NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of laparoscopic insertion of a magnetic ring for gastro-oesophageal reflux disease

Gastro-oesophageal reflux disease can occur when the ring of muscle between the food pipe (oesophagus) and the stomach does not close properly. Stomach acid can then travel up towards the throat (reflux), causing symptoms such as heartburn and nausea. This procedure is done under general anaesthesia. Using keyhole (laparoscopic) surgery, a ring of beads is placed around the outside of the food pipe, just above the stomach. Magnets inside the beads hold them together to keep the food pipe closed but are weak enough to move apart to allow food or liquid to be swallowed. The aim is to prevent acid reflux.

Contents

Abbreviations

Word or phrase	Abbreviation
Confidence interval	CI
Confidence limit	CL
Gastro-oesophageal reflux disease	GORD
Health-related quality of life	HRQL
Interquartile range	IQR
Laparoscopic Nissen fundoplication	LNF
Lower oesophageal sphincter	LOS
Magnetic sphincter augmentation	MSA
Manufacturer and User Facility Device Experience	MAUDE
Odds ratio	OR
Preferred reporting items for systematic reviews and meta-analysis	PRISMA
Proton pump inhibitor	PPI
Randomised controlled trial	TCT
Reflux Disease Questionnaire	RDQ
Reflux symptom index	RSI
Risk ratio	RR
Standard deviation	SD
Weighted mean difference	WMD

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in February 2022 and updated in August 2022.

Procedure name

- Laparoscopic insertion of a magnetic ring for gastro-oesophageal reflux disease

Professional societies

- Association of Upper Gastrointestinal Surgeons for Great Britain and Ireland (AUGIS)
- British Society of Gastroenterology (BSG)
- British Obesity and Metabolic Surgery Society (BOMSS)

Description of the procedure

Indications and current treatment

Gastro-oesophageal reflux disease (GORD) is a common condition in which acid from the stomach flows back up into the oesophagus. It is usually caused by the sphincter at the lower end of the oesophagus becoming weakened. Symptoms of GORD can be directly related to reflux episodes (such as heartburn, regurgitation, chest pain and nausea) or be caused by complications of the disease (such as dysphagia and respiratory difficulties). Repeated episodes of GORD can damage the lining of the oesophagus and lead to oesophageal ulceration, oesophageal stricture and Barrett's oesophagus.

NICE's guideline on GORD and dyspepsia in adults: investigation and management describes managing GORD in adults. The standard treatments for symptomatic GORD are lifestyle modification and drug therapy. People may be offered antireflux surgery (usually laparoscopic fundoplication) if their symptoms do not improve, or they develop complications despite medication or an intolerance to medication. Endoscopic interventions (such as endoscopic radiofrequency ablation at the gastro-oesophageal junction) and electrical stimulation of the lower oesophageal sphincter (LOS) can also be used.

What the procedure involves

The aim of laparoscopic insertion of a magnetic ring for GORD is to relieve reflux-related symptoms (such as heartburn or regurgitation) without impeding the ability to swallow, belch or vomit.

The procedure is done under general anaesthesia. Using a laparoscopic approach, a specially designed sizing tool is placed around the distal oesophagus to assess the size of implant needed. The sizing tool is then removed, and the implant is placed at the gastro-oesophageal junction, with the posterior vagus nerve trunk located outside the magnetic ring. The ends of the implant are secured together to hold it in place. Intraoperative endoscopy may be

used to help identify the anatomic gastro-oesophageal junction and to assess device position.

The implant consists of a ring of interlinked beads, each with a weak magnetic force that holds the beads together and reduces reflux. When the person swallows, the magnetic force is overcome, allowing the ring to open. After swallowing, magnetic attraction brings the beads together and the distal oesophagus is again closed.

