Apr ANZ Journal of Surgery 73(4):189-93,

Does not meet inclusion criteria

Brunner G;Creutzfeldt W;Omeprazole in the long-term management of patients with acid-related diseases resistant to ranitidine 1989Scandinavian Journal of Gastroenterology - Supplement 166:101-5; discussion 111-3,

Available meta-analysis

Bushkin FL;Neustein CL;Parker TH;Woodward ER;Nissen fundoplication for reflux peptic esophagitis 1977 Jun Annals of Surgery 185(6):672-7,

Does not meet inclusion criteria

Byrne WJ;Euler AR;Ashcraft E;Nash DG;Seibert JJ;Golladay ES;Gastroesophageal reflux in the severely retarded who vomit: criteria for and results of surgical intervention in twenty-two patients 1982 Jan Surgery 91(1):95-8,

Does not meet inclusion criteria

Cadiere GB;Himpens J;Rajan A;Muls V;Lemper JC;Bruyans J;Urbain D;Ham H;Laparoscopic Nissen fundoplication: laparoscopic dissection technique and results 1997 Jan Hepato-Gastroenterology 44(13):4-10,

Does not meet inclusion criteria

Cadiere GB;Himpens J;Vertruyen M;Bruyans J;Germay O;Leman G;Izizaw R;Evaluation of telesurgical (robotic) NISSEN fundoplication 2001 Sep Surgical Endoscopy 15(9):918-23,

Surgical technique description

Champault G;Volter F;Rizk N;Boutelier P;Gastroesophageal reflux: conventional surgical treatment versus laparoscopy. A prospective study of 61 cases 1996 Dec Surgical Laparoscopy & Endoscopy 6(6):434-40,

Does not meet inclusion criteria

Chiba N;De Gara CJ;Wilkinson JM;Hunt RH;Speed of healing and symptom relief in grade II to IV gastroesophageal reflux disease: a meta-analysis 1997 Jun Gastroenterology 112(6):1798-810,

Data available in subsequent meta-analysis

Chrysos E;Athanasakis E;Pechlivanides G;Tzortzinis A;Mantides A;Xynos E;The effect of total and anterior partial fundoplication on antireflux mechanisms of the gastroesophageal junction 2004 Jul American Journal of Surgery 188(1):39-44,

Does not meet inclusion criteria

Chrysos E;Prokopakis G;Athanasakis E;Pechlivanides G;Tsiaoussis J;Mantides A;Xynos E;Factors affecting esophageal motility in gastroesophageal reflux disease 2003 Mar Archives of Surgery 138(3):241-6,

Outcome not of interest

Chrysos E;Tsiaoussis J;Zoras OJ;Athanasakis E;Mantides A;Katsamouris A;Xynos E;Laparoscopic surgery for

Appendix B. List of Excluded Studies (continued)

gastroesophageal reflux disease patients with impaired esophageal peristalsis: total or partial fundoplication? 2003 *Journal of the American College of Surgeons* 197(1):8-15
Does not meet inclusion criteria

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] 2005 Feb *Gut* 54(2):183-6,
Gatekeeper not available in US

Civello IM;Brisinda G;Sganga G;De Fazio S;Maria G;Crucitti F;Modified Hill operation vs. Nissen fundoplication in the surgical treatment of gastro-esophageal reflux disease 1997 Mar *Hepato-Gastroenterology* 44(14):380-6,
Intervention not of interest

Coelho JC;Wiederkehr JC;Campos AC;Andrigueto PC;Conversions and complications of laparoscopic treatment of gastroesophageal reflux disease 1999 Oct *Journal of the American College of Surgeons* 189(4):356-61,
Mixed surgeries

Cohen JA;Arain A;Harris PA;Byrne DW;Holzman MD;Sharp KW;Richards WO;Surgical trial investigating nocturnal gastroesophageal reflux and sleep (STINGERS) 2003 Mar *Surgical Endoscopy* 17(3):394-400,
Does not meet inclusion criteria

Contini S;Bertele A;Nervi G;Zinicola R;Scarpignato C;Quality of life for patients with gastroesophageal reflux disease 2 years after laparoscopic fundoplication. Evaluation of the results obtained during the initial experience.[see comment] 2002 Nov *Surgical Endoscopy* 16(11):1555-60,
Does not meet inclusion criteria

Contini S;Bertele A;Nervi G;Zinicola R;Scarpignato C;Quality of life for patients with gastroesophageal reflux disease 2 years after laparoscopic fundoplication. Evaluation of the results obtained during the initial experience.[see comment] 2002 Nov *Surgical Endoscopy* 16(11):1555-60,
Does not meet inclusion criteria

Contini S;Zinicola R;Bertele A;Nervi G;Rubini P;Scarpignato C;Dysphagia and clinical outcome after laparoscopic Nissen or Rossetti fundoplication: sequential prospective study 2002 Sep *World Journal of Surgery* 26(9):1106-11,
Does not meet inclusion criteria

Coster DD;Bower WH;Wilson VT;Brebrick RT;Richardson GL;Laparoscopic partial fundoplication vs laparoscopic Nissen-Rosetti fundoplication. Short-term results of 231 cases.[see comment] 1997 Jun *Surgical Endoscopy* 11(6):625-31,
Does not meet inclusion criteria

Coster DD;Bower WH;Wilson VT;Butler DA;Locker SC;Brebrick RT;Laparoscopic Nissen fundoplication--a curative, safe, and cost-effective procedure for complicated gastroesophageal reflux disease 1995 Apr *Surgical Laparoscopy & Endoscopy* 5(2):111-7,
Does not meet inclusion criteria

Cremonini F;Di Caro S;DelgadoAros S;Sepulveda A;Gasbarrini G;Gasbarrini A;Camilleri M;Meta-analysis: the relationship between *Helicobacter pylori* infection and gastro-oesophageal reflux disease.[retraction in Cremonini F, Di Caro S, Delgado-Aros S, Sepulveda A, Gasbarrini G, Gasbarrini A, Camilleri M. *Aliment Pharmacol Ther.* 2004 Jan 1;19(1):145; PMID: 14687178] 2003 Aug 1 *Alimentary Pharmacology & Therapeutics* 18(3):279-89,
Intervention not of interest

Csendes A;Burdiles P;Korn O;Braghetto I;Huertas C;Rojas J;Late results of a

Appendix B. List of Excluded Studies (continued)

randomized clinical trial comparing total fundoplication versus calibration of the cardia with posterior gastropexy 2000 Mar British Journal of Surgery 87(3):289-97,
Intervention not of interest

Dallemagne B;Weerts JM;Jeahes C;Markiewicz S;Results of laparoscopic Nissen fundoplication 1998 Sep Hepato-Gastroenterology 45(23):1338-43,
Does not meet inclusion criteria

Dallemagne B;Weerts JM;Jeahes C;Markiewicz S;Causes of failures of laparoscopic antireflux operations 1996 Mar Surgical Endoscopy 10(3):305-10,
Does not meet inclusion criteria

Dassinger MS;Torquati A;Houston HL;Holzman MD;Sharp KW;Richards WO;Laparoscopic fundoplication: 5-year follow-up 2004 Aug American Surgeon 70(8):691-4; discussion 694-5,
Does not meet inclusion criteria

de Beaux AC;Watson DI;O'Boyle C;Jamieson GG;Role of fundoplication in patient symptomatology after laparoscopic antireflux surgery 2001 Aug British Journal of Surgery 88(8):1117-21,
Descriptive study

de Jong JR;van Ramshorst B;Timmer R;Gooszen HG;Smout AJ;The influence of laparoscopic adjustable gastric banding on gastroesophageal reflux 2004 Mar Obesity Surgery 14(3):399-406,
Does not meet inclusion criteria

DeMeester TR;Bonavina L;Albertucci M;Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients 1986 Annals of Surgery
Does not meet inclusion criteria

DeMeester TR;Johnson LF;Evaluation of the Nissen antireflux procedure by esophageal manometry and twenty-four hour pH monitoring 1975 Jan American Journal

of Surgery 129(1):94-100,
Does not meet inclusion criteria

Demos NJ;Stapled, uncut gastroplasty for hiatal hernia: 12-year follow-up 1984 Oct Annals of Thoracic Surgery 38(4):393-9,
Intervention not of interest

Desai KM;Soper NJ;Frisella MM;Quasebarth MA;Dunnegan DL;Brunt LM;Efficacy of laparoscopic antireflux surgery in patients with Barrett's esophagus 2003 Dec American Journal of Surgery 186(6):652-9,
Outcome not of interest

DeVault KR;Surgery versus medical therapy for gastroesophageal reflux disease 2001 Jun American Journal of Gastroenterology 96(6):1932-3,
Comment

Dobrilla G;Comberlato M;Steele A;Vallaperta P;Drug treatment of functional dyspepsia. A meta-analysis of randomized controlled clinical trials 1989 Apr Journal of Clinical Gastroenterology 11(2):169-77,
Population not of interest

Donahue PE;Samelson S;Nyhus LM;Bombeck CT;The floppy Nissen fundoplication. Effective long-term control of pathologic reflux 1985 Jun Archives of Surgery 120(6):663-8,
Does not meet inclusion criteria

Edwards SJ;Lind T;Lundell L;Systematic review of proton pump inhibitors for the acute treatment of reflux oesophagitis 2001 Nov Alimentary Pharmacology & Therapeutics 15(11):1729-36,
Limited individual comparisons (only esomeprazole vs. omeprazole)

Ellingson TL;Kozarek RA;Gelfand MD;Botoman AV;Patterson DJ;Iatrogenic achalasia. A case series 1995 Journal of Clinical Gastroenterology
Population not of interest

Appendix B. List of Excluded Studies (continued)

Erenoglu C;Miller A;Schirmer B;Laparoscopic Toupet versus Nissen fundoplication for the treatment of gastroesophageal reflux disease 2003 Oct International Surgery 88(4):219-25,
Does not meet inclusion criteria

Eriksson S;Langstrom G;Rikner L;Carlsson R;Naesdal J;Omeprazole and H2-receptor antagonists in the acute treatment of duodenal ulcer, gastric ulcer and reflux oesophagitis: a meta-analysis.[erratum appears in Eur J Gastroenterol Hepatol 1996 Feb;8(2):192] 1995 May European Journal of Gastroenterology & Hepatology 7(5):467-75,

Data available in subsequent systematic review

Eshraghi N;Farahmand M;Soot SJ;RandLuby L;Deveney CW;Sheppard BC;Comparison of outcomes of open versus laparoscopic Nissen fundoplication performed in a single practice 1998 May American Journal of Surgery 175(5):371-4,
Does not meet inclusion criteria

Ettinger;Paul RE;Moran JM;Gastric pseudotumor after fundoplication 1971 Sep Gastroenterology 61(3):299-304,
Outcome not of interest

Feldman LS;Mayrand S;Stanbridge D;Mercier L;Barkun JS;Fried GM;Laparoscopic fundoplication: a model for assessing new technology in surgical procedures 2001 Oct Surgery 130(4):686-93; discussion 693-5,
Does not meet inclusion criteria

Feretis C;Benakis P;Dimopoulos C;Dailianas A;Filalithis P;Stamou KM;Manouras A;Apostolidis N;Endoscopic implantation of Plexiglas (PMMA) microspheres for the treatment of GERD.[see comment] 2001 Apr Gastrointestinal Endoscopy 53(4):423-6,
Multiple reasons

Field SK;Sutherland LR;Does medical antireflux therapy improve asthma in asthmatics with gastroesophageal reflux?: a critical review of the literature 1998 Jul Chest 114(1):275-83,
Outcome: asthma symptoms

Finney JS;Kinnersley N;Hughes M;O'BryanTear CG;Lothian J;Meta-analysis of antisecretory and gastrokinetic compounds in functional dyspepsia 1998 Jun Journal of Clinical Gastroenterology 26(4):312-20,

Population not of interest

Fockens P;Bruno MJ;Gabbrielli A;Odegaard S;Hatlebakk J;Allescher HD;Rosch T;Rhodes M;Bastid C;Rey J;Boyer J;Muehldorffer S;van den HU;Costamagna G;Endoscopic augmentation of the lower esophageal sphincter for the treatment of gastroesophageal reflux disease: multicenter study of the Gatekeeper Reflux Repair System 2004 Aug Endoscopy 36(8):682-9,
Intervention not of interest

Fouad YM;Katz PO;Castell DO;Oesophageal motility defects associated with nocturnal gastro-oesophageal reflux on proton pump inhibitors 1999 Nov Alimentary Pharmacology & Therapeutics 13(11):1467-71,

Does not meet inclusion criteria

Frantzides CT;Carlson MA;Laparoscopic versus conventional fundoplication 1995 Jun Journal of Laparoendoscopic Surgery 5(3):137-43,

Does not meet inclusion criteria

Frantzides CT;Richards C;A study of 362 consecutive laparoscopic Nissen fundoplications 1998 Oct Surgery 124(4):651-4; discussion 654-5,
Does not meet inclusion criteria

Franzen T;Anderberg B;Tibbling GL;Johansson KE;Prospective evaluation of laparoscopic and open 360 degree fundoplication in mild and severe gastro-

Appendix B. List of Excluded Studies (continued)

oesophageal reflux disease 2002 European Journal of Surgery 168(10):539-45,

Does not meet inclusion criteria

Gadenstatter M, Wykypiel H, Schwab GP, et al Respiratory symptoms and dysphagia in patients with gastroesophageal reflux disease: a comparison of medical and surgical therapy 1999 Dec Langenbecks Archives of Surgery 384(6):563-7

Multiple reasons complicated GERD

Galvani C;Fisichella PM;Gorodner MV;Perretta S;Patti MG;Symptoms are a poor indicator of reflux status after fundoplication for gastroesophageal reflux disease: role of esophageal functions tests 2003 May Archives of Surgery 138(5):514-8; discussion 518-9,

Does not meet inclusion criteria

Gibson PG Gastro-oesophageal reflux treatment for asthma in adults and children 2005 Cochrane Database

Extra-esophageal GERD outcomes

Gill RC;Bowes KL;Murphy PD;Kingma YJ;Esophageal motor abnormalities in gastroesophageal reflux and the effects of fundoplication 1986 Aug Gastroenterology 91(2):364-9,

Outcome not of interest

Glise H;Hallerback B;Johansson B;Quality of Life assessments in the evaluation of gastroesophageal reflux and peptic ulcer disease before, during and after treatment 1995 Scandinavian Journal of Gastroenterology - Supplement

Does not meet inclusion criteria

Granderath FA;Kamolz T;Schweiger UM;Pointner R;Laparoscopic antireflux surgery for gastroesophageal reflux disease: experience with 668 laparoscopic antireflux procedures 2003 Jan International Journal of Colorectal Disease 18(1):73-7,

Does not meet inclusion criteria

Gundermann KJ;Godehardt E;Ulbrich M;Efficacy of a herbal preparation in patients with functional dyspepsia: a meta-analysis of double-blind, randomized, clinical trials 2003 Advances in Therapy

Population: non-ulcer dyspepsia; intervention: not H2-blocker or PPI

Hage E;Hendel L;Gustafsen J;Hendel J;Histopathology of the gastric oxyntic mucosa in two different patient groups during long-term treatment with omeprazole 2003 Jul European Journal of Gastroenterology & Hepatology 15(7):781-9,

All med tx before systematic review

Hagedorn C;Jonson C;Lonroth H;Ruth M;Thune A;Lundell L;Efficacy of an anterior as compared with a posterior laparoscopic partial fundoplication: results of a randomized, controlled clinical trial 2003 Aug Annals of Surgery 238(2):189-96,

Does not meet inclusion criteria

Hailey D;Endoscope-based treatments for gastroesophageal reflux disease 2004 Mar Issues in Emerging Health Technologies (54):1-4,

Poor quality

Halabi A;Kirch W;Cardiovascular effects of omeprazole and famotidine 1992 Sep Scandinavian Journal of Gastroenterology 27(9):753-6,

No Adverse events

Hasselgren G;HassanAlin M;Andersson T;ClaarNilsson C;Rohss K;Pharmacokinetic study of esomeprazole in the elderly 2001 Clinical Pharmacokinetics 40(2):145-50,

No Adverse events

Henderson RD;Marryatt G;Total fundoplication gastroplasty. Long-term follow-up in 500 patients 1983 Jan Journal of Thoracic & Cardiovascular Surgery 85(1):81-7,

Does not meet inclusion criteria

Appendix B. List of Excluded Studies (continued)

Hillman AL;Bloom BS;Fendrick AM;Schwartz JS; Cost and quality effects of alternative treatments for persistent gastroesophageal reflux disease 1992 Jul Archives of Internal Medicine 152(7):1467-72,

Outcome not of interest

Hillman LC;Chiragakakis L;Shadbolt B;Kaye GL;Clarke AC; Proton-pump inhibitor therapy and the development of dysplasia in patients with Barrett's oesophagus.[see comment] 2004 Apr Medical Journal of Australia 180(8):387-91,

Outcome not of interest

Hofstetter WL;Peters JH;DeMeester TR;Hagen JA;DeMeester SR;Crookes PF;Tsai P;Banki F;Bremner CG; Long-term outcome of antireflux surgery in patients with Barrett's esophagus 2001 Oct Annals of Surgery 234(4):532-8; discussion 538-9,

Outcome not of interest

Houston H;Khaitan L;Holzman M;Richards WO;First year experience of patients undergoing the Stretta procedure 2003 Mar Surgical Endoscopy 17(3):401-4,

Data available in a long-term study (Lutfu 2005)

Hunter JG;Smith CD;Branum GD;Waring JP;Trus TL;Cornwell M;Galloway K;Laparoscopic fundoplication failures: patterns of failure and response to fundoplication revision 1999 Oct Annals of Surgery 230(4):595-604; discussion 604-6,

Does not meet inclusion criteria

Hunter JG;Swanstrom L;Waring JP;Dysphagia after laparoscopic antireflux surgery. The impact of operative technique.[see comment] 1996 Jul Annals of Surgery 224(1):51-7,

Outcome not of interest

Incarbone R;Bonavina L;Reitano M;Peracchia A;Esophageal function studies in the management of gastroesophageal reflux disease 1999 International Journal of

Surgical Investigation 1(4):351-6,

Does not meet inclusion criteria

Jaakkimainen RL;Boyle E;Tudiver F;Is Helicobacter pylori associated with non-ulcer dyspepsia and will eradication improve symptoms? A meta-analysis.[see comment] 1999 Oct 16 BMJ 319(7216):1040-4,

Population: non-ulcer dyspepsia

Jobe BA;Wallace J;Hansen PD;Swanstrom LL;Evaluation of laparoscopic Toupet fundoplication as a primary repair for all patients with medically resistant gastroesophageal reflux 1997 Nov Surgical Endoscopy 11(11):1080-3,

Does not meet inclusion criteria

Joelson S;Joelson IB;Lundborg P;Walan A;Wallander MA; Safety experience from long-term treatment with omeprazole.[erratum appears in Digestion 1992;53(3-4):213]1992 Digestion 51 Suppl 1:93-101,

Data available in meta-analysis

Kamolz T;Granderath FA;Pointner R;The outcome of laparoscopic antireflux surgery in relation to patients' subjective degree of compliance with former antireflux medication 2003 Jun Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 13(3):155-60,

Does not meet inclusion criteria

KaplanMachlis B;Spiegler GE;Revicki DA; Health-related quality of life in primary care patients with gastroesophageal reflux disease 1999 Oct Annals of Pharmacotherapy 33(10):1032-6,

Outcome not of interest

Karim SS;Panton ON;Finley RJ;Graham AJ;Dong S;Storseth C;Clifton J; Comparison of total versus partial laparoscopic fundoplication in the management of gastroesophageal reflux disease 1997 May American Journal of Surgery 173(5):375-8,

Does not meet inclusion criteria

Appendix B. List of Excluded Studies (continued)

Katariya K;Harvey JC;Pina E;Beattie EJ;Complications of transhiatal esophagectomy 1994 Nov Journal of Surgical Oncology 57(3):157-63,
Intervention not of interest

Khoursheed MA;AlAsfoor M;AlShamali M;Ayed AK;Gupta R;Dashti HM;Behbehani AI; Effectiveness of laparoscopic fundoplication for gastro-oesophageal reflux 2001 Jul Annals of the Royal College of Surgeons of England 83(4):229-34,
Does not meet inclusion criteria

Kiroff GK;Maddern GJ;Jamieson GG; A study of factors responsible for the efficacy of fundoplication in the treatment of gastro-oesophageal reflux 1984 Apr Australian & New Zealand Journal of Surgery 54(2):109-12,
Outcome not of interest

Kiviluoto T;Luukkonen P;Salo J; Laparoscopic gastro-oesophageal antireflux surgery 1994Annales Chirurgiae et Gynaecologiae 83(2):101-6,
Adverse events, available in meta-analysis

Kiviluoto T;Siren J;Farkkila M;Luukkonen P;Salo J;Kivilaakso E; Laparoscopic Nissen fundoplication: a prospective analysis of 200 consecutive patients1998 Dec Surgical Laparoscopy & Endoscopy 8(6):429-34,
Does not meet inclusion criteria

Klok RM;Postma MJ;van Hout BA;Brouwers JR; Meta-analysis: comparing the efficacy of proton pump inhibitors in short-term use. [Review] [59 refs] 2003 May 15 Alimentary Pharmacology & Therapeutics 17(10):1237-45,
Data available in subsequent systematic review

Kuster E;Ros E;ToledoPimentel V;Pujol A;Bordas JM;Grande L;Pera C; Predictive factors of the long term outcome in gastro-oesophageal reflux disease: six year follow up of 107 patients 1994 Jan Gut 35(1):8-14,
Mixed cohort

Laheij RJ;van Rossum LG;Verbeek AL;Jansen JB;Helicobacter pylori infection treatment of nonulcer dyspepsia: an analysis of meta-analyses.[comment]2003 Apr Journal of Clinical Gastroenterology 36(4):315-20,
Population: non-ulcer dyspepsia; intervention: HP eradication

Laine L;Schoenfeld P;Fennerty MB;Therapy for Helicobacter pylori in patients with nonulcer dyspepsia. A meta-analysis of randomized, controlled trials.[see comment]2001 Mar 6 Annals of Internal Medicine 134(5):361-9,
Population: non-ulcer dyspepsia; intervention: HP eradication

Landreneau RJ;Wiechmann RJ;Hazelrigg SR;Santucci TS;Boley TM;Magee MJ;Naunheim KS;Success of laparoscopic fundoplication for gastroesophageal reflux disease1998 Dec Annals of Thoracic Surgery 66(6):1886-93,
Does not meet inclusion criteria

Larrain A, Carrasco E, Galleguillos F, et alMedical and surgical treatment of nonallergic asthma associated with gastroesophageal reflux1991 JunChest 99(6):1330-5
Deals with Asthma

