Anvari *et al.* trial[44–46]

Methods	**Randomisation:** computerised sequence generation **Allocation concealment:** apparently yes, although blocking used to ensure 1 : 1 randomisation ('blocking factor determined by data centre') **Blinding:** not possible; outcome assessment: at office visit (questionnaires before medical assessment) at 6 and 12 months, by telephone at 3 and 9 months **Follow-up:** 3, 6, 9 and 12 months and 3 years **Setting:** single centre in Canada (four experienced surgeons) **Inclusion criteria:** chronic symptoms of GORD requiring long-term therapy; dependent on PPIs for at least 12 months; adults aged 18–70 years; GORD symptom score of < 18 and a score of > 70 on visual analogue scale (VAS) (0–100) of symptom control at screening; % acid reflux > 4% at baseline **Exclusion criteria:** pregnancy, malignancy, aperistaltic esophagus, severe comorbidity and previous GORD surgery
Participants	**Sample size:** 216 (a priori) **Randomised:** 104; medical: 52 [50 received medication (96%)], surgical: 52 [51 received surgery (98%)] **Age, mean:** medical 42.1 years; surgical 42.9 years **Sex (M/F):** medical 26/26; surgical 29/23
Interventions	**Medical:** optimised PPI as per detailed symptom management algorithm **Surgical:** laparoscopic Nissen fundoplication. Comprised construction of 2.5- to 3-cm 360° wrap. Short gastric vessels divided routinely to achieve floppy wrap
Outcomes	**Primary outcome:** GERSS – includes heartburn, regurgitation, bloating, dysphagia and epigastric/retrosternal pain. Total scale score 0–60. Well controlled defined as score < 18 **Secondary outcomes:** oesophageal function: endoscopy, manometry and 24-hour pH; QoL: SF-36 (0–100), EQ-5D (0–1) and VAS 0–100 for patient satisfaction with symptom control. A score of 70 was considered the threshold for symptom control on the VAS
Type of trial design	On explanatory end of explanatory–pragmatic continuum
Clinical leadership	Upper gastrointestinal surgeon
Risk of bias	
Allocation concealment?	Probably concealed – explanation of randomisation and concealment given in methods, although blocking could have jeopardised this
Free of selective reporting?	One concern: heartburn-free days promoted to primary outcome at 3 years
Sequence generation?	Computerised sequence generation but blocked and size of block not stated
Incomplete outcome data addressed?	Some evidence to suggest differential loss to follow-up at 3 years: 8/52 vs 3/52; no responder analysis
Notes	Trial funded by the Canadian Institute of Health Research and Ontario Ministry of Health

LOTUS trial[47–50]

Methods	**Randomisation:** randomisation in blocks of four **Allocation concealment:** unclear **Blinding:** not possible; outcome assessment: primary outcome (treatment failure) dependent on clinical decision-making, which was not blinded **Follow-up:** 6 months and 1, 3 and 5 years **Setting:** 39 centres across 11 European countries **Inclusion criteria:** oesophagitis grade no more than Los Angeles grade B; GORD symptoms no more than mild; response to PPI in run-in phase **Exclusion criteria:** previous oesophageal, gastric or duodenal surgery; primary oesophageal disorders; inflammatory bowel disorders; any gastrointestinal absorption abnormality; other significant concomitant disease
Participants	**Sample size:** 550 – not clear if stated a priori **Randomised:** 554; medical: 266, surgical: 288 [248 received surgery (86%)] – specialist surgery **Age, mean (SD):** medical 45.4 (11.5) years; surgical 44.8 (10.9) years **Sex (M/F):** medical 199/67; surgical 199/89
Interventions	**Medical:** esomeprazole 20 mg once daily, which could be increased stepwise **Surgical:** laparoscopic anti-reflux surgery. Used crural repair and short floppy total fundoplication in standardised approach
Outcomes	**Primary outcome:** time to treatment failure **Secondary outcomes:** symptoms related to GORD (heartburn, acid regurgitation and dysphagia severity); other gastrointestinal symptoms (flatulence, diarrhoea, epigastric pain, bloating) from GSRS; endoscopy; QoL using QOLRAD; perioperative and postoperative mortality (< 30 days); dysphagia requiring further treatment; serious adverse events; rate of conversion to open surgery
Type of trial design	Principally explanatory with some pragmatic features (calls itself 'exploratory')
Clinical leadership	Upper gastrointestinal surgeon
Risk of bias	
Allocation concealment?	Unclear; randomisation in blocks of four, otherwise not reported
Free of selective reporting?	No evidence of selective reporting, although QOLRAD data only reported in supplementary table at 5 years
Sequence generation?	Unclear; randomisation in blocks of four
Incomplete outcome data addressed?	Not fully: follow-up at 3 years: 204/288 vs 208/266; at 5 years: 180/288 (62.5%) vs 192/266 (72.2%). No data on 14% allocated surgery who did not have an operation
Notes	Trial funded by AstraZeneca R&D, with three authors employed by AstraZeneca