Outcome measures

The DeMeester score is a composite score of the acid exposure during a prolonged ambulatory pH monitoring to categorise patients as GORD + or GORD -. The parameters that constitute the score are number of reflux episodes, number of episodes longer than 5 minutes, longest reflux duration, total percentage of monitoring time with pH below 4, and the percentage of time with pH below 4 in an upright position and supine position, respectively. The DeMeester score is the sum of the scores calculated for each of the 6 parameters. A score more than 14.7 is considered abnormal acid reflux, scores between 14.7 and 100 are regarded as mild-to-moderate GORD, and a score greater than 100 is regarded as severe GORD.

The GORD health-related quality of life (HRQL) scale measures symptomatic outcomes and therapeutic effects in patients with GORD. The scale has 10 items, and each item is scored from 0 to 5, with 0 indicating no symptoms and 5 presenting symptoms being incapacitating (unable to do daily activities).

Efficacy summary

GORD-HRQL

In a systematic review and meta-analysis of 15 studies (n=1,138), the pooled rate of GORD-HRQL improvement (at least 50% reduction) was 88% (95% confidence interval [CI] 83% to 93%, Cochrane Q P=0.11, I^2= 55%; 3 studies) within 1 year, and 85% (95% CI 78% to 91%, Cochrane Q P=0.52, I^2=0%; 2 studies) within 5 years. The total pooled rate was 88% (95% CI 84% to 92%; Cochrane Q P=0.17, I^2=40%; 4 studies). When comparing laparoscopic insertion of a magnetic ring with laparoscopic Nissen fundoplication (LNF), the weighted mean difference (WMD) in GORD-HRQL score was 0.20 (95% CI -1.60 to 2.00, p=0.83; Cochrane Q P=0.79, I^2=0%; 3 studies; Zhuang 2021).

In a systematic review and meta-analysis of 19 studies (n=12,697), when comparing laparoscopic insertion of a magnetic ring with fundoplication, the WMD in postoperative GORD-HRQL score was 0.34 (95% CI −0.70 to 1.37, p=0.525, I^2=70.6%; 3 studies; Guidozzi 2019).

In a systematic review and meta-analysis of 7 studies (n=1,211), the estimated pooled mean difference in postoperative GORD-HRQL score was −0.48 (95% CI -1.05 to 0.09, p=0.101, I^2=0.0%; 6 studies) between laparoscopic insertion of a magnetic ring and fundoplication (Aiolfi 2018).

In a randomised controlled trial (RCT) of 134 patients, the proportion of patients who had an at least 50% reduction in GORD-HRQL score was 81% (38/47) in the laparoscopic insertion of a magnetic ring group and 8% (7/87) in the twice-daily proton pump inhibitor (PPI) group (p<0.001) at 6-month follow up (Bell 2019). For all patients who had laparoscopic insertion of a magnetic ring (both primary and crossover groups) the mean GORD-HRQL score was 30±10 off PPIs and 24±10 on daily PPIs at baseline, and statistically significantly improved to 6 at 6 months and to 5 at 12 months (p<0.001). The proportion of patients who had an at least 50% reduction in GORD-HRQL score on PPIs was 81% (61/75). For the group who had medical treatment, no improvement in GORD-HRQL score was seen at study completion (exact data was not reported; Bell 2020).

In a non-randomised comparative study of 631 patients with GORD, there was a statistically significantly improvement in mean GORD-HRQL score at 3 years after treatment in both laparoscopic insertion of a magnetic ring (baseline, 22.0±9.1; 3 years, 4.6±6.0; mean change, -16.6±10.2, p<0.001) and fundoplication groups (baseline, 23.6±9.8; 3 years, 4.9±7.1; mean change, -17.8±10.6, p<0.001; Bonavina 2020).

In a case series of 553 patients with GORD, the mean GORD-HRQL total score statistically significantly improved from 33.8±18.7 at baseline to 7.2±9.0 (p<0.001) at a mean follow up of 10.3 months. The proportion of patients who had an at least 50% improvement in their GORD-HRQL total score was 84% (Ayazi 2020a).