Laycock WS;Trus TL;Hunter JG;New technology for the division of short gastric vessels during laparoscopic Nissen fundoplication. A prospective randomized trial1996 Jan Surgical Endoscopy 10(1):71-3,
Technique not of interest

Leeder PC;Watson DI;Jamieson GG;Laparoscopic fundoplication for patients with symptoms but no objective evidence of gastroesophageal reflux2002Diseases of the Esophagus 15(4):309-14,
Does not meet inclusion criteria

Leufkens H;Claessens A;Heerdink E;van Eijk J;Lamers CB;A prospective follow-up

Appendix B. List of Excluded Studies (continued)

study of 5669 users of lansoprazole in daily practice 1997 Oct *Alimentary Pharmacology & Therapeutics* 11(5):887-97,

Available meta-analysis

Lohegny A; Hauters P; Janssen P; Nakad A; Farchack E; Defrennes M; Quality of life assessment after Nissen fundoplication 2001 Jan *Acta Chirurgica Belgica* 101(1):20-4,

Does not meet inclusion criteria

Lord RV; Huprich JE; Katkhouda N; Images of interest. Gastrointestinal: complications of fundoplication 2000 Oct *Journal of Gastroenterology & Hepatology* 15(10):1221,

Case study

Ludemann R; Watson DI; Jamieson GG; Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication 2003 Aug *American Journal of Surgery* 186(2):143-7,

No Adverse events

Lundell L; Dalenback J; Hattlebakk J; Janatuinen E; Levander K; Miettinen P; Myrvold HE; Pedersen SA; Thor K; Junghard O; Andersson A; Outcome of open antireflux surgery as assessed in a Nordic multicentre prospective clinical trial. Nordic GORD-Study Group. [erratum appears in *Eur J Surg* 1999 Nov; 165(11):1104] 1998 Oct *European Journal of Surgery* 164(10):751-7,

Follow-up only to 12 mos

Lundell LR; Myers JC; Jamieson GG; Delayed gastric emptying and its relationship to symptoms of 'gas float' after antireflux surgery 1994 Mar *European Journal of Surgery* 160(3):161-6,

Does not meet inclusion criteria

Luostarinen M; Virtanen J; Koskinen M; Matikainen M; Isolauri J; Dysphagia and oesophageal clearance after laparoscopic versus open Nissen fundoplication. A randomized, prospective trial 2001 Jun *Scandinavian Journal of Gastroenterology*

36(6):565-71,

Follow-up only to 1 yr

Luostarinen ME; Isolauri JO; Randomized trial to study the effect of fundic mobilization on long-term results of Nissen fundoplication. [see comment] 1999 May *British Journal of Surgery* 86(5):614-8,

Does not meet inclusion criteria

Luostarinen ME; Koskinen MO; Isolauri JO; Effect of fundal mobilisation in Nissen-Rossetti fundoplication on oesophageal transit and dysphagia. A prospective, randomised trial 1996 Jan *European Journal of Surgery* 162(1):37-42,

Technique not of interest

Maher JW; Hocking MP; Woodward ER; Supradiaphragmatic fundoplication. Long-term follow-up and analysis of complications 1984 Jan *American Journal of Surgery* 147(1):181-6,

Supra diaphragm fundo

Matikainen M; Nissen-Rossetti fundoplication for the treatment of gastro-oesophageal reflux 1982 *Acta Chirurgica Scandinavica* 148(2):173-7,

Does not meet inclusion criteria

Maton PN; Vakil NB; Levine JG; Hwang C; Skammer W; Lundborg P; Esomeprazole S; Safety and efficacy of long term esomeprazole therapy in patients with healed erosive oesophagitis 2001 *Drug Safety* 24(8):625-35,

Available meta-analysis

McDonald ML; Trastek VF; Allen MS; Deschamps C; Pairolero PC; Pairolero PC; Barretts's esophagus: does an antireflux procedure reduce the need for endoscopic surveillance? 1996 Jun *Journal of Thoracic & Cardiovascular Surgery* 111(6):1135-8; discussion 1139-40,

Outcome not of interest

McDougall NI; Johnston BT; Collins JS; McFarland RJ; Love AH; Disease

Appendix B. List of Excluded Studies (continued)

progression in gastro-oesophageal reflux disease as determined by repeat oesophageal pH monitoring and endoscopy 3 to 4.5 years after diagnosis 1997 Dec European Journal of Gastroenterology & Hepatology 9(12):1161-7,

Does not meet inclusion criteria

McHardy G;Balart L;Reflux esophagitis in the elderly, with special reference to antacid therapy 1972 Journal of the American Geriatrics Society

Intervention: antacid Tx; tutorial but not SR

McKernan JB;Champion JK;Minimally invasive antireflux surgery 1998 Apr American Journal of Surgery 175(4):271-6,
Surgical Cohort before 2001 meta-analysis

Melvin WS;Needleman BJ;Krause KR;Schneider C;Ellison EC;Computer-enhanced vs. standard laparoscopic antireflux surgery 2002 Jan Journal of Gastrointestinal Surgery 6(1):11-5; discussion 15-6,

Does not meet inclusion criteria

Menguy R;A modified fundoplication which preserves the ability to belch 1978 Sep Surgery 84(3):301-7,

Does not meet inclusion criteria

Mosnier H;Leport J;Aubert A;Kianmanesh R;Sbai Idrissi MS;Guivarc'h M;A 270 degree laparoscopic posterior fundoplasty in the treatment of gastroesophageal reflux 1995 Sep Journal of the American College of Surgeons 181(3):220-4,

Does not meet inclusion criteria

Mossner J;Koop H;Porst H;Wubbolding H;Schneider A;Maier C;One-year prophylactic efficacy and safety of pantoprazole in controlling gastro-oesophageal reflux symptoms in patients with healed reflux oesophagitis 1997 Dec Alimentary Pharmacology & Therapeutics

11(6):1087-92,

All med tx before systematic review

Negre JB;Post-fundoplication symptoms. Do they restrict the success of Nissen fundoplication? 1983 Annals of Surgery
Surgical Cohort before 2001 meta-analysis

Negre JB;Markkula HT;Keyrilainen O;Matikainen M;Nissen fundoplication. Results at 10 year follow-up 1983 Nov American Journal of Surgery 146(5):635-8,
Does not meet inclusion criteria

Nelis GF;Engelage AH;Samson G;Does long-term inhibition of gastric acid secretion with omeprazole lead to small intestinal bacterial overgrowth? 1994 Sep Netherlands Journal of Medicine 45(3):93-100,
All med tx before systematic review

O'Rourke IC;Nissen fundoplication for gastro-oesophageal reflux 1979 Oct Medical Journal of Australia 2(8):441,

Case series

Orringer MB;Schneider R;Williams GW;Sloan H;Intraoperative esophageal manometry: is it valid? 1980 Jul Annals of Thoracic Surgery 30(1):13-8,
Not relevant to Q2

Oster G;Huse DM;Delea TE;Colditz GA;Richter JM;The risks and benefits of an Rx-to-OTC switch. The case of over-the-counter H2-blockers 1990 Sep Medical Care 28(9):834-52,

Population: non-ulcer dyspepsia; cost-effective analysis

O'Sullivan GC;DeMeester TR;Joelsson BE;Smith RB;Blough RR;Johnson LF;Skinner DB;Interaction of lower esophageal sphincter pressure and length of sphincter in the abdomen as determinants of gastroesophageal competence 1982 Jan American Journal of Surgery 143(1):40-7,
Outcome not of interest

Appendix B. List of Excluded Studies (continued)

Pace F;Bollani S;Molteni P;Bianchi PG;Natural history of gastro-oesophageal reflux disease without oesophagitis (NERD)--a reappraisal 10 years on2004 Feb Digestive & Liver Disease 36(2):111-5,
No interventions and prevalence data

Papp JP;Determination of the lower esophageal sphincter pressure in patients having a Nissen or Belsey fundoplication1979 Feb American Journal of Gastroenterology 71(2):154-7,
Does not meet inclusion criteria

Parshad R;Kumar MV;Bal S;Saraya A;Sharma MP;Laparoscopic Nissen fundoplication; results of a prospective pilot study2003 Jul Tropical Gastroenterology 24(3):152-6,
Does not meet inclusion criteria

Patti MG;Feo CV;De Pinto M;Archerito M;Tong J;Gantert W;Tyrrell D;Way LW;Results of laparoscopic antireflux surgery for dysphagia and gastroesophageal reflux disease1998 Dec American Journal of Surgery 176(6):564-8,
Does not meet inclusion criteria

Patti MG;Molena D;Fisichella PM;Perretta S;Way LW;Gastroesophageal reflux disease (GERD) and chest pain. Results of laparoscopic antireflux surgery2002 Apr Surgical Endoscopy 16(4):563-6,
Age not relevant

Peillon C;Manouvrier JL;Labreche J;Kaeffer N;Denis P;Testart J;Should the vagus nerves be isolated from the fundoplication wrap? A prospective study1994 Aug Archives of Surgery 129(8):814-8,
Not relevant to Q2

Pessaux P;Arnaud JP;Ghavami B;Flament JB;Trebuchet G;Meyer C;Huten N;Champault G;Laparoscopic antireflux surgery: comparative study of Nissen, Nissen-Rossetti, and Toupet fundoplication. Societe Francaise de Chirurgie Laparoscopique2000 Nov Surgical

Endoscopy 14(11):1024-7,
Does not meet inclusion criteria

Peters JH;DeMeester TR;Crookes P;Oberg S;de Vos SM;Hagen JA;Bremner CG;The treatment of gastroesophageal reflux disease with laparoscopic Nissen fundoplication: prospective evaluation of 100 patients with 'typical' symptoms1998 Jul Annals of Surgery 228(1):40-50,
Does not meet inclusion criteria

Peters JH;Silverman DE;Stein A;Lower esophageal sphincter injection of a biocompatible polymer: accuracy of implantation assessed by esophagectomy2003 Apr Surgical Endoscopy 17(4):547-50,
Evaluation of location of injection in esophageal resection specimens

Pitcher DE;Curet MJ;Martin DT;Castillo RR;Gerstenberger PD;Vogt D;Zucker KA;Successful management of severe gastroesophageal reflux disease with laparoscopic Nissen fundoplication1994 Dec American Journal of Surgery 168(6):547-53; discussion 553-4,
Does not meet inclusion criteria

Rabeneck L;Long-term treatment of erosive esophagitis with omeprazole: does it work?1995 Feb Gastroenterology 108(2):613-4,
Comment

Rabeneck L;Wray NP;Graham DY;Managing dyspepsia: what do we know and what do we need to know?1998 Jun American Journal of Gastroenterology 93(6):920-4,
Dyspepsia

Rantanen TK;Halme TV;Luostarinen ME;Karhumaki LM;Kononen EO;Isolaari JO;The long term results of open antireflux surgery in a community-based health care center.[see comment]1999 Jul American Journal of Gastroenterology 94(7):1777-81,
Outcome not of interest

Appendix B. List of Excluded Studies (continued)

Rantanen TK;Salminen JT;Makinen JE;Sipponen PI;Kiviluoto TA;Salo JA;Clinical significance of esophageal histologic findings after antireflux surgery2001 Jul Archives of Surgery 136(7):733-6,

Outcome not of interest

Rattner DW;Brooks DC;Patient satisfaction following laparoscopic and open antireflux surgery1995 Mar Archives of Surgery 130(3):289-93; discussion 293-4,

Does not meet inclusion criteria

Redstone HA;Barrowman N;Veldhuyzen van Zanten SJ;H2-receptor antagonists in the treatment of functional (nonulcer) dyspepsia: a meta-analysis of randomized controlled clinical trials2001 Sep Alimentary Pharmacology & Therapeutics 15(9):1291-9,

Population: non-ulcer dyspepsia

Ribet M;Mensier E;Pruvot FR;Barrett's esophagus and adenocarcinoma1987European Journal of Cardio-Thoracic Surgery 1(1):29-32,

Outcome not of interest

Richards WO;Scholz S;Khaitan L;Sharp KW;Holzman MD;Initial experience with the strepta procedure for the treatment of gastroesophageal reflux disease2001 Oct Journal of Laparoendoscopic & Advanced Surgical Techniques-Part A 11(5):267-73,

Duplicate of Houston paper

Richardson JD;Kuhns JG;Richardson RL;Polk HC;Properly conducted fundoplication reverses histologic evidence of esophagitis1983Annals of Surgery

Does not meet inclusion criteria

Rogers DM;Herrington JL;Morton C;Incidental splenectomy associated with Nissen fundoplication1980Annals of Surgery

Adverse events, before 1997

Rydberg L;Ruth M;Lundell L;Characteristics of secondary oesophageal peristalsis in operated and non-operated patients with chronic gastro-oesophageal reflux disease2000 Jul European Journal of Gastroenterology & Hepatology 12(7):739-43,

Outcome not of interest

Sandbu R;Khamis H;Gustavsson S;Haglund U;Long-term results of antireflux surgery indicate the need for a randomized clinical trial2002 Feb British Journal of Surgery 89(2):225-30,

Does not meet inclusion criteria

Schenk BE;Festen HP;Kuipers EJ;KlinkenbergKnol EC;Meuwissen SG;Effect of short- and long-term treatment with omeprazole on the absorption and serum levels of cobalamin1996 Aug Alimentary Pharmacology & Therapeutics 10(4):541-5,

Outcome not of interest

Schumacher MC;Jick SS;Jick H;Feld AD;Cimetidine use and gastric cancer1990 May Epidemiology 1(3):251-4,

All med tx before systematic review

Sharma VK;Leontiadis GI;Howden CW;Meta-analysis of randomized controlled trials comparing standard clinical doses of omeprazole and lansoprazole in erosive oesophagitis2001 Feb Alimentary Pharmacology & Therapeutics 15(2):227-31,

Limited individual comparisons (only lansoprazole vs. omeprazole)

Shirazi SS;Schulze K;Soper RT;Long-term follow-up for treatment of complicated chronic reflux esophagitis1987 May Archives of Surgery 122(5):548-52,

Cohort before 1995

Simon TJ;Bradstreet DC;Comparative tolerability profile of omeprazole in clinical trials1991 Oct Digestive Diseases & Sciences 36(10):1384-9,

All med tx before systematic review

Appendix B. List of Excluded Studies (continued)

Slim K;Bousquet J;Kwiatkowski F;Lescure G;Pezet D;Chipponi J;Quality of life before and after laparoscopic fundoplication2000 Jul American Journal of Surgery 180(1):41-5,

Does not meet inclusion criteria

So JB;Zeitels SM;Rattner DW;Outcomes of atypical symptoms attributed to gastroesophageal reflux treated by laparoscopic fundoplication1998 Jul Surgery 124(1):28-32,

Population not of interest

Solcia E;Fiocca R;Havu N;Dalvag A;Carlsson R;Gastric endocrine cells and gastritis in patients receiving long-term omeprazole treatment1992Digestion 51 Suppl 1:82-92,

All med tx before systematic review

Solcia E;Rindi G;Havu N;Elm G;Qualitative studies of gastric endocrine cells in patients treated long-term with omeprazole1989Scandinavian Journal of Gastroenterology - Supplement 166:129-37; discussion 138-9,

Available in subsequent meta-analysis

Solvell L;The clinical safety of omeprazole1989Scandinavian Journal of Gastroenterology - Supplement 166:106-10; discussion 111-3,

Available in subsequent meta-analysis

Sonnenberg A;Motion--Laparoscopic Nissen fundoplication is more cost effective than oral PPI administration: arguments against the motion2002 Sep Canadian Journal of Gastroenterology 16(9):627-31,

Population: non-ulcer dyspepsia

Soper NJ;Dunnegan D;Anatomic fundoplication failure after laparoscopic antireflux surgery1999 May Annals of Surgery 229(5):669-76; discussion 676-7,

Does not meet inclusion criteria

Spechler SJ;Jain SK;Tendler DA;Parker RA;Racial differences in the frequency of

symptoms and complications of gastro-oesophageal reflux disease.[see comment]2002 Oct Alimentary Pharmacology & Therapeutics 16(10):1795-800,

Available in subsequent meta-analysis

Starnes VA;Adkins RB;Ballinger JF;Sawyers JL;Barrett's esophagus. A surgical entity1984 May Archives of Surgery 119(5):563-7,

Outcome not of interest

Stein HJ;Feussner H;Siewert JR;Failure of antireflux surgery: causes and management strategies1996 Jan American Journal of Surgery 171(1):36-9; discussion 39-40,

Outcome not of interest

Stirling MC;Orringer MB;Surgical treatment after the failed antireflux operation1986 Oct Journal of Thoracic & Cardiovascular Surgery 92(4):667-72,

Intervention not of interest

Straathof JW;Ringers J;Masclée AA;Prospective study of the effect of laparoscopic Nissen fundoplication on reflux mechanisms2001 Nov British Journal of Surgery 88(11):1519-24,

Does not meet inclusion criteria

Swanstrom LL;Pennings JL;Laparoscopic control of short gastric vessels1995 Oct Journal of the American College of Surgeons 181(4):347-51,

Does not meet inclusion criteria

Talley NJ;Lauritsen K;The potential role of acid suppression in functional dyspepsia: the BOND, OPERA, PILOT, and ENCORE studies2002 May Gut 50 Suppl 4:iv36-41,

Population not of interest

Tardif C;Nouvet G;Denis P;Tombelaine R;Pasquis P;Surgical treatment of gastroesophageal reflux in ten patients with severe asthma1989Respiration 56(1-2):110-5,

Extra esophageal GERD

Appendix B. List of Excluded Studies (continued)

Tew S;Ackroyd R;Jamieson GG;Holloway RH;Belching and bloating: facts and fantasy after antireflux surgery2000 Apr British Journal of Surgery 87(4):477-81,
Outcome not of interest

Tew S;Jamieson GG;Holloway RH;Ferguson S;Tew P;A prospective study of the effect of fundoplication on primary and secondary peristalsis in the esophagus1997 Oct Diseases of the Esophagus 10(4):247-52,

Does not meet inclusion criteria

Thor KB;Silander T;A long-term randomized prospective trial of the Nissen procedure versus a modified Toupet technique1989 Dec Annals of Surgery 210(6):719-24,

Does not meet inclusion criteria

Torquati A;Houston HL;Kaiser J;Holzman MD;Richards WO;Long-term follow-up study of the Stretta procedure for the treatment of gastroesophageal reflux disease2004 Oct Surgical Endoscopy 18(10):1475-9,

Same patients reported with longer follow-up in Lutfu 2005

Tseng EE;Wu TT;Yeo CJ;Heitmiller RF;Barrett's esophagus with high grade dysplasia: surgical results and long-term outcome--an update2003 Feb Journal of Gastrointestinal Surgery 7(2):164-70; discussion 170-1,

Outcome not of interest

Tucker JG;Ramshaw BJ;Newman CL;Sims MS;Mason EM;Duncan TD;Lucas GW;Laparoscopic fundoplication in the treatment of severe gastroesophageal reflux disease: preliminary results of a prospective trial1996 Jan Southern Medical Journal 89(1):60-4,

Does not meet inclusion criteria

Urschel JD;Gastroesophageal leaks after antireflux operations1994 May Annals of Thoracic Surgery 57(5):1229-32,

Data available in subsequent meta-analysis

van Rensburg CJ;Honiball PJ;van Zyl JH;Grundling HD;Eloff FP;Spies SK;Simjee AE;Theron I;Fischer R;Louw JA;Safety and efficacy of pantoprazole 40 mg daily as relapse prophylaxis in patients with healed reflux oesophagitis-a 2-year follow-up1999 Aug Alimentary Pharmacology & Therapeutics 13(8):1023-8,

Available meta-analysis

Varga G;Kiraly A;Moizs M;Horvath OP;Effect of laparoscopic antireflux operation on esophageal manometry, 24 hours pH-metry and quality of life in gastroesophageal reflux disease1999 Acta Chirurgica Hungarica 38(2):213-8,

Does not meet inclusion criteria

Velanovich V;Comparison of symptomatic and quality of life outcomes of laparoscopic versus open antireflux surgery1999 Oct Surgery 126(4):782-8; discussion 788-9,

Does not meet inclusion criteria

Velanovich V;Medication usage and additional esophageal procedures after antireflux surgery2003 Jun Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 13(3):161-4,

Patients included with typical and atypical symptoms; results were not separately reported

Veldhuyzen van Zanten SJ;Cleary C;Talley NJ;Peterson TC;Nyren O;Bradley LA;Verlinden M;Tytgat GN;Drug treatment of functional dyspepsia: a systematic analysis of trial methodology with recommendations for design of future trials.[see comment]1996 Apr American Journal of Gastroenterology 91(4):660-73,

Population not of interest

Veldhuyzen van Zanten SJ;Talley NJ;Blum AL;BollingSternevald E;Sundin M;Junghard O;Combined analysis of the ORCHID and OCAY studies: does eradication of

Appendix B. List of Excluded Studies (continued)

Helicobacter pylori lead to sustained improvement in functional dyspepsia symptoms? 2002 May Gut 50 Suppl 4:iv26-30; discussion iv31-2,

Population not of interest

Viljakka M;Nevalainen J;Isolauri J;Lifetime costs of surgical versus medical treatment of severe gastro-oesophageal reflux disease in Finland 1997 Aug Scandinavian Journal of Gastroenterology 32(8):766-72,

Outcome not of interest

Viljakka M;Saali K;Koskinen M;Karhumaki L;Kossi J;Luostarinen M;Teerenhovi O;Isolauri J;Antireflux surgery enhances gastric emptying 1999 Jan Archives of Surgery 134(1):18-21,

Does not meet inclusion criteria

Washer GF;Gear MW;Dowling BL;Gillison EW;Royston CM;Spencer J;Duodenal diversion with vagotomy and antrectomy for severe or recurrent reflux oesophagitis and stricture: an alternative to operation at the hiatus 1986 Jul Annals of the Royal College of Surgeons of England 68(4):222-6,

Intervention not of interest

Watson A;Spychal RT;Brown MG;Peck N;Callander N;Laparoscopic 'physiological' antireflux procedure: preliminary results of a prospective symptomatic and objective study 1995 May British Journal of Surgery 82(5):651-6,

Does not meet inclusion criteria

Watson DI;Pike GK;Baigrie RJ;Mathew G;Devitt PG;Britten Jones R;Jamieson GG;Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels 1997 Nov Annals of Surgery 226(5):642-52,

Does not meet inclusion criteria

Wetscher GJ;Glaser K;Wieschemeyer T;Gadenstaetter M;Prommegger R;Profanter C;Tailored antireflux surgery for gastroesophageal reflux disease:

effectiveness and risk of postoperative dysphagia 1997 Jul World Journal of Surgery 21(6):605-10,