Mahon *et al.* trial[51–53]

Methods	**Randomisation:** 'computerised randomisation' – no details **Allocation concealment:** unclear, not reported **Blinding:** not possible **Follow-up:** 3 months and 1 year; separate follow-up of participants from one centre at 7 years **Setting:** two UK centres (two experienced surgeons) **Inclusion criteria:** GORD for at least 6 months, dependent on PPIs for at least 3 months and aged >16 to <70 years **Exclusion criteria:** significant oesophageal dysmotility and morbid obesity (BMI > 35 kg/m^2)
Participants	**Sample size:** a priori apparently 215 although basis not clear **Randomised**: 217; medical: 108, surgical: 109 (apparently all received surgery) **Age, median (range):** medical 47 (35–57) years; surgical 48 (39–56) years **Sex (M : F ratio):** medical 1 : 2.6; surgical 1 : 1.9
Interventions	**Medical:** one of four different PPI regimens, aiming to abolish symptoms **Surgical:** laparoscopic Nissen fundoplication. Used crural repair and short floppy wrap of 3 cm; division of short gastric vessels as deemed necessary
Outcomes	PGWI, GSRS, dysphagia, DeMeester score, operation time, length of stay, conversion to open surgery, reoperation rate, mortality rate, lower oesophageal sphincter pressure, postoperative complications, % time pH <4, cost, patient satisfaction only at 7 years (scale 1–3)
Type of trial design	At explanatory end of explanatory–pragmatic continuum
Clinical leadership	Upper gastrointestinal surgeon
Risk of bias	
Allocation concealment?	Unclear, not reported
Free of selective reporting?	Unclear, primary outcome not clearly prespecified
Sequence generation?	'Computerised randomisation'
Incomplete outcome data addressed?	Among 108 in medical group, well-being scores were available for 108 at baseline and 96 at one year; equivalent figures among 109 in surgical group were 104 and 99, respectively
Notes	Trial partially funded by Jansen Pharmaceutics; economic evaluation funded by Ethicon Endo-Surgery. All participants in medical group offered surgery at 1 year: 54/92 (59%) underwent surgery

REFLUX trial[1–3]

Methods	**Randomisation:** computer-generated sequence **Allocation concealment:** yes **Blinding:** not possible; outcome assessment by patient-completed postal questionnaires **Follow-up:** 3 months and annually for 5 years **Setting:** 21 UK centres **Inclusion criteria:** GORD symptoms for >12 months requiring PPI; evidence of GORD (endoscopy and/or pH monitoring) **Exclusion criteria:** BMI >40 kg/m^2; Barrett's esophagus >3 cm; paraoesophageal hernia; oesophageal stricture
Participants	**Sample size:** 600 (sample size recalculated from 600 to 392 after advice from DMC) **Randomised:** 357; medical: 179, surgical: 178 [111 received surgery (62%)] – by, or supervised by, experienced surgeon **Age, mean (SD):** medical 45.9 (11.9) years; surgical 46.7 (10.3) years **Sex (M/F):** medical 120/59; surgical 116/62
Interventions	**Medical:** best medical management after review. Lansoprazole was predominant PPI at study entry; omeprazole and lansoprazole most commonly reported at follow-up **Surgical:** laparoscopic surgery. Type of fundoplication was left to discretion of surgeon and all surgical techniques considered as a single policy
Outcomes	**Primary outcome:** REFLUX questionnaire score (heartburn, acid reflux, wind, eating and swallowing, bowel movements, sleep, work, physical and social activity) **Secondary outcomes:** QoL: EQ-5D and SF-36; serious morbidity; mortality; patient costs; NHS costs
Type of trial design	Pragmatic on explanatory–pragmatic continuum. Also included parallel, non-randomised preference groups
Clinical leadership	Upper gastrointestinal surgeon and gastroenterologist partnerships
Risk of bias	
Allocation concealment?	Allocation conducted by trials unit independent of all clinical teams
Free of selective reporting?	ITT and PP analysis presented as prespecified
Sequence generation?	Computerised randomisation
Incomplete outcome data addressed?	Adjusted treatment received and PP analyses reported in addition to ITT. Follow-up at 12 months: 154/178 (87%) vs 164/179 (92%)
Notes	Trial funded by NIHR HTA programme