In a case series of 124 patients with GORD who were followed up for 6 to 12 years after laparoscopic insertion of a magnetic ring, the mean total GORD-HRQL score statistically significantly improved from 19.9 at baseline to 4.01 (p<0.001) at a median follow up of 9 years. Clinically significant improvement in GORD-HRQL (>50% improvement) occurred in 93% of patients (Ferrari 2020).

In a non-randomised comparative study of 336 patients, the mean GORD-HRQL score statistically significantly improved from 19.2±7.7 at baseline to 3.8±5.7 at a mean follow up of 50.8 months in the non-severe GORD group and from 21.0±7.5 to 3.9±4.8 in the severe GORD group (all p<0.05). Comparison between groups showed that the mean score was statistically significantly higher in the severe GORD group than the non-severe GORD group at baseline (p=0.0479) but not at the final follow up (p=0.8870; Ferrari 2021).

In a non-randomised comparative study of 350 patients with GORD, the proportion of patients who had an at least 50% reduction in GORD-HRQL total score was 79% in the no hiatal hernia group, 78% in the small hiatal hernia group, 82% in the large hiatal hernia group, and 88% in the paraesophageal hernia group (p=0.77). The overall rate of clinical improvement in GORD-HRQL total score was 79% at a mean follow up of 13.6 months (Ayazi 2020b).

PPI use

In the systematic review and meta-analysis of 15 studies, the pooled rate of postoperative PPI use was 13% (95% CI 9.9% to 17.4%; Cochrane Q P =0.12, I^2=43%; 6 studies) within 1 year, 14% (95% CI 8.3% to 20.6%; Cochrane Q P=0.89, I^2=0%; 2 studies) within 2 years, and 19% (95% CI 9.9% to 35.9%; Cochrane Q P=0.13, I^2=55%; 2 studies) within 5 years. When comparing laparoscopic insertion of a magnetic ring with LNF, there was no statistically significant difference in postoperative PPI use (risk ratio [RR] 1.55, 95% CI 0.49 to 4.94, p=0.46, Cochrane Q P=0.27, I^2=19%; 2 studies; Zhuang 2021).

In the systematic review and meta-analysis of 19 studies, analysis of 13 single-cohort studies showed that the proportion of patients who needed postoperative PPI therapy was 13% (138/1,043). When comparing laparoscopic insertion of a magnetic ring with fundoplication, there was no statistically significant difference in postoperative PPI therapy (pooled odds ratio [OR] 1.08, 95% CI 0.40 to 2.95, p=0.877, I^2=72%; 5 studies; Guidozzi 2019).

In the systematic review and meta-analysis of 7 studies, there was no statistically significant difference in PPI suspension (pooled OR 0.81, 95% CI 0.42 to 1.58, p=0.548, I^2=63.9%; 6 studies) between the laparoscopic insertion of a magnetic ring group and the fundoplication group (Aiolfi 2018).

In the RCT of 134 patients, 91% (43/47) of patients in the laparoscopic insertion of a magnetic ring group discontinued PPIs at 6-month follow up (Bell 2019). At study completion (12 months), 91% (68/75) of patients who had laparoscopic insertion of a magnetic ring (both primary and crossover groups) stopped PPIs (Bell 2020).

In the non-randomised comparative study of 631 patients, the proportion of patients who used PPIs reduced from 98% (453/463) at baseline to 24% (76/314) at 3 years after laparoscopic insertion of a magnetic ring group and from 96% (158/165) to 20% (17/87) after fundoplication (Bonavina 2020).

In the case series of 553 patients, the proportion of patients who were free from PPI use was 93% at a mean follow up of 10.3 months (Ayazi 2020a).

In the case series of 124 patients, complete or at least 50% reduction in the average daily dose of PPI occurred in 79% and 90% of patients, respectively, at a median follow up of 9 years (Ferrari 2020).