Does not meet inclusion criteria

Wilton LV;Key C;Shakir SA;The pharmacovigilance of pantoprazole: the results of postmarketing surveillance on 11 541 patients in England 2003 Drug Safety 26(2):121-32,

Data available in subsequent systematic review

Winslow ER;Clouse RE;Desai KM;Frisella P;Gunsberger T;Soper NJ;Klingensmith ME;Influence of spastic motor disorders of the esophageal body on outcomes from laparoscopic antireflux surgery 2003 May Surgical Endoscopy 17(5):738-45,

Outcome not of interest

Wong WM;Lai KC;Lam KF;Hui WM;Hu WH;Lam CL;Xia HH;Huang JQ;Chan CK;Lam SK;Wong BC;Prevalence, clinical spectrum and health care utilization of gastro-oesophageal reflux disease in a Chinese population: a population-based study.[see comment] 2003 Sep 15 Alimentary Pharmacology & Therapeutics 18(6):595-604,

Outcome not of interest

Wykypiel H;Wetscher GJ;Klaus A;Schmid T;Gadenstaetter M;Bodner J;Bodner E;Robot-assisted laparoscopic partial posterior fundoplication with the DaVinci system: initial experiences and technical aspects 2003 Feb Langenbecks Archives of Surgery 387(11-12):411-6,

Does not meet inclusion criteria

Yau P;Watson DI;Devitt PG;Game PA;Jamieson GG;Laparoscopic antireflux surgery in the treatment of gastroesophageal reflux in patients with Barrett esophagus 2000 Jul Archives of Surgery 135(7):801-5,

Outcome not of interest

Appendix B. List of Excluded Studies (continued)

Zaninotto G;Anselmino M;Costantini M;Boccu C;Ancona E;Laparoscopic treatment of gastro-esophageal reflux disease: indications and results1995 Oct International Surgery 80(4):380-5,
Does not meet inclusion criteria

Zaninotto G;Costantini M;Anselmino M;Boccu C;Bagolin F;Polo R;Ancona E;Excessive competence of the lower oesophageal sphincter after Nissen fundoplication: evaluation by three-dimensional computerised imaging1995 Apr European Journal of Surgery 161(4):241-6,
Outcome not of interest

Zeitoun P;Comparison of omeprazole with ranitidine in the treatment of reflux oesophagitis1989Scandinavian Journal of Gastroenterology - Supplement 166:83-7; discussion 94,
Data available in subsequent systematic review

Zugel N;Jung C;Bruer C;Sommer P;Breitschaft K;A comparison of laparoscopic Toupet versus Nissen fundoplication in gastroesophageal reflux disease2002 Jan Langenbecks Archives of Surgery 386(7):494-8,
Does not meet inclusion criteria

Appendix C. Evidence Tables

Table 1. Comparative studies of medical vs. surgical management in patients with GERD

Author, Year	Intervention	Patient characteristics				Follow-up duration	Status at follow-up							Quality
		Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hiatial hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	Other med use data	QOL/ Satisfaction	EMS/ Others	
Lundell, 2001, 2000 RCT	Omeprazole (OME) vs. open anti-reflux surgery (OAS) OME n=154- >133 (f/u) 75% M Age <50 39% 50-64 42% >64 19% OAS n=144- >122 (f/u) Age <50 48% 50-65 38% >64 14%	Inclusion criteria includes esophagitis; but table 2 in paper (2000) shows: Grade 1 OME 6/154 (4%) OAS 10/144 (7%) Grade 0 OME 96% OAS 93%	OME 20% time < 4 OAS 19% time < 4 Estimated from fig.1 in paper	ND	Yes, proven by healed esophagitis after medical treatment	5-yr 3-yr	Similar results in the 2 groups in % of pts with moderate to severe heartburn at defined time points	At 3 yr, OME 22/133 (17%); 1 grade 3 OAS 16/119 (13%); no grade 3	After 12 mos, OME: 10% time < 4 OAS: 4% time < 4 (normalized) Estimated from fig.1 in paper	ND	ND	No difference in QOL assessment between 2 groups	At 5-year, % in remission (based on symptoms, PPI & surgery requirements, see paper for details): OME 49% OAS 68% (P<0.001) No difference in % Barrett's	B
Spechler, 2001, 1992 RCT	Continuous Medical (MEDc) vs. symptomatic Medical (MEDsx) vs. open Nissen fundoplication (ONF) N= 247 f/u= 208 (129 survivors; 79 deaths) 98% M 58 y (25-75) MEDc n=77 MEDsx n=88 ONF n=82	No; 30% with erosive esophagitis; 23% with esophageal ulcer; 40% with Barrett's	% time pH < 4 MEDc 20±19 MEDsx 23±22 ONF 23±22	LES in mm Hg MEDc 25±18 MEDsx 27±19 ONF 23±18	ND	Mean f/u MED 10.6 yr ONF 9.1 yr 1992 paper: 1 & 2 yr f/u	Long term: Symptom score better in ONF group compared to MED group during the wk when meds were stopped in both groups (P=0.003). At 1 & 2 yr, activity-index score improved in all 3 groups compared to baseline (P<0.03) Activity index score lower in ONF than MED	Long term: After 1 wk without meds, no significant difference in grade of esophagitis between the 2 groups. At 1 & 2 yr, grade of esophagitis improved in all 3 groups compared to baseline (P<0.03) Grades of esophagitis lower in ONF than MED during the 2 yr f/u (P<0.003)	Long term: % time pH < 4: MED 31% (62 SD) (n=38) ONF 17% (41 SD) (n=10) NS At 1 & 2 yr, % time pH < 4 improved in all 3 groups compared to baseline (P<0.03) At 1 yr, duration of acid reflux by pH monitoring lower in ONF than MEDsx	Long term: Off PPI: MED 36% (n=89) ONF 68% (n=37) P=0.002 Off any anti-reflux meds: MED 8% (n=90) ONF 38% (n=37) P<0.001	ND	Long-term: Difference between groups on SF-36 (P&M) =NS; subscale bodily pain was better in ONF (P=0.02) Majority in both groups were satisfied with their treatments. During the 2 yr f/u, pt satisfaction: ONF>MEDc (P=0.024) & MEDsx (P=0.006).	5 pts with esophageal CA after a mean f/u of 7.1 yrs (4-12); difference between MED & ONF: NS; 4 of 5 pts with CA had Barrett's at baseline; incidence rate of esophageal CA in pts with Barrett's vs. w/o: 0.4% vs.0.07% per year. LES higher in ONF than MED at 1 yr (significant, P	B

Appendix C. Evidence Tables

Author, Year Study design	Intervention N Enrolled/ Follow-up Gender/ Mean age	Patient characteristics				Follow-up duration	Status at follow-up						Quality		
		Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	Other med use data	QOL/ Satisfaction		EMS/ Others	
							throughout the 2 yr f/u (P<0.003)			(P<0.03)				value not reported).	
Mahon, 2005 RCT	PPI vs. Laparoscopic Nissen fundoplication (LNF) PPI 108 LNF 109 12 mos f/u PPI 97 LNF 106 66%M in LNF 48 yr 72%M in PPI 47 yr	No; 15% in PPI 21% in LNF	Mean DeMeester PPI 36.9 LNF 42.7 %time pH<4 PPI 9.5% LNF 12.9%	Mean LES in mm Hg PPI 8.1 LNF 6.3	Dependent on PPI	3 mos (pH, EMS study) 12 mos	GI-well being score improved at 3 mos & 12 mos; more improvement in LNF by ANCOVA (p=0.010 at 3 mos; P=0.003 at 12 mos)	ND	At 3 mos, Mean DeMeester PPI 17.7 LNF 8.6 (P <0.001, ANCOVA) %time pH<4 PPI 3.8% LNF (CI 2.9-11.2) 1.4% (P=0.002, ANCOVA)	ND	ND	Total well-being score improved more in LNF than PPI at 12 mos (p<0.001)	LES at 3 mos PPI 7.9 LNF 17.2 (P<0.001 by ANCOVA)	B	
Johansson, 1986 Open label medical comparison with surgical cohort	Maintenance ranitidine for 6 mos (RAN) vs. posterior partial fundoplication (OPA) 50% of pts received 8 wks of ranitidine before RAN or OPA (see paper) RAN n=16 38% M 60 y (35-73) OPA n=15 67% M 42 y (23-70)	No; > grade 3 RAN 6/16 (38%) OPA 2/15 (13%) +esophagitis RAN 15/16 OPA 13/15	Total reflux time= 7.7±7.3% before trial (n=28) + pH reflux test RAN 69% OPA 67%	LES in mm Hg RAN 5.6 (R 0-20) OPA 6.0 ± 6.7 (R 0-20) Hernia RAN 100% OPA 60%	Failed lifestyle modification prior to entry; half of the pts received 8 wks of ranitidine OR placebo then crossed over to other treatment; response to ranitidine not stated	6 mos	Heartburn & regurg ↓ after 8 wks of ranitidine in RAN & OPA (P<0.01). 6 mos later, no further improvement in RAN; in OPA, further improvement in heartburn, regurg & chest pain (P<0.05); all OPA pts symptom free except for 2 (mild dysphagia & chest pain)	After 8 wks of ranitidine, significant improvement in RAN (P<0.05), not in OPA. 6 mos later, no further improvement in RAN; all OPA pts had normal mucosa (p<0.01)	Total reflux time no significant ↓ after 8 wk of ranitidine (n=19). After OPA (n=15), total reflux time= 0.04±0.09%, which is lower than during RAN (p<0.01) Reflux was not seen in 10 subjects after OPA.	ND	ND	All OPA pts were satisfied (1 unable to belch). 5 pts in RAN dissatisfied with treatment.	LES increased to 10 ±4.6 mm in OPA (P<0.05).	C	

Appendix C. Evidence Tables

Author, Year Study design	Intervention N Enrolled/ Follow-up Gender/ Mean age	Patient characteristics				Follow-up duration	Status at follow-up							Quality
		Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	Other med use data	QOL/ Satisfaction	EMS/ Others	
Wetscher, 2001 Prospective Cohort with comparison to a retrospective surgical group	Continuous PPI and cisapride (MED) vs. laparoscopic anti-reflux surgery (LAS): included only if after LAS, Symptom free, no esophagitis, normal LES & pH study MED n=83 54% M Median age 59 y (21-74) LAS n=42 62% M Median age 53 y (26-67)	MED Yes; only pts with mild reflux were included. LAS No; 41% with severe esophagitis	Normal DeMeester score MED 16.9% LAS 19% ? normal pH study as a criterion of entry in LAS	LES in mm Hg MED 6 (2.5-8.0) LAS 4.7 (2.9-9.2) Defective esophageal contraction waves MED 0 LAS 10 (0-60)	In MED, must respond to PPI+cisapride In LAS, 12% failed PPI treatment	MED 2 yr LAS 3.5 yr	ND For LAS, see column 2	ND For LAS, see column 2	ND For LAS, see column 2	ND	ND	ND	LES – see column 2 regarding LAS inclusion criterion Barrett's developed in MED 12/83 (14.5%) LAS 0 Pts who developed Barrett's had more defective LES & more impaired esophageal peristalsis pre-treatment (p<0.05)	C
Tran, 2005 Retrospective comparison of 3 distinct cohorts from VA hospitals	Medical (MED) vs. Fundoplication (ARS) vs. no-GERD (Ctr) MED n=1892 ARS n=946 Ctr n=5676 Mean age 55y 98% M; No significant differences in all groups.	ND	ND	ND	ND	MED 10.6yr ARS 11.8yr Ctr 10.5yr	ND	ND	ND	ND	ND	ND	Esophageal CA: MED 8/20,115 patient-years (PY) 40/100,000 PY ARS 8/11,156 patient-years 72/100,000 PY (MED vs. ARS, NS) Ctr 0/59,439 PY	C

Appendix C. Evidence Tables

Author, Year Study design	Intervention N Enrolled/ Follow-up Gender/ Mean age	Patient characteristics				Follow-up duration	Status at follow-up							Quality
		Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	Other med use data	QOL/ Satisfaction	EMS/ Others	
Ye, 2001 Retrospective cohort analysis	Unoperated GERD (NoS) vs. surgery (ARS) NoS n=66,965 53% M Age 60 M 66 F ARS n=11,077 58% M Age 50 M 56 F	ND	ND	ND	ND	NoS f/u M 5.6 yr F 5.7 yr ARS f/u M 7.7 yr F 8.0 yr	ND	ND	ND	ND	ND	ND	Esophageal adeno-CA Incidence per 100,000 PY M: 22.4 (NoS); 37 (ARS) F: 6.6 (NoS); 0 (ARS) Esophageal adeno-CA Standardized Incidence Ratio M: 6.3 (NoS) (CI 4.5-8.7); 14.1 (ARS) (CI 8.0-22.8) F: 6.1 (NoS) (CI 2.9-11.2); 0 (ARS)	C
Fernando, 2002 Retrospective Cohort analysis	Medical Rx (MED) vs. laparoscopic anti-reflux surgery (LAS) MED n=51 -> 37 (f/u) 41% M Median age 48 y (17-82) LAS n=120 -> 101 (f/u) 50% M Median age 47 (17-80)	ND	ND	ND	ND PPI use MED 57% LAS 88% P<0.05 H2RA use MED 28% LAS 38%	MED Median f/u 23 mos LAS Median f/u 18 mos	ND	ND	ND	ND	ND	ND	Mean HRQOL better in LAS than MED (p<0.05) Better SF-36 in 6/8 domains in LAS than MED (p<0.05) Dissatisfied pts: MED 22% LAS 6%	C
Holzman,	MED vs. ARS	ND	ND	ND	ND	1 year	ND	ND	ND	ND	1 st year	ND	ND	C

Appendix C. Evidence Tables

Author, Year Study design	Intervention N Enrolled/ Follow-up Gender/ Mean age	Patient characteristics				Follow-up duration	Status at follow-up							Quality
		Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	Other med use data	QOL/ Satisfaction	EMS/ Others	
2001 Retrospective matched cohort from Tennessee Medicaid research database	MED n=250 39% M ARS n=135 40% M										after ARS: use of GERD drugs: ARS vs. MED, 123 days vs. 339 days (P<0.001)			
Khaitan, 2003 Follow-up results from above study	MED vs. ARS MED n=200 ARS n=111	ND	ND	ND	ND	4 year period	ND	ND	ND	ND	% of pts using GERD drugs was less in ARS than MED for each year of f/u; Year 4: 74% vs. 90%; P<0.001	ND	Fewer GERD outpatient visits in ARS	C
Isolauri, 1997 Retrospective Cohort	Medical Rx (MED) vs. Nissen-Rossetti (ONF) f/u 63%M 58 yr (36-83) MED n=81 -> 68 (f/u) ONR n=39 -> 37 (f/u)	Grade 3 MED 12% ONF 16% Grade 2 MED 34% ONF 57% Grade 0 None Must have erosive esophagitis to enroll.	ND	ND	Pts failed medical & lifestyle treatments before referral for ONF	Median observation time 10.9 yr (R 9.1-13.4yr)	No or mild heartburn: MED 53% ONF 84%	Grade 3 MED 4% ONF 0% Grade 2 MED 22% ONF 0% Grade 0 MED 46% ONF 86%	ND	MED: 14/68 (21%) on PPI or H2RA regularly; 22/68 (33%) occasionally ONF: 2/37 (5%) on H2RA occasionally	ND	ND	Barrett's baseline: MED 0 ONF 5/39 (13%) f/u MED 8/68 (12%) ONF 12/37(32%) 1 case of esophageal adeno-CA w/o Barrett's	C

M: male; F: female

Appendix C. Evidence Tables

Table 2. Studies on endoscopic procedures

Author, Year Study design	Study and patient characteristics					Follow up duration	Status at follow up						Quality	
	Intervention N Enrolled/ Follow up Gender/ Age	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/ hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI / Off all anti-secretory meds	Other med use data	QOL / satisfaction		EMS / Others
Deviere, 2005 RCT	Enteryx(ERX) vs. Sham 64 61 ERX n=32 62% M 49±10 SD Sham n=32 72% M 50±14 SD	Yes	Must have abnormal pH study while off PPI	Excluded hiatal hernia ≥ 5 cm	Yes	3 mos & 6 mos	Heartburn score improved ≥ 50% more in ERX vs. Sham at 3 mos (Ratio 3.05; CI, 1.55-6.33) Regurg score improved ≥ 50% more in ERX vs. Sham (Ratio 2.03; CI 1.14-3.75)	ND	Difference between groups=NS; Incomplete data Correlation not apparent between change in total time at pH≤4 and heartburn score.	At 3 mos, 68% in ERX off PPI vs. 41% in sham (ratio 1.67, CI 1.03-2.80)	At 3 mos, ≥ 50% ↓ in PPI use is 81% in ERX vs. 53% in Sham (ratio 1.52, CI 1.06-2.28)	SF-36 –P and SF-36-M improved in ERX; no significant change in sham at 3 mos. % change between the groups=NS, GERD-HRQL score improved by ≥ 50% significantly more in ERX at 3 months	6/9 retreated in ERX; 20/23 sham proceeded to ERX (ratio 0.42, CI 0.22-0.73) at 3 mos.	B
Corley, 2003 RCT with X-over at 6 mos	Radio-frequency (STR) vs. Sham 64 56 STR n=35 46% M 45±12 SD Sham n=29 59% M 52±15 SD	Yes	All have abnormal pH study	Median LES = 12.1 in Sham; 13 in STR	At least partially responsive to daily anti-acid meds	6 & 12 mos	At 6 mos, mean heartburn score improved compared to Sham (p=0.01)	At 6 mos, no difference between groups.	At 6 mos, no difference in median acid exposure between the 2 groups.	58% (STR) vs. 57% sham off PPI at 6 mos, p=NS	At 6 mos, daily PPI use ↓ 46% in STR vs. 29% in Sham p=NS; daily use of any meds: 61% in Sham vs. 55% in STR p=NS	At 6 mos, mean HRQL & SF-36-P improved compared to Sham (p=0.003, p=0.05)	No significant change in LES	B

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Author, Year Study design	Study and patient characteristics					Follow up duration	Status at follow up							Quality
	Intervention N Enrolled/ Follow up Gender/ Age	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/ hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI / Off all anti- secretory meds	Other med use data	QOL / satisfaction	EMS / Others	
Cohen, 2005; Included pts from Johnson, 2003 (UI14499767) & Johnson, 2003 (UI 12591037) Prospective Cohort	ERX 144 64 61%M Mean age 48 (12 SD)	Included 1 pt with > grade 3	Must have abnormal pH study	Included 12 with hiatal hernia ≥ 3 cm	Yes	Up to 24 mos	Heartburn score improved median 80% (CI 71%, 87%) compared to baseline off PPI. Regurg score improved median 88% (CI 79%, 92%) at 24 mos.	At 12 mos, unchanged in 59/107 (55%), improved in 14 (13%), ↑ in severity in 34 (32%) at 12 mos.	38/102 (37%) normalized at 12 mos (CI 28%, 47%).	43/64 (67%) off PPI at 24 mos (CI 54- 78%).	46/64 (72%) ≥ 50% ↓ in PPI use at 24 mos (CI 59-82%)	Improved GERD- HRQL in 78% (CI 69%, 85%) & SF-36-P 12% (CI 7.4%, 17%); no change for SF-36-M	No significant change in EMS data at 12 mos.	B
Deviere, 2002 Cohort, pilot study	ERX 15 15 Mean age 52	Yes	Must have abnormal pH study	Excluded hiatal hernia ≥ 3 cm; Excluded esophageal motility disorder other than associated with GERD	Yes	1 mos; 4-12 mos	Heartburn score improved at 1 month (p=0.038).	ND	ND	ND	4 patients resumed PPI at follow up (4-12 mos).	ND	LES=16.7 at 6- month (p=0.038 compared to baseline)	C
Schumacher, 2005 Prospective Cohort	ERX 93 76 68%M Mean age 48 (14 SD)	Yes	Must have abnormal pH study	Median LES = 10 mm Hg; Excluded hiatal hernia ≥ 3 cm	Yes	12 mos	Heartburn & regurg scores improved compared to off PPI levels (p<0.0001) & improved after treatment to a level similar to on PPI	No change in 55%; improved in 12%; worsened in 33%	28/54 (52%) normalized	65% off PPI at 12 mos;	86% ≥ 50% PPI ↓ dosage at 12 mos (CI 77-93%)	SF-36-P & SF-36-M improved compared to off PPI levels (p<0.0001 & p=0.0012), GERD- HRQL improved compared to off PPI levels	Median LES = 9 mm (NS); 6 pts retreated between months 1 & 3.	B

Appendix C. Evidence Tables

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Author, Year Study design	Study and patient characteristics					Follow up duration	Status at follow up							Quality
	Intervention N Enrolled/ Follow up Gender/ Age	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/ hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI / Off all anti-secretory meds	Other med use data	QOL / satisfaction	EMS / Others	
Filipi, 2001 RCT	Endocinch (ECH): Linear vs. circumferential plication 64 (52% in linear group) 51 70%M Mean age 46	Yes	Must have abnormal pH study while off meds; mean % time ≤ 4 = 0.63 (64 pts)	Mean LES= 16.1 mm Hg; Excluded hiatal hernia > 2 cm	Yes; responded to PPI, H2RA or antacids	Up to 6 mos	Heartburn & regurg score improved from baseline at 3 & 6 mos (p=0.0001)	No significant change in mean esophagitis grade	Mean % time ≤ 4 = 8.5 at 6- mos in 29 pts (p=0.011 compared to baseline)	62% of patients taking PPIs, H2RAs, antacids or prokinetics at baseline taking fewer than 4 doses of medication per month at 6 mos	ND	SF-36-P and SF-36-M, no significant change; significant change in 2 subscales.	LES=20.6 mm Hg at 6-month (no significant change); plication configuration did not affect Symptom or pH results.	C
Chadalavada, 2004 Non-randomized comparison	ECH vs. laparoscopic surgery (LAS) ECH n=47->44 (f/u) 32% M 47±2 SEM LAS n=40->40 (f/u) 30% M 44±2 SEM	Excluded erosive esophagitis in ECH; not in LAS	Abnormal pH: 16% in ECH vs. 18% in LAS	Excluded >2 cm hiatal hernia in ECH; not in LAS	No; had heartburn not responsive to med Rx	Mean 7 mos (ECH) Mean 8 mos (LAS)	ND	ND	ND	In ECH: 25% off an antisecretory med PPI/motility drug use: 32% in ECH vs. 13% in LAS (p=0.03)	Satisfied: 66% in ECH; 93% in LAS (NS)	3 ECH pts had LAS within 6 mos of ECH	C	
Velanovich, 2002 Case-control comparison, matched for gender, age & pre GERD-HRQL score	ECH vs. lap surgery (LAS) ECH n=27->27 (f/u) 33% M 47±4 SD LAS n=27->27 (f/u) no actual data on age	ND	Abnormal reflux on pH study in ECH	Excluded >2 cm hiatal hernia in ECH	ND	2mos,	See QOL column	ND	ND	ND	ND	GERD-HRQL improved in both groups (p<0.00001); difference between groups=NS; Satisfied: 78% in ECH; 98% in LAS (p<0.01)	ND	C