In the non-randomised comparative study of 336 patients, use of PPI statistically significantly reduced from 71% (167/234) of patients at baseline to 13% (31/234) of patients at a mean follow up of 50.8 months in the non-severe GORD group and from 86% (88/102) to 16% (16/102) in the severe GORD group (all $p<0.05$). Comparison between groups showed that PPI use was statistically significantly higher in patients with severe GORD than patients with non-severe GORD at baseline but not at the final follow up (Ferrari 2021).

In the non-randomised comparative study of 350 patients, the proportion of patients who were free from PPI use was 93% in the no hiatal hernia group, 92% in the small hiatal hernia group, 90% in the large hiatal hernia group and 94% in the paraesophageal hernia group ($p=0.96$). Overall, 92% of patients were free from PPI use at a mean follow up of 13.6 months (Ayazi 2020b).

DeMeester score

In the RCT of 134 patients, the median DeMeester score at baseline was 40.3 (interquartile range [IQR] 28.1 to 53.0) in patients who had laparoscopic insertion of a magnetic ring compared with 30.9 (IQR 24.3 to 39.5) in patients who had twice-daily PPIs. The mean score changed to 8 compared with 18 ($p=0.059$) at 6 months (Bell 2019). For patients who had laparoscopic insertion of a magnetic ring (both primary and crossover patients), the median DeMeester score improved from 40.5 (IQR 25.7 to 49.5) at baseline to 5.3 (IQR 1.2 to 18.5) at study completion (12 months), and DeMeester scores were normalised in 70% (48/69) of patients. For the step-down PPI patients, the median score remained elevated at 16.7 (IQR 1.9 to 164; exact baseline data was not reported) and scores were normal in 54% of patients at study completion (Bell 2020).

In the case series of 553 patients, the mean DeMeester score was 33.9±29.4 in all patients at baseline. At 1 year after the procedure, the score improved to 7.2±10.2 in patients (n=327) who had a small implant (sizes 13 and 14), 18.8±33.2 in patients (n=138) who had a medium implant (size 15) and 21.0±42.8 in patients (n=85) who had a large implant (sizes 16 and 17; between groups, $p<0.0001$). DeMeester scores were normalised in 82%, 69% and 66% respectively ($p=0.0349$; Ayazi 2020a).

In the case series of 124 patients with GORD, the mean DeMeester score statistically significantly improved from 40.7±26.5 at baseline to 16.3±18.8 at a median follow up of 9 years ($p<0.001$; Ferrari 2020).

In the non-randomised comparative study of 336 patients, the mean DeMeester score statistically significantly improved from 26.2±12 at baseline to 13.4±15.9 at a mean follow up of 50.8 months in the non-severe GORD group and from 58.3±33.5 to 17±16.3 in the severe GORD group (all p<0.05). Comparison between groups showed that the mean score was statistically significantly higher in the severe GORD group than the non-severe GORD group at baseline (p<0.0001) but not at the final follow up (p=0.0591). The proportion of patients with abnormal DeMeester scores was 28% in the non-severe GORD group and 42% in the severe GORD group at the final follow up (p=0.1476; Ferrari 2021).

In the non-randomised comparative study of 350 patients, DeMeester scores were normalised in 71% of patients without hiatal hernia, 79% of patients with small hiatal hernias, 66% of patients with large hiatal hernias, and 58% of patients with paraesophageal hernias (p=0.21). Overall, DeMeester scores were normal in 74% of patients at a mean follow up of 13.6 months (Ayazi 2020b).

Regurgitation

In the RCT of 134 patients, per protocol analysis showed that the proportion of patients who reported resolution of moderate-to-severe regurgitation was 89% (42/47) in the laparoscopic insertion of a magnetic ring group and 10% (10/101) in the twice-daily PPI group (p<0.001) at 6-month follow up. Intention-to-treat analysis revealed that relief of moderate-to-severe regurgitation occurred in 84% (42/50) and 10% (10/102), respectively (p<0.001). At 12 months, the proportion of patients who reported resolution of moderate-to-severe regurgitation was 96% (72/75) in the laparoscopic insertion of a magnetic ring group (both primary and crossover patients) and 19% (8/43) in the step-down PPI group. At the same end point, complete elimination of regurgitation was reported in 73% and 2%, respectively (p<0.001; Bell 2020).

In the case series of 124 patients with GORD, the proportion of patients with grade 2 to 4 regurgitation statistically significantly decreased from 60% at baseline to 10% postoperatively (p<0.01; Ferrari 2020).

Ability to belch

In the systematic review and meta-analysis of 15 studies, when comparing laparoscopic insertion of a magnetic ring and LNF, there was no statistically significant difference in ability to belch (RR 1.48, 95% CI 0.76 to 2.86, p=0.25; Cochrane Q P<0.00001, I^2=92%; 3 studies; Zhuang 2021).

In the systematic review and meta-analysis of 19 studies, laparoscopic insertion of a magnetic ring was associated with statistically significantly greater ability to belch compared with fundoplication (pooled OR 12.34, 95% CI 6.43 to 23.7; p<0.001; I^2=0%; 4 studies; Guidozzi 2019).

In the systematic review and meta-analysis of 7 studies (n=1,211), laparoscopic insertion of a magnetic ring was associated with statistically significantly greater ability to belch compared with fundoplication (pooled OR 5.53, 95% CI 3.73 to 8.19, p<0.001, I^2=8.2%; 7 studies; Aiolfi 2018).

In the non-randomised comparative study of 631 patients, the proportion of patients who appeared to be able to belch as needed changed from 97% (441/456) at baseline to 98% (284/291) at 3 years after laparoscopic insertion of a magnetic ring and from 94% (154/164) to 92% (77/84) after fundoplication (Bonavina 2020).

Ability to vomit

In the systematic review and meta-analysis of 7 studies, the estimated pooled OR of ability to vomit was 10.10 (95% CI 5.33 to 19.15, p<0.001, I^2=44%; 6 studies) between laparoscopic insertion of a magnetic ring and fundoplication (Aiolfi 2018).

In the non-randomised comparative study of 631 patients, the proportion of patients who reserved the ability to vomit decreased from 97% (343/355) at baseline to 91% (134/147) at 3 years after laparoscopic insertion of a magnetic ring and from 92% (115/125) to 68% (17/25) after fundoplication (Bonavina 2020).

Gas bloating

In the systematic review and meta-analysis of 15 studies, there was a statistically significantly lower risk of gas-bloat syndrome in the laparoscopic insertion of a magnetic ring group than the LNF group (RR 0.69, 95% CI 0.51 to 0.93, p=0.01; Cochrane Q P=0.39, I^2=0%; 2 studies; Zhuang 2021).

In the systematic review and meta-analysis of 19 studies, laparoscopic insertion of a magnetic ring was associated with statistically significantly less gas bloating compared with fundoplication (pooled OR 0.34, 95% CI 0.16 to 0.71, p=0.004; I^2=62.8%; 5 studies; Guidozzi 2019).

In the systematic review and meta-analysis of 7 studies, laparoscopic insertion of a magnetic ring was associated with statistically significantly fewer gas-bloat symptoms compared with fundoplication (pooled OR 0.39, 95% CI 0.25 to 0.61, p<0.001, I^2=49.6%; 5 studies, n=1,042; Aiolfi 2018).

In the RCT of 134 patients, frequent or continuous bloating was present in 58% of patients off PPIs and 55% of patients on PPIs at baseline. After the procedure, this statistically significantly reduced to 15% (11/75) of patients (both primary and crossover patients) and 27% of primary patients who had laparoscopic insertion

of a magnetic ring at study completion (p=0.0416). No change was seen in the patients who had medical treatment (exact data was not reported; Bell 2020).

Patient satisfaction

In the non-randomised comparative study of 631 patients, patient satisfaction (GORD-HRQL satisfaction with present condition) increased from 5% to 78% in the laparoscopic insertion of a magnetic ring group and from 4% to 77% in the fundoplication group (Bonavina 2020).