Appendix C. Evidence Tables

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Author, Year Study design	Study and patient characteristics					Follow up duration	Status at follow up							Quality
	Intervention N Enrolled/ Follow up Gender/ Age	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/ hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI / Off all anti- secretory meds	Other med use data	QOL / satisfaction	EMS / Others	
Abou-Rebyeh, 2005 Prospective Cohort	ECH 38 unclear f/u N 55%M 55 ± 10)	Yes	All have abnormal pH study while off medical therapy	ND	Yes	12 mos	39% improvement in heartburn, 14% free of heartburn	Esophagitis present in Baseline 41% 2 mos 31% 12 mos, 56%	Significant reduction in pathologic reflux in 84% after 2 mos and 66% after 1 yr; normalization in 24% after 2 mos and 14% after 1 yr	20% off PPI after 1 yr	PPI reduced from 6.5 to 1.9 days a week after 2 mos but increased to 4.3 days per week after 1 yr 63% reduced dose at 1 yr	ND	74% of sutures totally lost and 16% lose after 1 year, None had correct placement of initial sutures; EG had no effect on esophageal peristalsis or LES pressure	C
Arts, 2005 Prospective Cohort	ECH 20 20 50%M 45 ± 11 SD	Yes	All have abnormal pH study while off medical therapy	Excluded > 3 cm hiatal hernia	Failed or partial response	12 mos	Improved Symptom score at 12 mos (p<0.05 compared to before Rx, off PPI)	One healed at 12 mos. 3 of 4 had same grade at 12 mos.	6/20 (30%) normalized pH	6/20 (30%) off PPI (p<0.01)	6/20 (25%) now responds to dose that failed before Rx	ND	11 patients underwent 2 nd Endocinch	C
Chen, 2005 Prospective Cohort	ECH 85 81 44%M 48 (15 SD)	No; 10 had grade 3	All have abnormal pH study	Median LES= 17.6 mm; 9 had ≥ 2 cm hiatal hernia	Dependency on anti-secretory meds.	Up to 24 mos	~50% no heartburn & 69% no regurg at 24 mos (p<0.0001)	ND	27/68 (39.7%) normalized at 3-6 mos	30/74 (41%) off PPI at 24 mos.	21/74 (28%) ≥ 50% PPI ↓ dosage at 24 mos (p=0.0011).	ND	Median LES=17.1(NS); ↑ in residual LES (p=0.017); 2 had Nissen 2° to poor response	C
Mahmood, 2003 Prospective Cohort	ECH 26 22 13/22(59%M) Mean age 39 yr (R 22-62)	Excluded patients with an esophageal stricture or Barrett's esophagus	All have abnormal pH study while off medical therapy	Mean LES= 10.78 mm Hg; Excluded > 2 cm hiatal hernia	Many pts with breakthrough symptom while on PPIs	12 mos	Heartburn (p<0.0001) & regurg scores (p<0.001) improved at 12 mos	Esophagitis not worsened at 3 mos.	At 3 mos, DeMeester improved (p=0.028); total time pH<4, change=NS	64% off PPI at 12 months	36% need < 4 doses of PPI/month at 12 mos (p ≤ 0.001)	QOL improved at 12 mos (p ≤ 0.01)	At 3 mos, Mean LES=10.84 mm (NS)	C
Schiefke, 2005 Prospective Cohort	ECH 70 70 62%M Median age	No; 2/70 (2.9%) ≥ grade 3	All have abnormal pH study	LES= 7.mm; Excluded > 3 cm hiatal hernia	At least partial response to PPI	18 mos	Heartburn score improved (p=0.001)	No change: 40/70(57%); Improved: 20/70(29%); Worsened: 10/70 (14%)	16/54 (28%) normalized at 12 mos	4/70(6%) off PPI at 18 mos	> 50% PPI ↓ dosage: 47% at 6 mos; then 24% at 18 mos	14/70 considered responders based on pt satisfaction, heartburn &	LES 10.3(NS); All sutures retained in only 12/70 (17%) of patients;no	C

Appendix C. Evidence Tables

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Author, Year Study design	Study and patient characteristics					Follow up duration	Status at follow up							Quality
	Intervention N Enrolled/ Follow up Gender/ Age	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/ hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI / Off all anti- secretory meds	Other med use data	QOL / satisfaction	EMS / Others	
	48 y (R 22-77)											>50%↓ dose.	sutures in 18/70 (26%)	
Tam, 2004 Prospective Cohort	ECH 15 14 47%M Median age 46 yr (R 24- 64)	4 pts with grade A, 1 with grade B; excluded grade D pts	All have abnormal pH study	Mean fasting LES = 6.7 mm Hg; Post- prandial LES = 4.3 mm; Excluded > 2 cm hiatal hernia	Dependent on PPI or H2RA	6 mos, 12 mos	See QOL column	3 of 5 had same grade; 2 resolved; 2 new cases of grade A	4/15 (27%) normalized at 6 mos.	7/14 (50%) off PPI at 12 mos	8/15 (53%) at ↓ med dose at 6 mos	GERD- HRQL improved at 12 mos (P<0.05); SF-36-P ↑ at 12 mos (p<0.05); no significant Δ for -M	Mean fasting = 5.0 mm (NS); post-prandial = 6.2 mm (p<0.05); ↓ tLESRs (p<0.05)	C
Go, 2004 Prospective Cohort	Stretta (STR) Only > 3 mos f/u data were used in this study 50 44% M 47 yr(R 22-74) 37 (f/u)	ND	ND ?at least some had pH study	Excluded hiatal hernia	All on PPI	10 mos (R 3-32 mos)	Mean heartburn score improved (p=0.0012)	ND	ND	29% off PPI	ND	GERD- HRQL symptom satisfaction score improved (p=0.0001)	10 pts failed previous anti- reflux surgery; symptom satisfaction score improved in this group (p=0.0166); 4 pts had fundoplication after Stretta.	C
Lutfi, 2005 Prospective Cohort (includes patients from "Vanderbilt database": Houston, 2003, Torquati, 2004, Richards 2003, Richards 2001)	STR 85 had STR; only pts with f/u > 6 mos qualified for this study: 77 61 completed survey 39% M 52 yr (R20-82)	Yes	All have abnormal pH study	Excluded if LES < 8mm; excluded if hiatal hernia > 3 cm	All on PPI	26 mos (R 6-36 mos)	See QOL column	ND	24 had pH data at f/u: 10/24 (42%) normalized pH (all in off PPI & ≥ 50% PPI ↓ group)	26/61 (43%) off PPI	13/61 (21%) ≥ 50% PPI ↓ dosage	QOLRAD improved (p<0.001)	8 pts had Nissen after Stretta	C

Appendix C. Evidence Tables

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Author, Year Study design	Study and patient characteristics					Follow up duration	Status at follow up							Quality
	Intervention N Enrolled/ Follow up Gender/ Age	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/ hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI / Off all anti- secretory meds	Other med use data	QOL / satisfaction	EMS / Others	
Richards, 2003 Non-randomized comparison (Based on "Vanderbilt database")	STR vs. laparoscopic fundoplication (LAS) STR n=65 42% M 46±12 SEM LAS n=75 44% M 49±14 SEM	Some had esophagitis, actual data not reported	Acid exposure % time: STR – 11.3% LAS – 8.5% (p<0.01)	STR – LES= 25.4 mm; excluded hiatal hernia > 2 cm; LAS – LES= 18.2 mm (p<0.01); included hiatal hernia > 2 cm	ND	Mean f/u 7.3 mos (STR); 5.2 mos (LAS)	At 6 mos, GERD Symptom improved similarly in both groups (NS).	ND	At 7.2 mos, STR – 8/22 (36%) normal acid exposure; ND on LAS group	STR- 58% off PPI; LAS – 97% off PPI	STR – 31% ↓ PPI dose	At 6 mos, GERD-QOL & SF-12 improved in both groups (p<0.01) compared to baseline on-meds.	No significant change in mean LES in STR; ND in LAS	C
Tam et al, 2003 Prospective Cohort	STR 20 19 50%M Median age 51 (R 32-69)	2 Los Angeles grade A, 2 grade B, 1 grade C; Excluded pts with grade D	Mean DeMeester = 38.8	mean post-prandial basal LES=5.2 mm; Excluded >2 cm hiatal hernia	Dependent on daily acid suppressant	Up to 12 mos	See QOL column	10 grade A at 6 mos	4/20 (25%) had normal acid exposure at 12 mos; mean DeMeester = 24.1 (p<0.05).	13/20 (65%) off PPI at 12 mos	At 6 mos, 15/20 off PPI, 3 of remaining 5 on ↓ dose of PPI	GERD-HRQL, SF-36-P & SF-36-M improved at 12 mos (p<0.05)	At 6 mos, mean post-prandial basal LES=8 mm (p<0.01); ↓ TLESR (p<0.01)	C
Triadafilopoulos, 2002 & 2001 Included 9 pts from DiBaise, 2002 Prospective Cohort	STR 118 94 61%M Mean age 47 (12 SD)	Yes	All have abnormal pH study; median DeMeester off meds = 40	Median LES =15 mm Hg; Excluded >2 cm hiatal hernia	At least partial response to meds	Up to 12 mos	Heartburn score improved compared to baseline off med (p=0.0001)	Esophagitis (grades 1 or 2) present in 31% pre- and 25% post-Rx at 6 mos (NS)	DeMeester = 26.3 (p=0.0001) at 6 mos	At baseline, 88% on PPI, at 12 mos, 30% on PPI (p<0.0001); 40% off all meds	ND	GERD-HRQL improved at 12 mos compared to baseline on meds (p=0.0007); SF-36-P & M improved (p<0.0001)	At 6 mos, median LES=12.6 (p=0.007)	C
Triadafilopoulos, 2004 Post hoc analysis of data from Triadafilopoulos, 2002 & 2001	STR responder vs. non-responder 118 61%M Mean age 47 (R 22-75)	Responder: GERD-HRQL ≤ 10, heartburn severity score ≤ 1, no daily PPI or pt satisfaction score >4 Nonresponder: GERD-HRQL > 10, heartburn severity score > 1, daily PPI or pt satisfaction score ≤4					1. GERD-HRQL, satisfaction score, PPI responder subgroups improved in distal esophageal acid exposure time (p<0.001); nonresponders: change NS 2. Heartburn responder subgroup improved in distal esophageal acid exposure time from a baseline of 7.8% to 4.1% (p<0.001); nonresponders: 11.2% to 8% (p=0.04) 3. Changes in heartburn correlated with changes in esophageal acid exposure (r=0.26, p=0.01) 4. Changes in satisfaction negatively correlated with changes in esophageal acid exposure (r= -0.23, p=0.02).							C

Appendix C. Evidence Tables

Author, Year Study design	Study and patient characteristics					Follow up duration	Status at follow up							Quality
	Intervention N Enrolled/ Follow up Gender/ Age	Excluded \geq grade 3 esophagitis; $\% \geq$ grade 3	pH status	EMS/ hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI / Off all anti- secretory meds	Other med use data	QOL / satisfaction	EMS / Others	
Wolfsen, 2002 Survey	STR 558 from 33 institutions	ND	ND	ND	At least partial response to meds	Mean follow up = 8 mos	Satisfactory Symptom control: 26.3% at baseline on drugs compared to 77% after RF	ND	ND	At baseline, 70.6% pts on PPI twice daily, after RF, 51% required no antiseecretory meds.	ND	ND	ND	C
Pleskow, 2005, 2004 Prospective Cohort	Endoscopic Plication System 64 57 48%M 46 (13 SD)	Yes	All have abnormal pH study; mean DeMeester = 48.7	LES \geq 5mm Hg; excluded hiatal hernia > 2 cm	Dependent on antiseecretory meds	12 mos	Median Symptom scale improved from baseline off med ($p < 0.0001$); no change compared to baseline on med	ND	At 6 mos, mean DeMeester = 34.5; 30% normal pH score	36/53 (68%) off PPI at 12 mos (baseline 53/57 on PPI); 13/57 (23%) off all antiseecretory meds	ND	Median GERD- HRQL improved compared to baseline on & off meds ($p = 0.0237$, $p < 0.0001$)	No significant change in EMS data (from 2004 paper)	B

Appendix C. Evidence Tables

Table 3. Systematic Reviews and meta-analyses

Author, year Quality	Question			Database searched, year	Type of studies included (# studies)	Population	Intervention / Duration	Comparison group	Outcomes	Med vs. Med ¹	Med vs. Placebo ²	Med vs. Med ²	Med vs. Surg	Surg vs. Surg	Endo vs. Sham/ Surg
	Q1	Q2	Q3												
Caro, 2001 B	X			MEDLINE, Jun 1979- Jun 2000	RCTs (acute treatment: 26; maintenance treatment: 15)	endoscopically confirmed GERD for acute treatment; endoscopically confirmed healing of esophagitis for enrollment in the maintenance phase	PPI Duration: (acute treatment): 4-8 wk Follow-up (maintenance treatment): 6-12 mo	PPI (omeprazole) or H2RA (ranitidine)	acute treatment: symptom relief; esophageal ulcer healing (endoscopically confirmed) maintenance treatment: relapse rate (endoscopically confirmed) No significant difference between PPIs Results favored PPI when compared to H2RABlocker	X		X			
McDonagh, 2004 Oregon Report A	X		X	MEDLINE, 1966-Nov 2003 EMBASE, 1980-2003 Cochrane, 3/2003	RCTs (for PPI vs. PPI, acute treatment: 16; maintenance treatment: 4) (for PPI vs. H2RABlocker, acute treatment: 22; maintenance treatment: 1)	adults outpatients with symptoms of GERD; also adults with peptic ulcer or NSAIDs induced ulcer were analyzed separately	PPI Duration: (acute treatment): 8 wk Follow-up (maintenance treatment): 4 wk to 5 yr	PPI, H2RA, prokinetics, antacids	for acute treatment: symptom relief; healed esophagitis (endoscopically proved) for maintenance treatment: relapse of symptoms; esophagitis relapse	X		X			
Carlsson, 1997 B		X		ND	Individual Patient Data Meta-analysis based on 5 RCTs published between 1989-1995	endoscopically proven esophagitis healed; complete symptom resolution or mild residual symptoms at admission to maintenance phase	PPI (omeprazole) Follow-up (maintenance treatment): 6-12 mo	placebo or PPI (omeprazole) or H2RA (ranitidine)	endoscopic remission Results favored PPI (omeprazole 10 or 20 mg daily) Meta-regression: prognostic factors for the risk of relapse included pre-treatment severity of esophagitis or regurgitation, age, and smoking		X	X			

Appendix C. Evidence Tables

C-15	Donnellan, 2005 (Cochrane Database Systematic Review) A	X	X	MEDLINE, 1966-2003 EMBASE, 1980-2003 Cochrane, 2/2003 CINAHL, 1982-2003 National Research Register, 2/2003	RCTs: 51	reflux esophagitis healed (endoscopically proved) or ENRD with main presenting symptoms heartburn and /or acid reflux	PPI; H2RA; prokinetics; sucralfate; or combinations Follow-up (maintenance treatment): up to 12 mo	placebo or PPI, H2RAblocker, prokinetics, sucralfate	for reflux esophagitis: proportion of relapse; proportion of symptom relapse for ENRD: proportion of symptom relapse Results favored PPI	X	X			
	Corey, 2003 C	X		MEDLINE, 1966-Oct 2001	RCTs: 9; Cohorts: 25	BE by histologic confirmation	Surgery (not specified) Follow-up: ≥12 mo	medical treatment (not specified, PPI??)	incidence of adenocarcinoma by histologic confirmation no difference between medical and surgical groups				X	
	Catarci, 2004 A		X	MEDLINE, 1966-2002 EMBASE, 1980-2002 HealthSTAR, 1975-2002 Cochrane, 2/2002	RCTs (lap vs. open fundoplication: 6; partial vs. total wrap: 9)	GERD (not specified)	laparoscopic fundoplication partial wrap division of short gastric vessels Follow-up: 3 mo to >8 yr	open fundoplication total wrap	perioperative mortality was 0 for all procedures <u>lap vs. open fundoplication</u> <i>short-term outcomes:</i> significantly lower operative morbidity rate, shorter postoperative stay, and shorter sick leave for lap vs. open fundoplication <i>midterm /long-term follow-up:</i> no significant differences were found regarding the incidence of recurrence, dysphagia, bloating, and reoperation for failure <u>partial vs. total wrap</u> <i>short-term outcomes:</i> no significant differences in operative morbidity, and in operative time <i>midterm /long-term follow-up:</i> significantly lower incidence reoperation for failure after partial fundoplication; no significant differences regarding the incidence of recurrence and /or dysphagia					X

¹ Acute treatment (duration: 4-8 weeks)

² Maintenance treatment (duration ≥ 6 mo)

Appendix C. Evidence Tables

Table 4. RCTs on surgical interventions

Author, Yr Study design	Intervention Enrolled/ Final Other characteristics	Patient characteristics					Follow up duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality
		% ≥ grade 3 esophagitis	pH status	EMS / hiatal hernia	Responded to PPI or H2RA	Change in symptoms		Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction	EMS/ Others	
Ludemann, 2005	Laparoscopic total fundoplication Enrol/Final: 53/51 Age:50 yr for men and 57 for women (whole group) Gender: 35% men Setting: University hospital Country: Australia	24% Barretts/stricture	Abnormal mean score (performed in 34 patients)	LES:24% abnormal	ND	5	Heartburn: 90% improved	ND	ND	94% off PPI	ND	78% excellent or good global outcome 88% good QOL	ND	B
	Laparoscopic Partial fundoplication Enrol/Final: 54/50	21% Barretts/stricture	Abnormal mean score (performed in 35 patients)	LES: 20% abnormal	ND	5	Heartburn: 80% improved	ND	ND	98% off PPI	ND	86% excellent or good global outcome 98% good QOL	ND Men were younger than women in the whole group	
Hagedorn/Lundell	Open total fundoplication Enrol/Final: 65/nd (110 for the whole group) Age:53 (25-74) for the whole group Gender: 38% men for the whole group Setting:University hospital Country: Sweden	28% (whole group)	Abnormal mean score	7% abnormal	nd	11.5	Heartburn 90% Regurgitation 91%	ND	ND	ND	ND	ND	ND	B

Appendix C. Evidence Tables

Author, Yr Study design	Intervention Enrolled/ Final Other characteristics	Patient characteristics				Follow up duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality	
		% ≥ grade 3 esophag itis	pH status	EMS /hiatal hernia	Responde d to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ Others
	Open partial fundoplication Enrol/Final: 72/nd (110 for the whole group)		Abnormal mean score	6% abnormal			Heartburn 90% Regurgitation 91%	ND	ND	ND	ND	ND	ND	
Nilsson, 2004	Laparoscopic total fundoplication Enrol/Final: 30/17 Age:53 (25-74) for the whole group Gender: 38% men for the whole group Setting:University hospital Country: Sweden	1 patient Barretts	Abnormal mean score	Abnormal mean score	0% PPI	5	100%		Normal level Sig compared to baseline; but no differences between surgeries	94%	ND	PGWB Improved P<0.001	Increased and stable NS	B
	Open total fundoplication Enrol/Final: 30/24	4 patients Barretts	Abnormal mean score	Abnormal mean score	0% PPI		92%		Normal level Sig compared to baseline; but no differences between surgeries	74%	ND	PGWB Improved P<0.001	Increased and stable NS	

Appendix C. Evidence Tables

Author, Yr Study design	Intervention Enrolled/ Final Other characteristics	Patient characteristics				Follow up duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality	
		% ≥ grade 3 esophagitis	pH status	EMS /hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/Others
O'Boyle, 2002	Laparoscopic total fundoplication with division of gastric vessels Enrol/Final: 52/50 Age:47 Gender: 60% men for the whole group Setting:University hospital Country: Australia	19% Barretts or stricture	10.3% and only 50% underwent	Abnormal Mean pressure 56% hiatus hernia	Total n unclear on multiple meds	5	Heartburn 88% Regurgitation 90%	ND	ND	91%	ND	70% good QOL	ND	B
	Laparoscopic total fundoplication without division of gastric vessels Enrol/Final: 50/49 Age:47 Gender: 60%	24% Barretts or stricture	10.3% and only 50% underwent	Abnormal Mean pressure 53% hiatus hernia	Total n unclear on multiple meds	5	Heartburn 82% Regurgitation 96%		ND	91%	ND	76% good QOL	ND	

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Appendix C. Evidence Tables

Table 5. Non-randomized comparative studies on surgical interventions

Author, Yr Study design	Intervention Enrolled/ Final Other characteristics	Patient characteristics				Follow up duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality	
		% ≥ grade 3 esophagitis	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all antiretoretry meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ Others
Kamolz, 2002 UI 12430078 Prospective	Laparoscopic Nissen fundoplication Enrol/final: 104/69 Age: 52.1±9.8 (both groups) Gender: Male 55% (both groups) Country: Austria Setting: University hospital	69% for both groups	Mean DeMeester score abnormal	Abnormal mean score % data ND	0%	5	100% improved	ND	Normal mean DeMeester score	100% (antireflux meds)	NA	Mean score comparable to healthy Patient satisfaction 98%	Mean LES score normal % data ND	B
	Laparoscopic Toupet fundoplication Enrol/final: 65/33)		Mean DeMeester score abnormal	Abnormal mean score % data ND	0%	5	93% improved	ND	Normal mean DeMeester score	97% (antireflux meds)	ND	Mean score comparable to healthy Patient satisfaction: 96.9%	Mean LES score normal % data ND	
Granderath, 2002 11997816 Prospective	Laparoscopic Nissen fundoplication Enrol/final: 345/64 Age: 49.2 (29-79) whole group Gender: 58% (whole group) Country: Austria Setting: University hospital	ND	Abnormal mean DeMeester score	Mean score abnormal	0% PPI	5	Heartburn : 97.2% Regurgitation: 91.2% (data presented for both groups)	ND	Mean score normal range % data ND	ND	ND	ND	Mean score normal range % data ND	C