In the case series of 553 patients, 87% of patients were satisfied with the outcomes of the procedure (Ayazi 2020a).

In the case series of 124 patients, overall patient satisfaction was reported in 94% of patients who were followed up for more than 10 years (Ferrari 2020).

In the non-randomised comparative study of 350 patients, there was no statistically significant difference in patient satisfaction between groups (no hiatal hernia, 87%; small hiatal hernia, 88%; large hiatal hernia, 92%; paraesophageal hernia, 94%; p=0.73). The overall rate of patient satisfaction was 89% at a mean follow up of 13.6 months (Ayazi 2020b).

Safety summary

Overall morbidity and complication

Overall postoperative morbidity ranged from 0% to 3% of patients who had laparoscopic insertion of a magnetic ring and from 0% to 7% of patients who had fundoplication in the systematic review and meta-analysis of 7 studies (Aiolfi 2018).

The intraoperative complication rate was 2% in the laparoscopic insertion of a magnetic ring group and 1% in the fundoplication group, and the procedure-related complication rate was about 2% in each group in the non-randomised comparative study of 631 patients (Bonavina 2020).

Major complications were reported in 2 patients in the case series of 553 patients. These complications included CO_2 retention needing reintubation (n=1) and mediastinal abscess needing drainage and intravenous antibiotic (n=1; Ayazi 2020a).

Minor complications were described in 9% (49/553) of patients in the case series of 553 patients. These complications included poor postoperative pain control (n=4), significant nausea during immediate postoperative period (n=5), hypoxia needing supplemental oxygenation (n=7), lethargy (n=3), abdominal pain needing

additional evaluation (n=5), bothersome nausea or vomiting needing emergency department visit (n=11), dysphagia needing hospital admission (n=7), abdominal wall haematoma at gastric pacer insertion site (n=1), deep vein thrombosis (n=1), urinary retention (n=1), cardiac arrhythmia (n=1), dyspnoea (n=2), and aspiration pneumonia (n=1; Ayazi 2020a).

Overall complications were reported in 3% (n=2) of patients without hiatal hernia, 11% (n=23) of patients with small hiatal hernias, 14% (n=8) of patients with large hiatal hernias, and 27% (n=6) of patients with paraesophageal hernias (p=0.015) in the non-randomised comparative study of 350 patients. The overall complication rate was 11% (n=39), consisting of 2 major complications and 37 minor complications. Major complications happened in 2 patients with large hiatal hernias, and minor complications occurred in 2 patients without hiatal hernia, 23 patients with small hiatal hernias, 6 patients with large hiatal hernias, and 6 patients with paraesophageal hernias (Ayazi 2020b).

Dysphagia (needing treatment)

The pooled incidence of postoperative dysphagia was 29% in 1 year after laparoscopic insertion of a magnetic ring (95% CI 13% to 46%; Cochrane Q P<0.00001, I^2=96%; 6 studies) in the systematic review and meta-analysis of 15 studies. Only 1 study reported that 4% to 6% of patients complained of dysphagia at 1 year after laparoscopic insertion of a magnetic ring. The pooled rate of endoscopic dilation needed was 7.4% (95% CI 2.9% to 13.7%; Cochrane Q P=0.0005, I^2=80%; 5 studies) in 1 year. Comparison between laparoscopic insertion of a magnetic ring and LNF showed that there was no statistically significant difference in postoperative dysphagia (RR 1.21, 95% CI 0.92 to 1.60, p=0.18; Cochrane Q P=0.89, I^2=0%; 2 studies; Zhuang 2021).

Analysis of 13 single-arm cohort studies showed that postoperative dilation was reported in 8% of patients (164/2,112) in the systematic review and meta-analysis of 19 studies. When comparing laparoscopic insertion of a magnetic ring with fundoplication, there was no statistically significant difference in postoperative dysphagia (pooled OR 0.94, 95% CI 0.57 to 1.55, p=0.822; I^2=20.4%; 4 studies; Guidozzi 2019).

Dysphagia needing endoscopic dilation was described in 9% of patients who had laparoscopic insertion of a magnetic ring and 7% of patients who had fundoplication (OR=1.56, 95% CI 0.61 to 3.95, p=0.119; I^2=35%; 5 studies) in the systematic review and meta-analysis of 7 studies (Aiolfi 2018).

Dysphagia was reported in 32% (15/47) of patients at 6 months after laparoscopic insertion of a magnetic ring in the RCT of 134 patients having laparoscopic insertion of a magnetic ring or twice-daily PPIs. Intervention was needed in 7 patients (oral corticosteroids, n=3; endoscopic dilation, n=3;

laparoscopic hiatal hernia repair, n=1; Bell 2019). At study completion (12 months), the rate of dysphagia was 40% (n=19) in the primary laparoscopic insertion of a magnetic ring group and 33% (n=10) in the crossover group (Bell 2020).

Postoperative endoscopic dilation was needed in 169 patients (99 patients needed 1, and 70 needed more than 1) in the case series of 553 patients. The indications for endoscopic dilation were dysphagia (n=129), chest pain (n=14) and both dysphagia and chest pain (n=26; Ayazi 2020a).

Postoperative dysphagia was statistically significantly higher in the severe GORD group than the non-severe GORD group (25% compared with 14%, p=0.0124) in the non-randomised comparative study of 336 patients. Endoscopic dilation was needed in 3% and 2%, respectively (p=0.6562). At baseline, dysphagia was also statistically significantly higher in the severe group (12%) than the non-severe group (6%, p=0.0460; Ferrari 2021).

Postoperative dysphagia was reported in 16% of patients without hiatal hernia, 16% of patients with small hiatal hernias, 6% of patients with large hiatal hernias, and 6% of patients with paraesophageal hernias (p=0.08) at a mean follow up of 13.6 months in the non-randomised comparative study of 350 patients. Endoscopic dilation was needed in 20%, 26%, 24% and 5%, respectively (n=0.12; Ayazi 2020b).

Dysphagia needing device removal was reported in 292 patients at a mean of 10.9 months after implantation in a review of the MAUDE database and the Ethicon's complaint database of 27,779 patients implanted with LINX devices (DeMarchi 2021).

Device erosion

Analysis of 13 single-arm cohort studies revealed that the overall rate of oesophageal erosion was less than 1% (31/11,530) in the systematic review and meta-analysis of 19 studies (Guidozzi 2019).

Erosion needing device removal was reported in 27 patients at a mean of 25 months after LINX device implantation in the review of the MAUDE database and the Ethicon's complaint database. The cumulative risk of erosion at 7 years was 0.28% (95% CI 0.17% to 0.46%; DeMarchi 2021).

Device removal

Device removal was reported in 15 patients (5 studies) at 5-year follow up in the systematic review and meta-analysis of 15 studies (Zhuang 2021). Fourteen patients had their implants removed because of persistent dysphasia, chest pain or unresolved GORD symptoms, and 1 patient was because of implant erosion.

Analysis of 13 single-arm cohort studies showed that device removal or reoperation was reported in 3% of patients (69/2,098) in the systematic review and meta-analysis of 19 studies. When comparing laparoscopic insertion of a magnetic ring with fundoplication, there was no statistically significant difference in postoperative reoperation (pooled OR 1.23, 95% CI 0.26 to 5.8; p=0.797; I^2=48.5%; 4 studies; Guidozzi 2019).

Device removal was reported in 1.5%, 2.0% and 2.4% of patients at 1, 2 and 3 years after laparoscopic insertion of a magnetic ring in the non-randomised comparative study of 631 patients with GORD (Bonavina 2020).

Device removal was reported in 7% (37/553) of patients in the case series of 553 patients (Ayazi 2020a). The reasons for removals included troublesome dysphagia or chest pain not responding to dilation (n=20), recurrence of hernia and migration of the device (n=3), recurrence of hernia and mediastinal abscess (n=1), worsening typical reflux symptoms (n=4), worsening atypical reflux symptoms (n=3), possible titanium allergy (n=1), unexplained leukocytosis (n=1), need for subsequent operation (n=2), and removal indicated by device malfunction (n=2).