Appendix C. Evidence Tables

Author, Yr Study design	Intervention Enrolled/ Final Other characteristics	Patient characteristics				Follow up duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality	
		% ≥ grade 3 esophagitis	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all antiretortory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ Others
	Laparoscopic Toupet fundoplication Enrol/final: 155/39	ND	Abnormal mean DeMeester score	Mean score abnormal with weak peristalsis	0% PPI	5		ND	Mean score normal range % data ND	ND	ND	ND	Mean score normal range % data ND Patients with poor esophageal motility underwent Partial fundoplication	
Pelgrims, 2001 Retrospective analysis	Open Nissen fundoplication Enrol/final: 61/nd Age: 55 (28-76) Gender: 66% Country: Belgium Setting: University hospital	18% 3.5% had Barrett's	5 patients underwent and all abnormal	Normal LES score 81% hiatal hernia	0% All patients had recurrent symptoms after withdrawal of meds	6	91.8% improved	ND	ND	85% off all meds	ND	ND	ND	C

Appendix C. Evidence Tables

Author, Yr Study design	Intervention Enrolled/ Final Other characteristics	Patient characteristics				Follow up duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality	
		% ≥ grade 3 esophagitis	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all antiretorety med	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/Others
	Laparoscopic Nissen fundoplication Enrol/final: 149/nd Age: 47.5 (24-81) Gender: 58%	18% 5% had Barrett's	77 patients underwent and all abnormal	Normal LES score 90% hiatal hernia	0%	4	94%	ND	ND	88% off all meds	ND	ND	The records indicate the open procedure was abandoned after the year 1994	
Patti, 2003 Retrospective analysis	Laparoscopic total fundoplication Enrol/final: 94/94 Age: 55±15 (15-93) whole group Gender: 55% Males (whole group) Country: USA Setting: University hospital	Barrett's 16%	Abnormal mean score	Normal peristalsis Hiatal hernia: 62%	ND	5.5	85%	ND on Barrett's	72%	92% (off PPI)	ND	ND	Mean LES pressure normal range 20% follow-up for objective tests	C
	Laparoscopic partial fundoplication Enrol/final: 141/141	Barrett's 19%	Abnormal mean score Difference BW: P=0.01	Weak peristalsis Hiatal hernia: 74%	ND	5.9	67%	ND on Barrett's	44%	75% (off PPI)	ND	ND	Mean LES pressure normal range 34% follow-up for objective tests	

Appendix C. Evidence Tables

Table 6. Cohorts (non-comparative) studies on surgical interventions

Author, Yr Study design	Intervention Enrolled/ Final Population and study characteristics	Patient characteristics				Follow up /duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality	
		% ≥ grade 3 esophagitis	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ Others
Anvari, 2001 Prospective Cohort	Laparoscopic Nissen Fundoplication	ND	Mean acid reflux (%) 8.43±0.53	Lower esophageal sphincter: abnormal 7.16±0.33	36%	5	Improved GERD symptom score P<0.0001	ND	Reduced P<0.0001	88%	ND	Satisfaction: 86%	Lower esophageal sphincter: normal range P<0.001	B
	Enrol/Final: 332/181 Age: 46.5±14.1 Gender: Male 38% Country: Canada Setting: University Hospital		abnormal	Hiatal hernia: ND								Re-surgery Acceptance: 89%	Tightness of wrap varied with pre-op Lower esophageal sphincter	
Booth, 2002 Prospective Cohort	Laparoscopic Nissen Fundoplication	20% (≥ grade 2)	5% abnormal	ND	ND	8	Heart Burn: Improved 93%	ND	ND	86%	ND	Satisfaction: 91%	ND	C
	Enrol/Final: 179/48 Age: 41 median (9-82) Gender: Male 66% Country: UK Setting: Hospital						Regurg: Improved 91%							
Lafullarde, 2001 Prospective Cohort	Laparoscopic Nissen Fundoplication	ND	ND	ND	ND	6	No reflux symptoms : 87%	ND	ND	89%	ND	High mean score for satisfaction	ND	C

Appendix C. Evidence Tables

Author, Yr Study design	Intervention Enrolled/ Final Population and study characteristics	Patient characteristics				Follow up /duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality		
		% ≥ grade 3 esophagitis	pH status	EMS /hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ Others	
	Enrol/Final: 178/176 Age: nd Gender: nd Country: Australia Setting: University Hospital												Re-surgery acceptance: 90%		
Bammer, 2001 Retrospective Cohort	Laparoscopic Nissen Fundoplication Enrol/Final: 171/171 Age: 52±14 Gender: Male 63% Country: US Setting: Hospital	ND	Mean score abnormal	Mean score abnormal	ND	6.4	Heartburn : 5.8% Regurg: Improved 93.6%	ND	ND	86%	ND	Overall well being score improved P <0.0001 Satisfaction: 93%	12.7% had barretts before surgery and none reported development of dysplasia/adenocarcinoma	C	
Granderath, 2002 11918872 Prospective Cohort	Laparoscopic Toupet Fundoplication Enrol/Final: 155/39 Age: 50.2 (29-74) Gender: Male 59% Country: Austria Setting: University hospital	33.6 %	100% abnormal	Lower esophageal sphincter: abnormal 100%	0%	5	Heartburn : Improved 97.4% Regurg: Improved 96.7%	ND	4.5%	97.4%	ND	Improved to normative healthy data	ND	C	

Appendix C. Evidence Tables

Author, Yr Study design	Intervention Enrolled/ Final Population and study characteristics	Patient characteristics				Follow up /duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality	
		% ≥ grade 3 esophagitis	pH status	EMS /hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ Others
Kamolz, 2002 UI 12236479	Laparoscopic antireflux procedures (excluded redo-surgery)	ND	Abnormal mean DeMeester score 100%	ND	0%	5	ND	ND	ND	ND	ND	Mean score comparable to healthy (NA compared to PPI at 5 yr)	ND	C
	Enrol/Final: 511/107 Age: 47.6 (28-79) Gender: 55% Country: Spain Setting: University hospital											Difference sig compared to untreated patients		
Franzen, 1999 Prospective Cohort	Posterior Partial Fundoplication	25%	70% abnormal	99% abnormal	ND	10	Clinically improved 92%	ND	24% pathological reflux	94%	ND	ND	ND	
	Enrol/Final: 101/87 Age: ~57(70 yrs; 53; 53; 63) grade 1-4 esophagitis Gender: Male 52% Country: Sweden Setting: University Hospital				11% had dysphagia compared to 66% preop 2% new dysphagia Useful surgical procedure except in severe esophagitis									

Appendix C. Evidence Tables

Author, Yr Study design	Intervention Enrolled/ Final Population and study characteristics	Patient characteristics				Follow up /duration (yr)	Status at follow up (P-value compared to preoperative values)						Quality	
		% ≥ grade 3 esophagitis	pH status	EMS /hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/ Others
Henderson, 1985 Prospective Cohort	Open Total Nissen Fundoplication	51%	91.9% +ve status	Lower esophageal sphincter: abnormal 46.2%	ND	6.5	93.1% excellent results	ND	ND	ND	ND	ND	ND	C
	Enrol/Final: 351/335 Age: 45.5 (17-75) Gender: 35% Country: Canada Setting: University hospital			Hiatal hernia: 68.9%										
Grande, 1994 Prospective Cohort	Open Total Nissen Fundoplication	32%	ND (not taken into account for surgery)	ND	0%	20	85% grade 1 and 2 score	ND	ND	85% of meds	ND	89% satisfied and willing for re-surgery	92% success rate in controlling symptoms over the 20yr period from actuarial analysis	B
	Enrol/Final: 160/157 Age: 53±4 Gender: 55% Country: Spain Setting: University hospital			(not taken into account for surgery)										
Luostarinen, 1993	Open Total Nissen Fundoplication	69%	ND	ND	ND	~6	70%	ND	pH status 71% improved	ND	ND	ND	ND	C
	Enrol/Final: 127/72 Age: 48 (22-74) Gender: 57% men Country: Finland Setting: University hospital			ND										

Appendix C. Evidence Tables

Table 7a. Age as modifying factor for outcomes after laparoscopic fundoplication

Author Yr Country Setting Study design	Pre-operative variable assessed Age	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Sex	Excluded \geq grade 3 esophagitis; % \geq grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Khajanchee 2002 USA Private center Ambi-directional case-matched control	71	Nissen 90% Nissen/Collis 3% Toupet 7% 30/30	57% male	23% Stricture 23% Barrett's	Abnl 84 \pm 58		7.6 \pm 7.4 LES mmHg 17% Impaired motility	22 mo	No difference between groups for heartburn, dysphagia, cough, regurgitation, chest pain	ND	No difference between groups for DeMeester scores	No	2 (7%) intermittent meds	No difference between groups for time to normal activities; No difference between groups for SF-36 HRQOL (elderly n=7 vs non-elderly n=8)	No difference between groups for LES	C
	44	Nissen 97% Toupet 3% 30/30	53% male	17% Stricture 17% Barrett's	Abnl 88 \pm 57 DeMeester	Non-responsive	7.0 \pm 4.0 LES mmHg 7% Impaired motility Type II hiatal hernia excluded	19 mo				No	2 (7%) intermittent meds			
Brunt 1999 USA University hospital Prospective cohort	69 (65-82)	Nissen 97% Toupet 3% 36/36	42% male			ND	8.3 \pm 6.3 LES mmHg 1 (3%) dysmotility	27 mo (med)	No difference between groups for heartburn, dysphagia, regurgitation, epigastric/ substernal pain	ND	ND	94%	ND	No difference between groups for time to normal activities	ND	C
	44 (18-64)	Nissen 90% Toupet 10% 303/303	56% male	ND	ND	ND	8.4 \pm 6.0 LES mmHg 31 (10%) dysmotility					ND				

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Author Yr Country Setting Study design	Pre-operative variable assessed Age	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Sex	Excluded \geq grade 3 esophagitis; % \geq grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Stewart 2004 UK Hospital Ambi-directional cohort	44	Anterior partial 55% Nissen 27% Open Nissen 17% 357 (questionnaire)	61% male	ND	ND	ND	ND	3.7 2.3 3.5 yr (med)	No association between symptom level and age	ND	ND	Use of PPI, antacids, & H2RA correlate to DeMeester score $p < 0.001$	ND	68%-77% reported excellent or good results, 7% reported poor results	ND	C
Jackson 2001 USA University hospital Prospective cohort	≤ 50 yr 44(54%) > 50 yr 37(46%)	Nissen 95% Toupet 5% 100/81	54% male	62% esophagitis 22% Barrett's	93% abnl DeMeester	21% with partial or no response to PPI	65% hiatal hernia	15 mo	Good response by Visick score 91%, 9% reported poor response, findings confirmed by GERD- HRQL; ≤ 50 yr predictive of good outcomes $p < 0.021$	ND	ND	ND	ND	12 days to work, 37 days to full physical activity	ND	C

Appendix C. Evidence Tables

Author Yr Country Setting Study design	Pre-operative variable assessed Age	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up							Quality
			Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction	EMS/ others	
Power 2004 UK University hospital Case-control	43	Nissen 131 131	47% male	48% esophagitis 7.6% Barrett's	40 DeMeester	ND	ND	71 mo	117 were free of symptoms; 7 pt with symptom recurrence	ND, 13 of failure group had study	ND, 13 of failure group had study	97% 127/131	ND	ND	Age not predictive of failure (14 pt with symptom recurrence, intractable dysphagia, or short-term AE)	B
O'Boyle 2002 Australia Public hospital Case-control	<40 32% 40-60 48% >60 20% (n=258)	Nissen 262/ 262	63% male	22% no esophagitis 66% moderate esophagitis 11% severe esophagitis (n=218)	13/119 (11%) abnl (>4.4%)	ND	116/246 (47%) hiatal hernia	5 yr	No difference in post- op heartburn scores by age	ND	ND	ND	ND	No difference in post-op satisfaction scores by age	ND	C
Sandbu 2002 Sweden Public hospitals- low vs high volume Amibdirectional cohort	52 54	Low volume Antireflux 220/208 High volume Antireflux 225/200	62% male 60% male	ND	ND	ND	ND	4 yr	Age not correlated to symptoms	ND	ND	89% low vol vs 80% high vol	ND	Age not correlated to patient satisfaction	ND	C

Appendix C. Evidence Tables

Author Yr Country Setting Study design	Pre-operative variable assessed Age	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Horvath 1999 USA Hospital Case-control	50 (30-73)	Toupet 48/48	69% male	~43% gr III or IV; 28% Stricture; 28% Barrett's (Savary-Miller)	Conducted off meds 5 days prior DeMeester	ND	LES 6.8 mmHg	22 mo	ND	ND	ND	ND	ND	ND	Age is not predictive of failure (abnl pH)	C
Blom 2002 USA University hospital Case-control	48 med (15-78)	Nissen 163/103 (preop dysphagia (n=60) excluded from analyses)	73% male	33 (20%) Stricture; 36 (22%) Barrett's (Savary-Miller)	ND Abnl > 14.72 DeMeester	ND	ND	14 mo (med)	Age not factor for dysphagia after surgery	ND	ND	ND	ND	ND	ND	C
Fernando 2003 USA University hospital Retrospective cohort	68 med (60-80)	Nissen 96% Nissen/Collis 4% 43/35	28% male	ND	71	ND	13 LES mmHg	18 mo (med)	No difference between groups for heartburn, dysphagia, cough, regurgitation, chest pain, HRQOL for heartburn	ND	ND	No difference between groups for PPI 17% vs 19% H2RA 9% vs 6% Antacids 14% vs 5%	ND	Time to normal activities similar in both groups; no difference between groups for SF-36 mental & physical	ND	C
	41 med (15-59)	150/102	55% male		69 DeMeester		9.5 LES mmHg	17 mo (med)								
Campos 1999 USA University hospital Prospective cohort	<50 yr (n=102) >50 yr (n=97) (15-77)	Nissen 233/199	70% male	41% erosive esophagitis; 24% Barrett's	86% abnl >14.7 DeMeester	Unknown meds/dose; Rspn to acid suppression therapy: 7% complete 71% partial 17% minor 5% none	75% structurally defective LES; 70% hiatal hernia	15 mo	87% excellent/good & 13% poor symptomatic outcomes; age not factor for outcomes	ND	ND	Unknown number of pts on meds	ND	ND	ND	C

Appendix C. Evidence Tables

Author Yr Country Setting Study design	Pre-operative variable assessed Age	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Sex	Excluded \geq grade 3 esophagitis; % \geq grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Kamolz 2001 Austria Hospital Prospective cohort		Nissen 71% Toupet 29% 72/72	83 (79-95) 68% male	None	61 NI < 17.5 DeMeester	Non-responsive to omeprazole 20-60 mg/day	2.3 LES mmHg 95% hiatal heenia	3 yr	All GERD symptoms resolved	ND	ND	100%	NA	Pt satisfaction 84% excellent, 16% good; 97% would undergo surgery again; GIQLI 120 vs 86 at baseline ↑	ND	B
Bammer 2002 USA Private hospital Retrospective cohort		Nissen (83%) Toupet (17%) 30/28	83 (79- 95) 37% male	13% stricture, 17% Barrett's	64 DeMeester	Non-responsive	7.7 LES mmHg	3.1 yr	96% reported excellent significant improvement for heartburn, dysphagia, cough, regurgitation, chest pain p<0.02 – 0.001	3 had endoscopy – 1 Barrett's surveillance, 2 for dysphagia	ND	19% on PPI or promotility meds	ND	92% satisfied with surgery decision; Well- being score improved significantly p=0.03		C

Appendix C. Evidence Tables

Table 7b. Age as modifying factor for outcomes after endoscopic therapy

Author, Year Study design	Pre-operative risk assessed Age Mean(SD)	Study and patient characteristics					Follow up duration	Status at follow up						Quality	
		Intervention N Enrolled/ Follow up Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI / Off all anti-secretory meds	Other med use data	QOL / satisfaction		EMS / Others
Schumacher 2005 Prospective Cohort	48 yr (14)	ERX 93 76 68%M	Yes	Must have abnormal pH study	Median LES = 10 mm Hg; Excluded hiatal hernia ≥ 3 cm	Yes	12 mo	Heartburn & regurg scores improved compared to off PPI levels (p<0.0001) & improved after treatment to a level similar to on PPI	No change in 55%; improved in 12%; worsened in 33%	28/54 (52%) normalized	65% off PPI at 12 mos;	86% ≥ 50% PPI ↓ dosage at 12 mos (CI 77-93%)	SF-36-P &-SF-36-M improved compared to off PPI levels (p<0.0001 & p=0.0012), GERD-HRQL improved compared to off PPI levels	Median LES = 9 mm (NS); 6 pts retreated between months 1 & 3.	B
Triadafilopoulos 2002 & 2001 Included 9 pts from DiBaise, 2002 Prospective Cohort	47 yr (12)	STR 118 94 61%M	Yes	All have abnormal pH study; median DeMeester off meds = 40	Median LES =15 mm Hg; Excluded >2 cm hiatal hernia	At least partial response to meds	Up to 12 mo	Heartburn score improved compared to baseline off med (p=0.0001)	Esophagitis (grades 1 or 2) present in 31% pre- and 25% post-Rx at 6 mos (NS)	DeMeester = 26.3 (p=0.0001) at 6 mos	At baseline, 88% on PPI, at 12 mos, 30% on PPI (p<0.0001); 40% off all meds	ND	GERD-HRQL improved at 12 mos compared to baseline on meds (p=0.0007); SF-36-P &-M improved (p<0.0001)	At 6 mos, median LES=12.6 (p=0.007)	C

Appendix C. Evidence Tables

Table 8. Sex as modifying factor for outcomes after laparoscopic fundoplication

Author Yr	Pre-operative risk assessed Sex	Intervention Enrolled/ Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH Status	Off PPI/ Off all anti-secretory meds/)	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Stewart 2004	61% male	Anterior partial 55% Nissen 27%ONF 17% 357 (questionnaire)	44	ND	ND	ND	ND	3.7 2.3 3.5 yr (med)	Females had significantly higher level of symptoms: Abdominal pain Diarrhea Indigestion Constipation p=0.043 - 0.001	ND	ND	Use of PPI, antacids, & H2RA correlate to DeMeester score p<0.001	ND	68%-77% reported excellent or good results, 7% reported poor results	Females reported significantly more bloating p=0.001 & inability to vomit p=0.021	C
Sandbu 2002	Low vol hospitals 62% male	Antireflux 220/208	52	ND	ND	ND	ND	4 yr	Sex not correlated to symptoms	ND	ND	89% low vol vs 80% high vol	ND	Sex not correlated to patient satisfaction	ND	C
Sweden Public hospital Ambi-directional cohort	High vol hospitals 60% male	Antireflux 225/200	54													C
Jackson 2001	54% male	Nissen 95% Toupet 5% 100/81	48 (med)	62% esophagitis 22% Barrett's	93% abnl DeMeester	21% with partial or no response to PPI	65% with hiatal hernia	15 mo	Good response by Visick score 91%, 9% reported poor response, findings confirmed by GERD-HRQL; Sex not predictive of outcomes	ND	ND	ND	ND	ND	ND	C
Khajanchee 2004	62% male	Nissen 223/223	51	62% severe esophagitis	93% abnl (off meds) DeMeester (>14.7)	ND	58% hiatal hernia	8.8 mo	89% had reduction or were symptom-free; Sex (?) is risk factor for poor outcomes	ND	9.7% abnl (133/193 asymptomatic tested)	ND	ND	ND	ND	C

Appendix C. Evidence Tables

Author Yr	Pre-operative risk assessed Sex	Intervention Enrolled/ Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age	Excluded \geq grade 3 esophagitis; % \geq grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH Status	Off PPI/ Off all anti-secretory meds/)	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
O'Boyle 2002 Australia Public hospital Case-control	63% male	Nissen 262/ 262	<40 32% 40-60 48% >60 20% (n=258)	22% no esophagitis 66% moderate esophagitis 11% severe esophagitis (n=218)	13/119(11%) abnl	ND	116/246 (47%) hiatal hernia	5 yr	Better heartburn scores associated with males p=0.018	ND	ND	ND	ND	Higher satisfaction score associated with males p=0.015	ND	C
Horvath 1999 USA Hospital Case-control	69% male	Toupet 48/48	50	~43% gr III or IV; 28% Stricture; 28% Barrett's (Savary-Miller)	Conducted off meds 5 days prior DeMeester	ND	LES 6.8 mmHg	22 mo	ND	ND	Sex not factor for abnormal DeMeester score	ND	ND	ND	ND	C
Blom 2002 USA University hospital Case-control	27% female	Nissen 163/103 (preop dysphagia (n=60) excluded from analyses)	48 med (15-78)	33 (20%) Stricture; 36 (22%) Barrett's (Savary-Miller)	ND Abnl > 14.72) DeMeester	ND	ND	14 mo (med)	Female sex not factor for postop dysphagia	ND	ND	ND	ND	ND	ND	C
Campos 1999 USA University hospital Prospective cohort	70% male	Nissen 199/199	49 med (15-77)	41% erosive esophagitis; 24% Barrett's	86% (abnl >14.7, off meds) DeMeester	Unknown meds/dose; response to acid suppression therapy: 7% complete 71% partial 17% minor 5% none	75% structurally defective LES; 70% hiatal hernia	15 mo	87% excellent/good & 13% poor symptomatic outcomes; sex not factor for outcomes	ND	ND	Unknown number of pts on meds	ND	ND	ND	C

Appendix C. Evidence Tables

Table 9. Preoperative esophagitis as a modifying factor for surgical, or endoscopic treatment outcome

Author, Year	Preop Factor(s) Assessed	Intervention Enrolled/Final	Patient characteristics				Follow up duration	Status at follow up						Quality	
			Excluded ≥ grade 3 esophagitis ; % ≥grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/Others
Desai, 2003 case control	Esophagitis	LNF or LPA 597 414	58% ≥grade 3	mean DeMeester score was abnormal (unknown if on/off meds)	ND	ND	range: 6-109 mo	Dysphagia: Factor: 25% No Factor: 14% p<.05 No difference in overall symptomatic improvement No difference in rates of any symptom assessed ²	ND	ND	No difference in rates of patients off all meds No difference in rates of patients off PPIs	ND	No difference in % satisfied	No difference in rates of reoperation	C
O'Boyle, 2002 case control	Esophagitis	ONF 262 262	~77% ≥grade 3	11% had abnormal % time at low pH (unknown if on/off meds)	47% had hiatal hernia	ND	5 yr	No difference in heartburn or dysphagia scores	ND	ND	ND	ND	No difference in satisfaction score	ND	C

Appendix C. Evidence Tables

C-35	Campos, 1999 prospective cohort	Esophagitis	LNF 233 199	ND	85% had abnormal DeMeester score (off meds)	75% had incompetent LES, 70% had hiatal hernia	78%	median: 15 mo	ND	ND	ND	No difference in rates of patients off all meds ¹	ND	ND	ND	B
	Power 2004 case control	Esophagitis	LNF 131 131	11% ≥grade 3	mean % time at low pH: 25% (unknown if on/off meds)	ND	ND	mean: 70.6 mo	No difference in rates of GER symptoms or dysphagia ¹	ND	ND	ND	ND	ND	ND	B
	Blom, 2002 case control	Esophagitis	LNF 163 103	ND	100% had abnormal DeMeester score (unknown if on/off meds)	ND	ND	median: 14 mo	No difference in rates of dysphagia	ND	ND	ND	ND	ND	ND	C
	Jackson, 2001 prospective cohort	Esophagitis	LNF or LPA 100 81	≥22% ≥grade 3	93% had abnormal DeMeester score (unknown if on/off meds)	74% had structurally defective LES, 65% had hiatal hernia	79%	average: 15 mo	No difference in Visick grade ¹	ND	ND	ND	ND	ND	ND	B

Appendix C. Evidence Tables

Triadafilopoulos, 2002 Prospective Cohort	Esophagitis	STR 118 94	Excluded ≥grade 3	100% had abnormal pH study; median DeMeester = 40 (off meds)	Median LES = 15 mm Hg; Excluded >2 cm hiatal hernia	100% had at least partial response to meds	Up to 12 mo	No difference in heartburn score	ND	No difference in % time at low pH	No difference in rates of patients off PPIs or off all meds	ND	ND	ND	C
Schumacher, 2005 Prospective Cohort	Esophagitis	ERX 93 76	Excluded ≥grade 3	100% had abnormal pH study (off meds)	Median LES = 10 mm Hg; Excluded hiatal hernia ≥ 3 cm	100%	12 mo	No difference in heartburn or regurgitation scores	No difference in changes in esophagitis severity	No difference in pH status	No difference in rates of patients off PPIs	No difference in rates of ↓PPI dose	No difference in SF-36 or GERD-HRQL scores	No difference in LES pressures	B
Cohen, 2005 Prospective Cohort	Esophagitis	ERX 144 64	Included 1 pt with ≥ grade 3	100% had abnormal pH study (unknown if on/off meds)	Included 12 pts with hiatal hernia ≥ 3 cm	100%	Up to 24 mo					No difference in rates of ↓PPI dose ^{1,4}			C
Khajanchee, 2004 case control	Esophagitis grade	ONF 223 223	ND	93% had abnormal DeMeester score (off meds)	58% had hiatal hernia	ND	median: 8.8 mo	No difference in rates of heartburn/regurgitation ≥1x/wk ¹	ND	ND	ND	ND	ND	ND	B
Deviere, 2005 RCT	Esophagitis grade	ERX 32 31	Excluded ≥grade 3	100% had pH study (off PPI)	Excluded hiatal hernia ≥ 5 cm	100%	3 mos	ND	ND	ND	ND	No difference in rates of PPI reduction ≥ 50% pre-endo dose	ND	ND	B

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Appendix C. Evidence Tables

Bell, 1999 case control	Grade 2-4 esophagitis	LPA 143 138	≥ 36% ≥grade 3	mean DeMeester score abnormal (off meds)	ND	ND	mean: 30 mo	No difference in rates of dysphagia ¹	ND	ND	ND	ND	ND	ND	C
Horvath, 1999 case control	Grade 3-4 Esophagitis	LPA 48 39	≥~40% ≥grade 3	mean DeMeester score was abnormal (off meds)	~48% had low LES pressure (<5mmHg), 63% had hiatal hernia	ND	mean: 22 mo	ND	ND	Abnormal DeMeester score: Factor: 16/21 (76%) No Factor³: 6/27 (22%) p<.05¹	ND	ND	ND	ND	C
Blom, 2002 case control	Stricture	LNF 163 103	ND	100% had abnormal DeMeester score (unknown if on/off meds)	ND	ND	median: 14 mo	No difference in rates of dysphagia	ND	ND	ND	ND	ND	ND	C
Horvath, 1999 case control	Stricture	LPA 48 39	≥~40% ≥grade 3	mean DeMeester score was abnormal (off meds)	~48% had low LES pressure (<5mmHg), 63% had hiatal hernia	ND	mean: 22 mo	ND	ND	No difference in rates of abnormal DeMeester score ¹	ND	ND	ND	ND	C

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Appendix C. Evidence Tables

Jackson, 2001 prospective cohort	Barrett's esophagus	LNF or LPA 100 81	≥22% ≥grade 3	93% had abnormal DeMeester score (unknown if on/off meds)	74% had structurally defective LES, 65% had hiatal hernia	79%	average: 15 mo	No difference in Visick grade ¹	ND	ND	ND	ND	ND	ND	B
Horvath, 1999 case control	Barrett's esophagus	LPA 48 48	≥~40% ≥grade 3	mean DeMeester score was abnormal (off meds)	~48% had low LES pressure (<5mmHg), 63% had hiatal hernia	ND	mean: 22 mo	ND	ND	No difference in rates of abnormal JD score ¹	ND	ND	ND	ND	C
Blom, 2002 case control	Length of Barrett's esophagus (continuous)	LNF 163 103	ND	100% had abnormal DeMeester score (unknown if on/off meds)	ND	ND	median: 14 mo	No difference in rates of dysphagia	ND	ND	ND	ND	ND	ND	C

¹ Significance adjusted for covariates

² Symptoms assessed were: heartburn, regurgitation, water brash, nocturnal aspiration, chest pain, bloating and ability to belch

³ Factor and No Factor: patients with and without the preoperative modifying factor assessed in the study

⁴ Outcome for multivariate analysis not explicitly stated, but assumed to be the primary outcome of the study, >50% reduction in PPI use from baseline

Appendix C. Evidence Tables

Table 10. Preoperative esophageal pH status as a modifying factor for medical, surgical, or endoscopic treatment outcome

Author, Yr Study design	Preop Factor(s) Assessed ²	Intervention Enrolled/ Final	Patient characteristics				Follow up duration	Status at follow up						Quality	
			Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ Others
O'Boyle, 2002 case control	Abnormal % time at low pH ³	ONF 262 262	~77% ≥grade 3	11% had abnormal % time at low pH (unknown if on/off meds)	47% had hiatal hernia	ND	5 yr	Heartburn score: Factor: 2 No factor ⁴ : 3 p<.01 Dysphagia score: Factor: 2 No factor ⁴ : 5 p=.002	ND	ND	ND	ND	Satisfaction score: Factor: 8 No factor ⁴ : 5 P<.001	ND	C
Campos, 1999 prospective cohort	% time at low pH ³ (continuous)	LNF 233 199	ND	78% had abnormal % time at low pH (off meds)	75% had incompetent LES, 70% had hiatal hernia	78%	median: 15 mo	ND	ND	ND	No difference in rates patients were off all meds ¹	ND	ND	ND	B
Anvari, 2003 prospective cohort	% time at low pH ³ (continuous)	LNF 332 181	ND	Mean % time at low pH: 8% (off meds)	Mean LES pressure: 7.2 mmHg	36%	5 yr	No difference in GERD symptom score P=.67 ¹	ND	ND	ND	ND	ND	ND	B
Power, 2004 case control	% time at low pH ³ (continuous)	LNF 131 131	11% ≥grade 3	mean % time at low pH: 25% (unknown if on/off meds)	ND	ND	mean: 70.6 mo	No difference in rates of GER symptoms/dysphagia ¹	ND	ND	ND	ND	ND	ND	B
Triadafilopoulos, 2002 Prospective Cohort	% time at low pH ³ (continuous)	STR 118 94	Excluded ≥grade 3	100% had abnormal pH study; median DeMeester = 40 (off meds)	Median LES =15 mm Hg; Excluded >2 cm hiatal hernia	100% had at least partial response to meds	Up to 12 mo	No difference in heartburn score	ND	No difference in % time at low pH ³	No difference in rates of patients off PPIs or off all meds	ND	ND	ND	C

Appendix C. Evidence Tables

Author, Yr Study design	Preop Factor(s) Assessed ²	Intervention Enrolled/ Final	Patient characteristics				Follow up duration	Status at follow up						Quality	
			Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hialatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ Others
Topart, 1999 case control	% time at low pH ³ (continuous)	LNF, LPA, ONF or OPA 88 88	26% ≥grade 3	mean % time at low pH: 20.6% (unknown if on/off meds)	mean LES pressure: 9.5 mmHg, 76% had hialatal hernia	ND	Mean: 30.6 mo	ND	ND	ND	ND	ND	ND	No difference in symptoms with esophagitis and/or hialatal hernia	B
Costantini, 1996 non-randomized controlled trial	% time at low pH ³ (continuous)	H2RA or OME 55 55	≤24% ≥grade 3	100% had abnormal DeMeester score (off meds)	34% had defective LES	Not applicable	median: 31 mo	ND	ND	ND	No difference in rates of patients off all meds	ND	ND	ND	B
Deviere, 2005 RCT	% time at low pH ³ (continuous)	ERX 32 31	Excluded ≥grade 3	100% had pH study (off PPI)	Excluded hialatal hernia ≥ 5 cm	100%	3 mos	ND	ND	ND	ND	No difference in rates of PPI reduction ≥ 50% pre-endo dose	ND	ND	B
Power, 2004 case control	% supine time at low pH ³ (continuous)	LNF 131 131	11% ≥grade 3	mean % time at low pH: 25% (unknown if on/off meds)	ND	ND	mean: 70.6 mo	No difference in rates of GER symptoms/ dysphagia ¹	ND	ND	ND	ND	ND	ND	B
Costantini, 1996 non-randomized controlled trial	% supine time at low pH ³ (continuous)	H2RA or OME 55 55	≤24% ≥grade 3	100% had abnormal DeMeester score (off meds)	34% had defective LES	Not applicable	median: 31 mo	ND	ND	ND	No difference in rates of patients off all meds	ND	ND	ND	B

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Appendix C. Evidence Tables

Author, Yr Study design	Preop Factor(s) Assessed ²	Intervention Enrolled/ Final	Patient characteristics				Follow up duration	Status at follow up							Quality	
			Excluded \geq grade 3 esophagitis; \geq grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	\downarrow PPI dose or now responds to dose that failed before Rx	QOL/satisfaction	EMS/Others		
Power, 2004 case control	% upright time at low pH ³ (continuous)	LNF 131 131	11% \geq grade 3	mean % time at low pH: 25% (unknown if on/off meds)	ND	ND	mean: 70.6 mo	\uparrow Factor ⁴ associated with \uparrow GER symptoms/dysphagia p=.04 ¹	ND	ND	ND	ND	ND	ND	ND	B
Costantini, 1996 non-randomized controlled trial	% upright time at low pH ³ (continuous)	H2RA or OME 55 55	\leq 24% \geq grade 3	100% had abnormal DeMeester score (off meds)	34% had defective LES	Not applicable	median: 31 mo	ND	ND	ND	No difference in rates of patients off all meds	ND	ND	ND	ND	B
Khajanchee, 2004 case control	Abnormal DeMeester score (>14.7)	ONF 223 223	ND	93% had abnormal DeMeester score (off meds)	58% had hiatal hernia	ND	median: 8.8 mo	Heartburn/regurgitation \geq 1x/wk: <u>Factor:</u> 17/208 (8%) <u>No factor</u> ⁴ : 6/15 (40%) p<.05 ¹	ND	ND	ND	ND	ND	ND	ND	B
Campos, 1999 prospective cohort	DeMeester score (continuous)	LNF 233 199	ND	85% had abnormal DeMeester score (off meds)	75% had incompetent LES, 70% had hiatal hernia	78%	median: 15 mo	ND	ND	ND	<u>Off all meds:</u> <u>Factor:</u> 154/170 (91%) <u>No factor</u> ⁴ : 19/29 (66%) p<.001 ¹	ND	ND	ND	ND	B
Power, 2004 case control	DeMeester score (continuous)	LNF 131 131	11% \geq grade 3	mean % time at low pH: 25% (unknown if on/off meds)	ND	ND	mean: 70.6 mo	No difference in rates of GER symptoms/dysphagia ¹	ND	ND	ND	ND	ND	ND	ND	B

Appendix C. Evidence Tables

Author, Yr Study design	Preop Factor(s) Assessed ²	Intervention Enrolled/ Final	Patient characteristics				Follow up duration	Status at follow up							Quality
			Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/hialal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction	EMS/Others	
Blom, 2002 case control	DeMeester score (continuous)	LNF 163 103	ND	100% had abnormal DeMeester score (unknown if on/off meds)	ND	ND	median: 14 mo	No difference in rates of dysphagia	ND	ND	ND	ND	ND	ND	C
Jackson, 2001 prospective cohort	DeMeester score (continuous)	LNF or LPA 100 81	≥22% ≥grade 3	93% had abnormal DeMeester score (unknown if on/off meds)	74% had structurally defective LES, 65% had hiatal hernia	79%	avg: 15 mo	No difference in Visick grade ¹	ND	ND	ND	ND	ND	ND	B
Horvath, 1999 case control	DeMeester score (continuous)	LPA 48 39	≥~40% ≥grade 3	mean DeMeester score was abnormal (off meds)	~48% had low LES pressure (<5 mmHg), 63% had hiatal hernia	ND	mean: 22 mo	ND	ND	↑Factor ⁴ associated with ↑DeMeester score p<.05 ¹	ND	ND	ND	ND	B
Cohen, 2005 Prospective Cohort	"esophageal acid exposure"	ERX 144 64	Included 1 pt with ≥ grade 3	100% had abnormal pH study (unknown if on/off meds)	Included 12 pts with hiatal hernia ≥ 3 cm	100%	Up to 24 mo					No difference in rates of ↓PPI dose ⁵			C

¹ Significance adjusted for covariates

² Unless otherwise indicated, all pH studies were performed for 24 hours.

³ Low pH is defined as < 4 by virtually all studies. An abnormal percentage of time spent at low pH is defined as 4.4% by virtually all studies

⁴ Factor and No Factor: patients with and without the preoperative modifying factor assessed in the study

⁵ Outcome for multivariate analysis not explicitly stated, but assumed to be the primary outcome of the study, >50% reduction in PPI use from baseline

Appendix C. Evidence Tables

Table 11. Preoperative esophageal manometric status as a modifying factor for medical, surgical or endoscopic treatment outcome

Author, Yr Study design	Preop Factor(s) Assessed	Intervention Enrolled/ Final	Patient characteristics				Follow up duration	Status at follow up							Quality
			Excluded \geq grade 3 esophagitis; % \geq grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	\downarrow PPI dose or now responds to dose that failed before Rx	QOL/satisfaction	EMS/Others	
LOWER ESOPHAGEAL SPHINCTER (LES) INCOMPETENCE²															
Campos, 1999 prospective cohort	Incompetent LES	LNF 233 199	ND	78% had abnormal % time at low pH, 85% had abnormal DeMeester score (off meds)	75% had incompetent LES, 70% had hiatal hernia	78%	median: 15 mo	ND	ND	ND	No difference in rates of patients off all meds ¹	ND	ND	ND	B
Bell, 1999 case control	Incompetent LES	LPA 143 138	$\geq 36\%$ \geq grade 3	mean DeMeester score abnormal (off meds)	ND	ND	mean: 30 mo	No difference in rates of dysphagia	ND	ND	ND	ND	ND	ND	C
Ritter, 1998 prospective cohort	Incompetent LES	LNF 123 103	ND	100% with abnormal % time at low pH (unknown if on/off meds)	68% had structurally defective LES	ND	median: 18 mo	No difference in severity of GER Symptoms/dysphagia	ND	ND	ND	ND	ND	ND	C
ESOPHAGEAL SEGMENTS LENGTH															
Yau, 2000 prospective cohort	Esophageal length (continuous)	LAS 774 484	26% \geq grade 3	ND	52% had hiatal hernia	ND	median: 2 yr	ND	ND	ND	ND	ND	ND	No difference in overall rates of reoperation	B
Blom, 2002 case control	Esophageal length: monometric, total and abdominal (all continuous)	LNF 163 103	ND	100% had abnormal DeMeester score (unknown if on/off meds)	ND	ND	median: 14 mo	No difference in rates of dysphagia for any of the factor factors	ND	ND	ND	ND	ND	ND	C

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Khajanchee, 2004 case control	total LES length (continuous)	ONF 223 223	ND	93% had abnormal DeMeester score (off meds)	58% had hiatal hernia	ND	median: 8.8 mo	No difference in rates of heartburn/regurgitation $\geq 1x/wk^1$	ND	ND	ND	ND	ND	ND	B
LOWER ESOPHAGEAL SPHINCTER (LES) PRESSURE															
Horvath, 1999 case control	low LES pressure (<5 mmHg)	LPA 48 39	$\geq \sim 40\%$ \geq grade 3	mean DeMeester score was abnormal (off meds)	$\sim 48\%$ had low LES pressure (<5 mmHg), 63% had hiatal hernia	ND	mean: 22 mo	ND	ND	abnormal DeMeester score: <u>Factor:</u> $\sim 16/24$ (67%) <u>No factor²:</u> $\sim 8/24$ (33%) $p < .05^1$	ND	ND	ND	ND	B
Costantini, 1996 non-randomized controlled trial	defective LES ³	H2RA or OME 55 55	$\leq 24\%$ \geq grade 3	100% had abnormal DeMeester score (off meds)	34% had defective LES ³	Not applicable	median: 31 mo	ND	ND	Off all meds: <u>Factor:</u> $1/14$ (7%) <u>No factor²:</u> $13/27$ (48%) $p < .05$	ND	ND	ND	ND	B
Patti, 2003 retrospective cohort	LES pressure	LNF or LPA 520 280	30% \geq grade 3	mean reflux score was abnormal (off meds)	61% had hiatal hernia	ND	avg: 17 mos	NS difference in heartburn, regurgitation or dysphagia							C
Khajanchee, 2004 case control	LES pressure (continuous)	ONF 223 223	ND	93% had abnormal DeMeester score (off meds)	58% had hiatal hernia	ND	median: 8.8 mo	No difference in rates of heartburn/regurgitation $\geq 1x/wk^1$	ND	ND	ND	ND	ND	ND	B
Anvari, 2003 prospective cohort	LES pressure (continuous)	LNF 332 181	ND	mean % time at low pH: 8.4 (off meds)	Mean LES pressure: 7.2 mmHg	36%	5 yr	No difference in GERD symptom score ¹	ND	ND	ND	ND	ND	ND	B
Power, 2004 case control	LES pressure (continuous)	LNF 131 131	11% \geq grade 3	mean % time at low pH: 25% (unknown if on/off meds)	ND	ND	mean: 70.6 mo	No difference in rates of GER symptoms/dysphagia ¹	ND	ND	ND	ND	ND	ND	B

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Blom, 2002 case control	LES pressure (continuous)	LNF 163 103	ND	100% had abnormal DeMeester score (unknown if on/off meds)	ND	ND	median: 14 mo	↑Factor ⁷ associated with ↑dysphagia p=.004	ND	ND	ND	ND	ND	ND	C
Triadafilopoulos, 2002 Prospective Cohort	LES pressure (continuous)	STR 118 94	Excluded ≥grade 3	100% had abnormal pH study; median DeMeester = 40 (off meds)	Median LES =15 mm Hg; Excluded >2 cm hiatal hernia	100% had at least partial response to meds	Up to 12 mo	No difference in heartburn score	ND	No difference in % time at low pH	No difference in rates of patients off PPIs or off all meds	ND	ND	ND	C
Topart, 1999 case control	LES pressure (continuous)	ARS 88 88	26% ≥grade 3	mean % time at low pH: 20.6% (unknown if on/off meds)	mean LES pressure: 9.5 mmHg, 76% had hiatal hernia	ND	mean: 30.6 mo	ND	ND	ND	ND	ND	ND	No difference in symptoms with esophagitis and/or hiatal hernia	B
DISORDERED ESOPHAGEAL MOTILITY															
Booth, 2002 prospective cohort	Esophageal hypomotility (Castell criteria)	LNF 117 117	ND	100% had abnormal % time at low pH (off meds)	43% had hiatal hernia	ND	1 yr	No difference in dysphagia scores No difference in DeMeester Symptom Scores	ND	No difference in % time at low pH	ND	ND	ND	No difference in LES pressure Dilation/ Re-operation: <u>Factor</u> : 0/35 (0%) <u>No factor</u> ² : 10/82 (12%) p=.03	A
Triadafilopoulos, 2002 Prospective Cohort	Amplitude of contractions (continuous)	STR 118 94	Excluded ≥grade 3	100% had abnormal pH study; median DeMeester = 40 (off meds)	Median LES =15 mm Hg; Excluded >2 cm hiatal hernia	100% had at least partial response to meds	Up to 12 mo	No difference in heartburn score	ND	No difference in % time at low pH	No difference in rates of patients off PPIs or off all meds	ND	ND	ND	C

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Costantini, 1996 non-randomized controlled trial	Amplitude of contractions (continuous)	H2RA or OME 55 55	≤24% ≥grade 3	100% had abnormal DeMeester score (off meds)	34% had defective LES ³	Not applicable	median: 31 mo	ND	ND	ND	No difference in rates of patients off all meds	ND	ND	ND	B
Horvath, 1999 case control	Esophageal hypomotility, dysmotility, low distal wave amplitude (<30 mmHg) ⁴	LPA 48 39	≥~40% ≥grade 3	mean DeMeester score was abnormal (off meds)	~48% had low LES pressure (<5 mmHg), 63% had hiatal hernia	ND	mean: 22 mo	ND	ND	No difference in rates of abnormal DeMeester score for any of the factor factors ¹	ND	ND	ND	ND	B
Jackson, 2001 prospective cohort	low distal wave amplitude (<30 mmHg)	LAS 100 81	≥22% ≥grade 3	93% had abnormal DeMeester score (unknown if on/off meds)	74% had incompetent LES, 65% had hiatal hernia	79%	mean: 15 mo	No difference in Visick grade ¹	ND	ND	ND	ND	ND	ND	B
Winslow, 2003 prospective cohort	High distal wave amplitude (>71 mmHg)	LAS 168 124	≥ 23% ≥grade 3	mean DeMeester score was abnormal (unknown if on/off meds)	59% had hiatal hernia	ND	mean: 18.4 mo	No difference in rates of heartburn/ regurgitation	ND	ND	ND	ND	ND	ND	C
Winslow, 2003 prospective cohort	Nonspecific spastic disorder ⁵	LAS 168 124	≥ 23% ≥grade 3	mean DeMeester score was abnormal (unknown if on/off meds)	59% had hiatal hernia	ND	mean: 18.4 mo	Heartburn/ regurgitation: Factor: 25% No factor ² : 7% p=.012	ND	ND	Off all meds: Factor: 81% No factor ² : 95% p=.014	ND	No difference in change in overall health	ND	C
MISCELLANEOUS															
Blom, 2002 case control	Competent LES	LNF 163 103	ND	100% had abnormal DeMeester score (unknown if on/off meds)	ND	ND	median: 14 mo	Dysphagia: Factor: 3/80 (4%) No factor ² : 5/23 (22%) p=.01	ND	ND	ND	ND	ND	ND	C

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Klaus, 2003 open, single-arm trial	Defective LES and impaired peristalsis ⁶	OME	excluded ≥grade 3	median DeMeester score was abnormal (off meds)	80% had defective LES	No history of med use	1 yr	ND	ND	ND	ND	ND	Symptoms +/- esophagitis: <u>Normal LES/peristalsis:</u> 8% <u>Defective LES + Normal peristalsis:</u> 38% <u>Defective LES/peristalsis:</u> 80% p<.05	ND	C
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¹ Significance adjusted for covariates

² Incompetent LES is defined by: LES length < 2cm, intra-abdominal length < 1cm and/or LES resting pressure criteria. In studies by Campos, 1999 and Ritter, 1998 the LES pressure criteria is < 6mmHg. In the study by Bell, 1999 the criteria is <10 mmHg

³ Defective LES was defined as an LES vector volume (calculated by Bombeck criteria) <5% below normal controls

⁴ Esophageal hypomotility was defined as contraction amplitudes <30 mmHg at 2 or more levels. Dysmotility was defined as the presence of >60% tertiary or simultaneous contractions or >60% dropped peristalses.

⁵ Nonspecific spastic disorder is defined as any one or a combination of the following: high distal wave amplitude, prolonged distal wave duration, excessive double peaked waves or any triple peaked waves

⁶ Defective LES was defined as resting pressure <9 mmHg. Impaired peristalsis was defined as defective contraction waves ≤ 20%

⁷ Factor and No Factor: patients with and without the preoperative modifying factor assessed in the study

Appendix C. Evidence Tables

Table 12. Preoperative presence of hiatal hernia as a modifying factor for surgical or endoscopic treatment outcome

Author, Yr Study design	Preop Factor(s) Assessed	Intervention Enrolled/ Final	Patient characteristics				Follow up duration	Status at follow up						Quality	
			Excluded \geq grade 3 esophagitis ; % \geq grade 3	pH status	EMS/hiatal hernia	Responded to PPI or H2RA		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/Others
O'Boyle, 2002 case control	hiatal hernia	ONF 262 262	~77% \geq grade 3	11% had abnormal % time at low pH (unknown if on/off meds)	47% had hiatal hernia	ND	5 yr	No difference in heartburn or dysphagia scores ¹	ND	ND	ND	ND	No difference in satisfaction score ¹	ND	C
Khajanchee, 2004 case control	hiatal hernia, excluded para-esophageal (type 2 or 3) hernias	ONF 223 223	ND	93% had abnormal DeMeester score (off meds)	58% had hiatal hernia	ND	median: 8.8 mo	No difference in symptom score ¹	ND	ND	ND	ND	ND	ND	B
Campos, 1999 prospective cohort	hiatal hernia >2cm, excluded para-esophageal hernias	LNF 233 199	ND	78% had abnormal % time at low pH, 85% had abnormal DeMeester score (off meds)	75% had incompetent LES, 70% had hiatal hernia	78%	median: 15 mo	ND	ND	ND	No difference in rates of patients off all meds ¹	ND	ND	ND	B
Power, 2004 case control	hiatal hernia >3cm	LNF 131 131	11% \geq grade 3	mean % time at low pH: 25% (unknown if on/off meds)	ND	ND	mean: 70.6 mo	Factor ³ associated with \uparrow GERD symptoms/dysphagia P=.003 ¹	ND	ND	ND	ND	ND	ND	B
Blom, 2002 case control	hiatal hernia >2 cm	LNF 163 103	ND	100% had abnormal DeMeester score (unknown if on/off meds)	ND	ND	median: 14 mo	No difference in rates of dysphagia by presence or size of hernia	ND	ND	ND	ND	ND	ND	B

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Jackson, 2001 prospective cohort	hiatal hernia	LNF or LPA 100 81	≥22% ≥grade 3	93% had abnormal DeMeester score (unknown if on/off meds)	74% had structurally defective LES, 65% had hiatal hernia	79%	avg: 15 mo	No difference in Visick grade ¹	ND	ND	ND	ND	ND	ND	B
Cohen, 2005 Prospective Cohort	hiatal hernia	ERX 144 64	Included 1 pt with ≥ grade 3	100% had abnormal pH study (unknown if on/off meds)	Included 12 pts with hiatal hernia ≥ 3 cm	100%	up to 24 mo	ND	ND	ND	ND	No difference in rates of ↓PPI dose ^{1,2}	ND	ND	C
Horvath, 1999 case control	hiatal hernia, excluded para-esophageal hernias	LPA 48 48	≥~40% ≥grade 3	mean DeMeester score was abnormal (off meds)	~48% had low LES pressure (<5 mmHg), 63% had hiatal hernia	ND	mean: 22 mo	ND	ND	No difference in rates of abnormal DeMeester score	ND	ND	ND	ND	B
Deviere, 2005 RCT	hiatal hernia <5cm	ERX 32 31	Excluded ≥grade 3	100% had pH study (off PPI)	Excluded hiatal hernia ≥ 5 cm	100%	3 mo	ND	ND	ND	ND	No difference in rates of PPI reduction ≥ 50% pre-endo dose	ND	ND	B

¹ Significance adjusted for covariates

² Outcome for multivariate analysis not explicitly stated, but assumed to be the primary outcome of the study, >50% reduction in PPI use from baseline

Appendix C. Evidence Tables

Table 13. Patient response to anti-secretory medications as modifying factor for outcomes after laparoscopic fundoplication

Author Yr	Pre-operative variable assessed	Intervention	Baseline patient characteristics				Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH normalized	Off PPI/ Off all anti-secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Power 2004 UK University hospital Case-control	ND	Nissen 131/ 131	43 47% male	48% esophagitis 7.6% Barrett's	40 DeMeester PH study not required if severe esophagitis & rspn to PPI	Unknown # of hiatal hernia > 3 cm	71 mo	117 were free of symptoms, 7 pt with symptom recurrence	ND, 13/14 in failed group had study	ND, 13/14 in failed group had study	97% 127/131	ND	ND	Non-response to preop PPI were predictive of surgical failure p<0.001	B
Anvari 2003 Canada Hospital Cohort	All on PPI; 120 (36%) had adequate control to PPI up to 120 mg/day	Nissen 332/ 181	47 38% male	ND	ND; obtained off meds 5 day prior; reflux criteria pH<4	7.2 LES mmHg hiatal hernia: 36(11%) > 3 cm 16(4.8%) >7 cm 8 pts with >50% stomach herniated through hiatus	5 yr	Improved symptom score - scores obtained off meds; responders to PPI tx correlated to symptomatic response to surgery p=0.004	ND	9 (5%) had abnl pH	21 (12%) back on anti-secretory meds for heartburn or dyspepsia	ND	86% satisfied, but 89% would undergo surgery again; no difference in satisfaction between responders & non-responders	Hernia reduced successfully for all cases	C

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Author Yr	Pre-operative variable assessed	Intervention	Baseline patient characteristics				Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH normalized	Off PPI/ Off all anti-secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Jackson 2001 USA University hospital Prospective cohort	79% complete response, 21% with partial or no response to PPI	Nissen 95% Toupet 5% 100/81	48 (med) 54% male	62% esophagitis 22% Barrett's	93% abnl DeMeester	65% with hiatal hernia	15 mo	Good response by Visick score 91%, 9% reported poor response	ND	ND	ND	ND	12 days - return to work, 37 days - full physical activity; GERD-HRQL scores highly associated with Visick grade p<0.00001	Complete response to acid suppression tx associated with good outcomes (Visick score) p<0.0007	C
Campos 1999 USA University hospital Prospective cohort	Response to acid suppression therapy: 71% complete 17% partial 5% none Unknown meds/dose	Nissen 199/199	49 med (15-77) 70% male	41% erosive esophagitis; 24% Barrett's	86% (abnl >14.7, off meds) DeMeester	75% structurally defective LES; 70% hiatal hernia	15 mo	87% excellent/good & 13% poor symptomatic outcomes; response vs no response to therapy is factor for successful outcomes, 92% vs 68% p=0.00008	ND	ND	Unknown number of pts on meds	ND	ND	ND	C

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Appendix C. Evidence Tables

Table 14. Patient symptoms as modifying factor for outcomes after laparoscopic fundoplication

Author Yr Country Setting Study design	Pre-operative risk assessed Symptoms	Intervention Enrolled/ Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded \geq grade 3 esophagiti s; $\% \geq$ grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretor y meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfactio n		EMS/ others
Ritter 1998 USA University hospital Prospective cohort	85% typical symptoms (heartburn, regurgitation, dysphagia); 15% atypical (cough, asthma, chest pain, & other complaint)	Nissen 123/103	49 74% male	ND	ND	ND	68% structurally defective LES	18 mo (med)	Symptomatic outcomes rated excellent /good in 90%, fair/poor in 10%; pts w/typical vs atypical symptoms had significantly better symptomatic outcomes	ND	ND	Unknown number of pts on meds	ND	ND	ND	C

Appendix C. Evidence Tables

Author Yr Country Setting Study design	Pre-operative risk assessed Symptoms	Intervention Enrolled/ Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagiti s; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretor y meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfactio n		EMS/ others
Power 2004 UK University hospital Case-control	Graph data: ~88% heartburn ~30% regurgitation ~40% foregut flatulence ~25% vomiting ~15% dysphagia ~7% respiratory compromise	Nissen 131/ 131	43 47% male	48% esophagitis, 7.6% Barrett's	40 DeMeester PH study not required if severe esophag itis & rspn to PPI	ND	Unknown # of hiatal hernia > 3 cm	71 mo	117 were free of symptoms; 7 pt with symptom recurrence	ND, 13/14 in failed group had study	ND, 13/14 in failed group had study	97% 127/131	ND	ND	Prepsy mptoms of heartbur n or dysphag ia not predictiv e of treatmen t failure	B

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Author Yr	Pre-operative risk assessed Symptoms	Intervention Enrolled/ Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Anvari 2003 Canada Hospital Cohort	Graph data: ~40 symptom score for heartburn, regurgitation, bloating, dysphagia, epigastric or retrosternal pain, cough Scores obtained on & off meds	Nissen 332 181	47 38% male	ND	Study conducted off meds 5 day prior; reflux criteria pH<4	All on PPI; 120 (36%) had adequate control to PPI up to 120 mg/day	7.2 LES mmHg Hiatal hernia: 36(11%) > 3 cm 16(4.8%) >7 cm 8 pts with >50% stomach herniated through hiatus	5 yrs	21 had recurrence of heartburn or dyspepsia; Severe preop GERD symptom score correlated well to symptomatic response to surgery p<0.001	ND	9 (5%) had abnl pH	21 (12%) back on anti-secretory meds for heartburn or dyspepsia	ND	86% satisfied, but 89% would undergo surgery again	Hernia reduced for all pts	C
Jackson 2001 USA University hospital Prospective cohort	76 (94%) typical symptoms (heartburn, regurgitation); 63 (78%) atypical symptoms (hoarseness, cough, respiratory complaints)	Nissen 95% Toupet 5% 100/81	48 (med) 54% male	62% esophagitis 22% Barrett's	93% abnl DeMeester	21% with partial or no response to PPI	65% with hiatal hernia	15 mo	Good response by Visick score 91%, 9% reported poor response; typical symptoms associated with good outcomes p<0.002	ND	ND	ND	ND	12 days to work, 37 days to full physical activity; GERD-HRQL scores highly associated with Visick grade p<0.00001	ND	C

Appendix C. Evidence Tables

Author Yr	Pre-operative risk assessed Symptoms	Intervention Enrolled/ Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded \geq grade 3 esophagitis; % \geq grade 3	pH status	Responded to PPI or H2RA	EMS/Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/others
Bell 1999 USA Hospital Case-control	Visick symptom scale	Toupet 143/138	ND ND	ND	Study conducted off meds (n=80) DeMeester	36 PPI > 8 wk, 22 unkn meds or duration, 14 no meds	ND	ND "pts seen up to 3 mo & every 6 mo"	21 failures (15%): 19 with recurrent symptoms, 2 had dysphagia	ND	ND	ND	1 pt responding with PPI	ND	Heartburn, reflux, dysphagia not predictor for success/failure	C
Horvath 1999 USA Hospital Case-control	Heartburn Dysphagia Pulmonary Water-brash Odynophagia Nausea/ emesis	Toupet 48/48	50 69% male	~43% gr III or IV; 28% Stricture; 28% Barrett's (Savary-Miller)	Conducted off meds 5 days prior DeMeester	ND	LES 6.8 mmHg	22 mo	ND	ND	ND	ND	ND	ND	Preop symptoms & symptom yrs not predictors for failure (abnl pH)	C
Blom 2002 USA University hospital Case-control	ND	Nissen 163/103 (preop dysphagia (n=60) excluded from analyses)	48 med (15-78) 73% male	33 (20%) Stricture; 36 (22%) Barrett's (Savary-Miller)	ND (abnl > 14.72) DeMeester	ND	ND	14 mo (med)	Symptoms not factor for postop dysphagia	ND	ND	ND	ND	ND	ND	C

Appendix C. Evidence Tables

Author Yr	Pre-operative risk assessed Symptoms	Intervention Enrolled/ Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagiti s; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretor y meds	PPI dose or now responds to dose that failed before Rx	QOL/ satisfactio n		EMS/ others
Campos 1999 USA University hospital Prospective cohort	80% Typical (heartburn, regurgitation, dysphagia) 20% Atypical (hoarseness, cough, wheeze, chest pain)	Nissen 199/199	49 med (15-77) 70% male	41% erosive esophagitis; 24% Barrett's	86% (abnl >14.7, off meds) DeMeester	Unknown meds/dose; response to acid suppression therapy: 7% complete 71% partial 17% minor 5% none	75% structurally defective LES; 70% hiatal hernia	15 mo	87% excellent/goo d& 13% poor symptomatic outcomes; typical vs atypical symptoms factor for successful outcomes, 92% vs 68% p=0.0001	ND	ND	Unknown number of pts on meds	ND	ND	ND	C

Appendix C. Evidence Tables

Table 15. Weight as modifying factor for outcomes after ARS

Author Yr	Pre-Op Risk(s) Assessed (R) Weight	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/others
Sandhu ¹ 2002	Low volume hospital	ARS 220/208	52 62% male	ND	ND	ND	ND	4 yr	ND	ND	ND	89% low vol vs 80% high vol	ND	Increasing BMI correlated to patient satisfaction P=0.0006	ND	C
Sweden Public hospital Ambidirectional cohort	BMI 26.4 High volume hospital BMI 26.3	ARS 225/200	54 60% male													
O'Boyle 2002	<70Kg 50 (22%) 70-90Kg 123 (54%) >90Kg 54 (24%) (n=227)	Nissen 262/262	<40 32% 40-60 48% >60 20% (n=258) 63% male	22% no esophagitis 66% moderate esophagitis 11% severe esophagitis (n=218)	13/119 abnl (>4.4%)	ND	116/ 246 (47%) hiatal hernia	5 yr	No difference in post-op heartburn scores by weight	ND	ND	ND	ND	No difference in post-op satisfaction scores by weight	ND	C
Bell 1999	ND	Toupet 143/138	ND ND	ND	ND (n=80, off meds) DeMeester	36 PPI > 8 wks, 22 unk duration, 14 no meds	ND	ND "pts seen up to 3 mo & every 6 mo"	21 failures (15%): 19 recurrent symptoms, 2 had dysphagia	ND	ND	ND	1 pt responding with PPI	ND	BMI not factor for success / failure	C

Appendix C. Evidence Tables

Author Yr	Pre-Op Risk(s) Assessed (R) Weight	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Winslow 2003 USA University hospital Cohort	NI BMI < 25 82 (16%)	Nissen 90% Toupet 10% 505/505	47 28% male	51% Esophagitis 11% Barretts 15% Stricture	51	Majority of patients on medication	LES 10 mmHg 34% hiatal hernia*	35 mo	Reduced symptoms of heartburn, water brash, regurgitation; no difference between groups	ND	ND	ND	All groups had reduced requirement for meds	No difference between groups for number of return to work days; no difference for patient satisfaction	No difference for complications, reoperation, anatomical failure; overall improvement	C
	Overweight BMI 25-29.9 210 (42%)		47 69% male	63% Esophagitis 20% Barretts 17% Stricture	57		LES 9 mmHg 51% hiatal hernia									
	Obese BMI ≥ 30 212 (42%)		48 36% male	53% Esophagitis 12% Barretts 18% Stricture	59 (modified DeMeester)		LES 9 mmHg 47% hiatal hernia *p=0.03									

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Author Yr	Pre-Op Risk(s) Assessed (R) Weight	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/others
Perez 2001	NI BMI<25 78 (42%) Overweight BMI 25-29.9 74 (40%) Obese BMI ≥30 35 (19%)	Nissen 187/187	47 53% male	No 31 (17%) Barrett's	100% abnl (Unkn # pts tested)	All pts symptomatic failures on meds, refused life-long meds, or had structural complications of GERD	Hiatal hernia: 86% none/small 14% >3 cm	34 mo	Recurrences of 5.1%, 5.4%, 22.9% for nl, overweight, obese p=0.03	ND	ND	ND	ND	ND	ND	C
Khajanchee 2004	ND	Nissen 223/223	51 62% male	62% severe esophagitis	93% abnl (off meds) DeMeester (>14.7)	ND	58% hiatal hernia	8.8 mo	89% had reduction or were symptom-free; weight not factor for symptomatic failure	ND	9.7% abnl (133/193 asymptomatic tested)	ND	ND	ND	ND	C
Blom 2002	ND	Nissen 163/103 (preop dysphagia (n=60) excluded from analyses)	48 med (15-78) 73% male	33 (20%) Stricture; 36 (22%) Barrett's (Savary-Miller)	ND Abnl > 14.72) DeMeester	ND	ND	14 mo (med)	Weight not factor for postop dysphagia	ND	ND	ND	ND	ND	ND	C

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Appendix C. Evidence Tables

Author Yr	Pre-Op Risk(s) Assessed (R) Weight	Intervention Enrolled/Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	Excluded ≥ grade 3 esophagitis; % ≥ grade 3	pH status	Responded to PPI or H2RA	EMS/Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/satisfaction		EMS/others
Campos 1999 USA University hospital Prospective cohort	Normal BMI 19-25: 47(24%) Overweight BMI 25-35: 144(72%) Severely obese BMI>35: 8(4%)	Nissen 199/199	49 med (15-77) 70% male	41% erosive esophagitis; 24% Barrett's	86% (abnl >14.7, off meds) DeMeester	Unknown meds/dose; response to acid suppression therapy: 7% complete 71% partial 17% minor 5% none	75% structurally defective LES; 70% hiatal hernia	15 mo	87% excellent/good & 13% poor symptomatic outcomes; weight not factor for outcomes	ND	ND	Unknown number of pts on meds	ND	ND	ND	C
Fraser 2001 Australia University hospital Ambi-directional cohort	Normal BMI<25: 40(21%) Overweight BMI 25-29.9: 88(45%) Obese BMI>30: 66(34%) Morbidly obese & obese groups combined	Nissen 194/194	47 (17-74) 60% male	ND	ND	ND	ND	3.2 yr	Weight not factor for dysphagia; heartburn scores higher in normal weight group compared to overweight & obese groups p=0.001	ND	ND	ND	ND	No difference in patient satisfaction between groups	ND	C

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[†] type of procedures not specified

Appendix C. Evidence Tables

Table 16. Psychological profile as modifying factor for outcomes after laparoscopic fundoplication

Author Yr	Pre-operative risk(s) assessed (R)	Intervention	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality		
			Country Setting Study design	Psychological profile	Enrolled Final	Age Sex	% ≥ grade 3 eophagitis		pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia	Change in symptoms	Esophagitis status	pH status		Off PPI/ Off all anti-secretory meds	↓ PPI dose or now responds to dose that failed before Rx
Velanovich 2001	Major depression (5) Anxiety disorders (4), (diagnosed prior to surgical consult)	LAS 82% Open anti-reflux fundoplication 18%	USA University hospital Retrospective cohort	94/94	ND ND	ND	ND	ND	6 wk	GERD-HRQL symptoms score for pt w/o vs with psychiatric disorders – 10.5 vs 1	ND	ND	Most pts dissatisfied with symptomatic outcome restarted H2RA or PPIs	"Mixed results"	11% psychiatric pt satisfied with surgery vs 95% for non-psychiatric pt p<0.000001	Greater improvement for median total GERD-HRQL score for pt w/o vs with psychiatric disorders p<0.03	C
Kamolz 2003	Case: Concomitant major depression	Nissen 39% Toupet 61% 38/38	Austria Public hospital Matched case-control	51 37% male	26% more gr 0, fewer gr IV p<0.05	55 DeMeester, Greater % dominant upright reflux p<0.05	Persistent or recurrent symptoms on 20-80 mg omeprazole @ day 18 mos	LES 3.1 mmHg 87% hiatal hernia	1 yr	Significant improvement for both groups for heartburn, regurgitation, chest pain, bloating; Cases reported more chest pain, bloating, & dysphagia p<0.01	ND	100% normal, no difference between groups	No meds at 28 months follow-up	NA	GIQLI 99 for cases vs 122 controls p<0.05	Normal LES - no difference between groups	C
	Control: NA	Nissen 39% Toupet 61% 38/38		49 37% male	55%	61 DeMeester	Persistent or recurrent symptoms on 20-80 mg omeprazole @ day 13 mos	LES 2.7 mmHg 95% hiatal hernia									
Kamolz 2000	Locus of control score: Internal 29.4 Social external 23.3 Fatalistic external 22.6 Factor of Reinforcement 27.1 Scores within average range of comparable population	Nissen 90/87	Austria Hospital Cohort	51 60% male	ND	69 DeMeester (>17.5)	Persistent or recurrent symptoms on 20-80 mg omeprazole @ day 13 .5 mos	LES 3.1 mmHg	3 mos	Resolved for all pts Negative correlation for subjective dysphagia & internal control p<0.001 vs positive correlation for fatalistic external control p<0.01, significant between 2 traits	ND	15.6 (nl < 17.5) 3 pts w/abnl score	ND	ND	GIQLI score 125 vs 92 at baseline	2/87 abnl esophageal motility; LES 12 mmHg; Correlation for LES & subjective dysphagia, NS	C

Appendix C. Evidence Tables

Author Yr Country Setting Study design	Pre-operative risk(s) assessed (R) Psychological profile	Intervention Enrolled Final	Baseline patient characteristics					Follow-up duration	Status at follow up						Quality	
			Age Sex	% ≥ grade 3 eophagitis	pH status	Responded to PPI or H2RA	EMS/ Hiatal hernia		Change in symptoms	Esophagitis status	pH status	Off PPI/ Off all anti- secretory meds	↓ PPI dose or now responds to dose that failed before Rx	QOL/ satisfaction		EMS/ others
Power 2004 UK University hospital Case-control	4 pts with varying issues from sexual abuse (1), depression (2), inorganic GI dysfunction (1)	Nissen 131/ 131	43 47% male	48% esophagi- tis 7.6% Barrett's	40 DeMeester	ND	ND	71 mos	117 were free of symptoms; 7 pt with symptom recurrence	ND, 13/14 in failed group had study	ND, 13/14 in failed group had study	97% 127/131	ND	ND	Psychiatric history was significant factor in predicting failure p=0.002	B

Appendix C. Evidence Tables

Table 17. Intraoperative complications (and those occurring within 30 days) for surgical and endoscopic procedures

	Surgical								Endoscopic					
	ONF		LNF		ONF /LNF		LNF /LPA		ECH		ERX	NDO plication	STR	
Mortality N (%)	Catarci 2004 Parrilla 2003	0 0	Coelho 2003 Catarci 2004 Fernando 2002 Mohan 2005 Power 2004	1(1.3) 0 0 0 0	Flum 2002	0	Carlson 2001	8(<1)	Filipi 2001	0	ND	ND	Triadafilopoulos 2002 Corley 2003	0 0
Re-operation N(%)	ND		O'Boyle 2000	3(<1)	ND		ND		ND		ND	ND	Richards 2003	2(3.3)
Conversion N(%)	ND		Catarci 2004 Leggett 2000 Power 2004 Coelho 2003 Fernando 2002	17(7.3) 4(4) 2(1.5) 0 0	ND		Carlson 2001	271 (3.1)	ND		ND	ND	ND	ND

Appendix C. Evidence Tables

	Surgical								Endoscopic								
	ONF		LNF		ONF /LNF		LNF /LPA		ECH		ERX		NDO plication		STR		
GI injury /perforation N (%)	ND		Leggett 2000 injury 4(3.4)	Fernando 2002 perforation 1(<1)	Flum 2002 injury	1,283 (1.4)	Richard s 2003 enterot omy 1(1.7)	Walsh 2003 perforat ion 3(1.2)	Carlson 2001 injury 62(<1)	Mahmood 2003 injury 1(3.8)	Filipi 2001 injury perforatio n 2(3) 1(2)	Chadalav ada 2004 injury perforatio n 1(2) 0	Cohen 2003	0	Plesko w 2004; 2005 perfora tion 1(1.6) 1(1.6)	Triadafilo poulos 2002; 2001 injury perforatio n 8 (6.8) 0	Corley 2003 0
Pneumothorax N (%)	ND		Chadalava da 2004 1(3)	Coelho 2003 2(2.6)	Fernando 2002 2(1.6)	Leggett 2000 2(1.4)	ND	Carlson 2001 67(<1)	ND	ND	ND	ND	Plesko w 2004; 2005 1 (1.6)	ND	ND		
Splenic injury N (%)	Parrilla 2003 splene ctomy 1(1.7)	Mohan 2005 2(1.8)	Coelho 2003 1(1.3)	Sato 2002 1(<1)	Flum 2002 splene ctomy 2065 (2.2)	Walsh 2003 1(<1)	Carlson 2001 injury splene ctomy 16(<1) 4(<1)	ND	ND	ND	ND	ND	ND	ND			

Appendix C. Evidence Tables

	Surgical					Endoscopic											
	ONF	LNF		ONF /LNF	LNF /LPA		ECH		ERX	NDO plication		STR					
Bleeding N(%)	ND	Sato 2002 8(5)	Coelho 2003 1(1.3)	Leggett 2000 1(1)	ND	Walsh 2003 2(<1)	Carlson 2001 49(<1)	Schiefke 2005 8(11)	Mahmood 2003 2(7.7)	Chen 2005 3(4.4)	Filipi 2001 2(3)	Chadalavada 2004 1(2)	Tam 2004 0	ND	ND	DiBaise 2002 1(5.6)	Corley 2003 1(3)
Pulmonary N (%)	ND	Fernando 2002 embolism 3(2.5)	ND	Walsh 2003 aspiration 1 (<1)	Carlson 2001 embolism 11 (<1)	effusion 12 (<1)	atelectasis 10 (<1)	Chadalavada 2004 aspiration 2(4)	Chen 2005 bronchospasm 1(1.2)	ND	Pleskow 2004; 2005 dyspnea 2 (3.1)	ND	ND				

Appendix C. Evidence Tables

	Surgical						Endoscopic							
	ONF		LNF		ONF /LNF	LNF /LPA		ECH		ERX	NDO plication		STR	
Gastrointestinal N (%)	Parrilla 2003 inability to belch, vomit	13 (22)	Seelig 1999 para- esophageal hernia /re- operation	2(<1)	ND	Carlson 2001 wrap herniation	85(1.3)	ND		ND	Pleskow 2004; 2005 eructation	9 (14)	Richards 2003; 2001; Houston 2003 gastroparesis /esophagitis	1 (4)
			Fernando 2002 gastric outlet obstruction gastric dilation	1(<1)		Walsh 2003 acute recurrence hiatal hernia	1(<1)				not specified	11 (17)		
			Anvari 2003;1996 esophageal leak	1(<1)		pancreatitis	1(<1)							
Infection/ Fever N (%)	ND		Fernando 2002 pneumonia	1(<1)	ND	Carlson 2001 wound infection	7(<1)	Abou- Rebyeh 2005 fever	2(5.3)	ND	ND		Tam 2003 pain / mediastinitis	1 (3.8)
			wound infection	1<1)		Walsh 2003 fever pneumonia	37(<1)	Tam 2004 sepsis	0				Triadafilopoulos 2002 fever	2 (1.7)
			Power 2004 umbilical port site infection	1(<1)			18(26)							

Appendix C. Evidence Tables

	Surgical							Endoscopic							
	ONF		LNF		ONF /LNF	LNF /LPA		ECH		ERX		NDO plication		STR	
Dysphagia N (%)	Parrilla 2003	17(29)	Coelho 2003	2(2.6)	ND	Walsh 2003	6(3.6)	Mahmood 2003	2(7.7)	Cohen 2003	35(24)	Pleskow 2004; 2005	7 (11)	Triadafilopoulos 2002; 2001	1(<1)
								Arts 2005	1(5)	Schumacher 2005	12(13)				
								Chen 2005	1(1.2)	Devriere 2002	1(6.7)				
Bloating N (%)	ND		Power 2004	1(<1)	ND	ND		Mahmood 2003	2(7.7)	ND		ND		Corley 2003	1(3)
Nausea /vomiting N (%)	ND		Chadalavada 2004	3(8)	ND	ND		Schiefke 2005	12(17)			Pleskow 2004; 2005	4(6)	ND	
								Filipi 2001	9(14)						
								Mahmood 2003	2(7.7)						
								Chadalavada 2004	2(4)						
								Abou-Rebyeh 2005	1(2.6)						

Appendix C. Evidence Tables

	Surgical				Endoscopic			
	ONF	LNF	ONF /LNF	LNF /LPA	ECH	ERX	NDO plication	STR
Other N (%)	ND	Coelho 2003 acute delirium acute urinary retention 1(1.3) acute ischemia lower extremity 1(1.3) Chadalava da 2004 urinary retention 1(3) Fernando 2002 atrial fibrillation dehydration 1(<1) 1(<1) Mohan 2005 liver injury 1(<1) Power 2004 port site hematoma urinary retention atrial fibrillation 1(<1) 1(<1) 1(<1)	ND	Carlson 2001 myocardi al infarction 5(<1) trocar hernia 12 (<1) Walsh 2003 stroke 1(<1) deep venous thrombosi s 1(<1) 1(<1) myocardi al infarction 1(<1) arrhythmi a 1(<1)	Chadalavad a 2004 pharyngitis 27(57) Filipi 2001 pharyngitis 20(31) Chadalavad a 2004 hypoxia 6(13) Filipi 2001 hypoxia 4(6) Chen 2005 hypoxemia 2(2.4)	ND	Plesko w 2004; 2005 phary ngitis 26 (41)	Triadafilop oulos 2002 submental swelling hypotensio n 1(<1) 1(<1)

Carlson 2001: systematic review; 6,542 cases including 61.4% Nissen, 23.8% Toupet, 13.4% Nissen-Rossetti, and 1.4% other procedures; results on each procedure separately are not given

Appendix C. Evidence Tables

Catarci 2004: meta-analysis; peri-operative morbidity (not specified): 77(18%) for open Nissen, 32(10.4%) for Lap Nissen, 8(7.5%) for open Toupet, and 2(12.5%) for Lap Toupet

Flum 2002: two retrospective population-based cohort studies using the Washington State discharge database and the United States Health Care Utilization Project (HCUP) database; patients underwent Nissen fundoplication surgery: 86,411; the percentage of laparoscopic and open procedures is not specified

Arts 2005: Mild throat ache and mild epigastric pain were commonly observed immediately after the procedure (specific results not given)

Cohen 2003: it includes 8 patients with short-term dysphagia from Johnson 2003 study (2 publications: one with 6-mo follow-up and another with 12-mo follow-up)

O'Boyle 2000: specifically focused on patients with iatrogenic stomach herniation as adverse event; other adverse events may have happened, as well but they were not reported

Seelig 1999: specifically focused on patients with para-esophageal hernia as adverse event; other adverse events may have happened, as well but they were not reported

Appendix C. Evidence Tables

Table 18. Complications occurring more than 30 days after surgical or endoscopic procedures

	Surgical								Endoscopic					
	ONF		LNF		OPA		LPA		LNF /LPA		ERX		STR	
Re-operation N (%)	Catarci 2004	9 (3.4)	Catarci 2004	19 (5.6)	Catarci 2004	2 (2.2)	Ludemann 2005	3 (6)	Catarci 2004	1 (1)	ND		ND	
Bleeding N (%)	ND		ND		ND		ND		ND		ND		Triadafilopoulos 2002	0
Gastrointestinal N (%)	ND		Ludemann 2005 inability to belch normally	22 (43)	ND		Ludemann 2005 inability to belch normally	10 (20)	Klaus 2003 diarrhea	15 (17.9)	Cohen 2003 injury	0	Richards 2003; 2001; Houston 2003 pancreatitis	1 (4)
			diarrhea	14 (27)			diarrhea	12 (24)	Carlson 2001 reflux	206 (3.5)			Triadafilopoulos 2002; 2001 ulcer stricture	0 0
			Coelho 2003 ulcer	2 (2.6)			increased flatulence	31 (62)					Torquati 2004 ulceration	0
			Dally 2004 penetratio n of Teflon pledgets	7 (<1)										0

Appendix C. Evidence Tables

	Surgical								Endoscopic					
	ONF		LNF		OPA		LPA		LNF /LPA		ERX		STR	
Dysphagia N (%)	Catarci 2004	42 (13.1)	Ludemann 2005	14 (27)	Catarci 2004	14 (13.2)	Ludemann 2005	9 (18)	Carlson 2001	188 (2.5)	Schumacher 2005	12 (13)	Triadafilopoulos 2002; 2001	0
			Catarci 2004	55 (15.1)			Catarci 2004	6 (5.2)	Richards 2003	0	Johnson 2003	8 (10.3)	Lufti 2005; Torquati 2004	0
			Sato 2002	9 (6.5)							Cohen 2003	1 (<1)		
			Mahon 2005	5 (4.6)										
Bloating N (%)	Catarci 2004	24 (12.8)	Ludemann 2005	38 (75)	ND		Ludemann 2005	22 (44)	Klaus 2003	16 (19)	ND		Lufti 2005	0
			Anvari 2001; 1998	45 (32)					Carlson 2001	239 (9.4)				
			Catarci 2004	23 (12.2)					Richards 2003	0				
			Coelho 2003	6 (7.8)										
Pain N (%)	ND		ND		ND		ND		ND		ND		Triadafilopoulos 2002 chest	0

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Carlson 2001: systematic review; 6,542 cases including 61.4% Nissen, 23.8% Toupet, 13.4% Nissen-Rossetti, and 1.4% other procedures; results on each procedure separately are not given

Catarci 2004: meta-analysis

Dally 2004: specifically focused on patients with symptomatic luminal penetration of Teflon pledgets as adverse event; other adverse events may have happened, as well but they were not reported; some of these patients were re-operated for that complication (specific number could not be extracted)

O'Boyle 2000: specifically focused on patients with iatrogenic stomach herniation as adverse event; other adverse events may have happened, as well but they were not reported

Seelig 1999: specifically focused on patients with para-esophageal hernia as adverse event; other adverse events may have happened, as well but they were not reported

Appendix C. Evidence Tables

Table 19. Complications of uncertain time period occurring after surgical and endoscopic procedures

	Surgical		Endoscopic
	LNF	LNF /LPA	ERX
Mortality N (%)	ND	Walsh 2003 1(<1)	ND
Re-operation N (%)	Mahon 2005 4(3.7) Bammer 2001 5(2.9) Leggett 2000 2(2) Fernando 2002 2(1.7) Anvari 2003; 1996 5 (1.5)	Sandbu 2002 18 (4.4) Walsh 2003 8 (3) Carlson 2001 162 (2.7)	ND
Pulmonary N (%)	Legget 2000 Atelectasis: 4 (1.6)	ND	Schumacher 2005 Effusion: 1 (1.1)
GI N (%)	Fernando 2002 Diarrhea 21 (12.3) Leggett 2000 Ileus: 1 (1)	Sandbu 2002 Difficult to vomit 193 (47.3) Difficult or unable to belch 154 (37.7) Klaus 2003 Constipation 3 (2.8)	Johnson 2003 Nausea /vomiting 12 (14.1) Schumacher 2005 Belching 6 (7.1) Regurgitation 1 (1.1) Deviere 2005 Belching 1 (3.1)

Appendix C. Evidence Tables

	Surgical		Endoscopic
	LNF	LNF /LPA	ERX
Infection/ Fever N (%)	Mohan 2005 Respiratory tract infection: 2 (1.8) Leggett 2000 Pneumonia: 1 (<1) Mediastinitis: 1 (<1)	Chadalavada 2004 Gastrostomy tube site infection: 1 (3)	Schumacher 2005 Fever 24 (26) Deviere 2005 Fever 7 (21.9) Johnson 2003 Fever 10 (11.8)
Dysphagia N (%)	Power 2004 131 (100) Sato 2002 33 (24) Fernando 2002 21(18) Bammer 2001 21(12.5) Blom 2002 8(4.9) Coelho 2003 2 (2.6)	Sandbu 2002 32 (7.8) Chadalavada 2004 20 (51) Walsh 2003 67 (25.2)	Deviere 2005 9 (28.1) Schumacher 2005 12 (13)
Bloating N (%)	Fernando 2002 54 (46) Bammer 2001 35 (20.5)	Sandbu 2002 145 (35.5) Walsh 2003 2 (<1)	Johnson 2003 5 (5.9) Deviere 2005 1(1.3) Schumacher 2005 1 (1.1)

Appendix C. Evidence Tables

	Surgical		Endoscopic
	LNF	LNF /LPA	ERX
Pain /discomfort N (%)	ND	Chadalavada 2004 Chest: 12 (30) Klaus 2003 Abdominal: 6 (5.5)	Cohen 2005 Retrosternal 122 (85) Schumacher 2005 Chest 72(77) Johnson 2003 Shoulder: 3 (3.5) Rib: 1 (1.2) Breast: 1 (1.2) Deviere 2005 Retrosternal /epigastric 22 (68.8)
Other N (%)	Bammer 2001 Trocar wound problems /scars: 10 (6) Leggett 2000 Atrial fibrillation: 1 (<1) Biloma: 1 (<1)	Walsh 2003 Recurrent hiatal hernia: 9 (3.4) Richards 2003 Incisional hernia: 2 (3.3)	Schumacher 2005 Flu syndrome: 1 (1.1) Bradycardia: 1 (1.1) Johnson 2003 Pharyngitis: 9 (10.6) Body odor /bad taste: 4 (4.7) Dry mouth: 2 (2.4) Anxiety: 2 (2.4) Flu syndrome: 1 (1.2)

Carlson 2001: systematic review; 6,542 cases including 61.4% Nissen, 23.8% Toupet, 13.4% Nissen-Rossetti, and 1.4% other procedures; results on each procedure separately are not given

Appendix D. Peer Reviewers

Peer Reviewers

Comparative Effectiveness of Management Strategies for Gastroesophageal Reflux Disease

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Appendix D. Peer Reviewers (continued)

NDO Surgical
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Tufts University School of Medicine
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Tufts-New England Medical Center
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Common Esophagitis Grading Scales

Savary-Miller

Grade I: one or more supravestibular, non-confluent reddish spots, with or without exudates

Grade II: erosive and exudative lesions in the distal esophagus, which may be confluent but not involving entire circumference

Grade III: circumferential erosions in the distal esophagus, covered by hemorrhagic and pseudomembranous exudates

Grade IV: presence of chronic complications such as deep ulcers, stenosis, or scarring with Barrett's metaplasia

Los Angeles Classification

Not present: No breaks (erosions) in the esophageal mucosa (edema, erythema, or friability may be present)

Grade A: One or more mucosal breaks confined to the mucosal folds, each not more than 5 mm in maximum length

Grade B: One or more mucosal breaks more than 5 mm in maximum length, but not continuous between the tops of two mucosal folds

Grade C: Mucosal breaks those are continuous between the tops of two or more mucosal folds, but which involve less than 75% of the esophageal circumference

Grade D: Mucosal breaks, which involve at least 75% of the esophageal circumference. The presence or absence of strictures, ulcers, and /or Barrett's esophagus must be noted separately, e.g., "Grade B with stricture"

Description of Endoscopic Treatments and Preliminary Findings

As we did our systematic literature search of MEDLINE in February of 2005, there has been much information on endoscopic treatments presented either in abstracts or society meetings in the last four months. The following is a distillation of current information regarding this topic.

Endoscopic treatments

Three endoscopic therapies are currently available for use in the United States. A fourth procedure, Enteryx™, was voluntarily recalled from the market due to safety concerns during final preparation of this report. The physiologic basis for improvement in symptoms or objective measures of GERD is unclear, although several mechanisms have been proposed for each technique.

- The Stretta™ procedure (Curon Medical, Fremont, CA) involves application of radiofrequency energy to the lower esophageal sphincter. Proposed mechanisms whereby radiofrequency energy might lead to improvement in GERD include a reduction in the number of transient lower esophageal sphincter relaxations and a reduction in the distensibility of the gastroesophageal junction.¹
- Enteryx™ involves injection of a biopolymer (Enteryx™, Boston Scientific, Natick, MA) into the lower esophageal sphincter. Enteryx™ contains 8 percent ethylene vinyl alcohol copolymer (EVOH) dissolved in dimethyl sulfoxide (DMSO). The DMSO diffusate results in solidification of the EVOH, which forms a spongy solid mass. The precise mechanisms whereby it improves GERD are not understood, although it is hypothesized that the physical properties of the implant might augment the lower esophageal sphincter mechanism.²
- EndoCinch™ Suturing System (Bard, Murray Hill, NJ) involves creation of plication in the region of the gastric cardia using a device that allows for sutures to be placed endoscopically. The stitches typically penetrate only as far as the submucosa. Preclinical studies suggested that the sutures increase lower esophageal sphincter pressure.^{3,4}
- NDO Plicator™ (NDO Plicator™, NDO Surgical, Mansfield, MA) also involves creation of a plication in the region of the gastric cardia. However, unlike Endocinch™, the device allows for a transmural plication. Animal studies suggested that plication increases the threshold of intragastric pressure needed to cause a reflux episode.⁵

Other devices continue to be developed but are not included in this report. One of the devices for which clinical trials are emerging rapidly is the “Gatekeeper™ reflux repair system (Medtronic, Minneapolis, MN), which involves implantation of a self-expanding bioprosthesis into the lower esophageal sphincter.^{6,7}

Preliminary findings and studies in progress

Our literature search identified only two sham-controlled studies that have been published in final form (one for Stretta⁸ and the other for Enteryx™⁹). Sham controlled trials for the other procedures are in progress but only interim results have been presented in preliminary form.¹⁰⁻¹² A second, multicenter, sham-controlled trial of the Enteryx™ procedure is ongoing.¹³

None of the studies directly compared endoscopic therapy to continued (or intensified) medical therapy or compared one endoscopic procedure to another. At least one comparison of

Appendix F. Description of Endoscopic Treatments and Preliminary Findings (continued)

EndoCinch™ with Enteryx™ is ongoing and has been presented in preliminary form.¹⁴ The preliminary results show similar efficacy on symptoms, quality of life and pH status.

A benefit on esophageal pH exposure compared with sham could not be demonstrated for either Enteryx™ or Stretta™. A preliminary report of a United States Multicenter sham-controlled trial of Enteryx™ suggests a benefit on pH, but the study has not yet been completed.¹³

The preliminary results of one ongoing sham-controlled trials of Endocinch™ raise additional concerns related to its efficacy when considered in the context of two earlier reports showing loss of sutures in the majority of patients.^{15,16} This study reported a similar proportion of patients relapsed and there were no differences in esophageal pH exposure between sham and Endocinch™ treated patients after one year.¹⁰ A preliminary report of another sham-controlled trial found significant improvement in heartburn frequency but not severity, regurgitation, quality of life or the ability to discontinue all anti-secretory therapy after three months compared with the sham procedure.¹¹

A preliminary report of 46 patients who had participated in a United States open label trial of Enteryx™¹⁷ found that two-thirds had sustained symptom control and reduction or discontinuation of PPI use for up to 36 months.¹³ However, the original study included 144 patients and the disposition of the remaining 98 patients is unclear.

References

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Appendix F. Description of Endoscopic Treatments and Preliminary Findings (continued)

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Gastroesophageal Reflux Disease-Health-Related Quality-of-Life Scale

Scoring Scale

- 0 = No symptoms
- 1 = Symptoms noticeable but not bothersome
- 2 = Symptoms noticeable and bothersome but not every day
- 3 = Symptoms bothersome every day
- 4 = Symptoms affect daily activities
- 5 = Symptoms are incapacitating – unable to do activities

Questions about symptoms (*circle one of each question*)

1. How bad is your heartburn?	0	1	2	3	5
2. Heartburn when lying down?	0	1	2	3	5
3. Heartburn when standing up?	0	1	2	3	5
4. Heartburn after meals?	0	1	2	3	5
5. Does heartburn change your diet?	0	1	2	3	5
6. Does heartburn wake you from sleep?	0	1	2	3	5
7. Do you have difficulty swallowing?	0	1	2	3	5
8. Do you have pain with swallowing?	0	1	2	3	5
9. If you take medication, does this affect your daily life?	0	1	2	3	5
10. How satisfied are you with your present condition?	Satisfied	Neutral	Dissatisfied		

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