Device removal was done in 3 patients between 6 to 12 years after laparoscopic insertion of a magnetic ring in the case series of 124 patients. The reasons for device removal were heartburn/continued reflux symptoms (n=1), dysphagia (n=1) and need of magnetic resonance study/planned magnetic resonance imaging (n=1; Ferrari 2020).

Device removal was reported in 8 patients with severe GORD and 24 patients with non-severe GORD in the non-randomised comparative study of 336 patients (Ferrari 2021).

Device removal was reported in 2% (609/27,779) of patients at a mean of 14.6 months after implantation in the review of the MAUDE database and the Ethicon's complaint database. The overall 7-year cumulative risk of explant was 5% (95% CI 4.31% to 5.36%; DeMarchi 2021). The reasons for device removal included dysphagia (n=292), persistent or recurrent GORD (n=125), erosion (n=27), abdominal pain or pain (n=46), discontinuous device (n=17), need for MRI (N=11), vomiting (n=16), gastroparesis (n=4), device migration (n=3) and other unknown reasons (n=68).

Device removal was reported in 6% of patients without hiatal hernia, 6% of patients with small hiatal hernias, 2% of patients with large hiatal hernias, and 0% of patients with paraesophageal hernias (p=0.28) at a mean follow up of 13.6 months in the non-randomised comparative study of 350 patients. The overall rate of device removal was 5% at a mean follow up of 13.6 months, and

all the removals were for persistent dysphagia or oesophageal spasm unresponsive to endoscopic dilation (Ayazi 2020b).

Reoperation

Reoperation was needed in 13 patients who had laparoscopic insertion of a magnetic ring (12 device removals and 1 crural release) and 11 patients who had fundoplication (5 herniation of the fundic wrap, 3 persistent GORD, 2 retroesophageal abscess and 1 crural release) in the systematic review and meta-analysis of 7 studies. The estimated pooled OR of reoperation was 0.54 (95% CI 0.22 to 1.34, p=0.183, I^2=0.0%; 3 studies) between groups (Aiolfi 2018).

The surgical intervention rate at 1, 2 and 3 years after treatment was 1.6%, 1.2% and 0.6% of patients who had laparoscopic insertion of a magnetic ring and 1.9%, 0% and 0% of patients who had fundoplication in the non-randomised comparative study of 631 patients. The intervention for the laparoscopic insertion of a magnetic ring group was the removal of device for dysphagia (45%), ongoing GORD (18%), vomiting/regurgitation (18%), gastric pain (9.5%) and need for MRI (9.5%). The intervention for the fundoplication group was revision of a Nissen wrap because of ongoing GORD, reherniation, and a sigmoid resection secondary to diverticulitis (Bonavina 2020).

Reoperation was needed in 7 of the 24 patients who were found to have hiatal hernia recurrence on endoscopy at a mean follow up of 13.6 months in the non-randomised comparative study of 350 patients. Of these 24 patients, 20 patients had small hernias, 1 patient had large hernias, and 3 patients had paraesophageal hernias. The incidence of recurrent hiatal hernia increased in direct correlation with the preoperative hiatal hernia size (small hiatal hernia, 10%; large hiatal hernia, 17%; paraesophageal hernia, 20%; p=0.032). When comparing with patients with a full dissection, patients with a minimal dissection had a statistically significantly higher hiatal hernia recurrence rate (minimal dissection, 21%; full dissection, 8%; p=0.033), and were more likely to need reoperation (minimal dissection, 11%; full dissection, 2%; p=0.0133; Ayazi 2020b).

Readmission

Readmission was reported in 31 patients within 90 days after the procedure in the case series of 553 patients. Of these patients, 23 patients were readmitted to hospital within 30 days and 8 patients were readmitted between 30 to 90 days (Ayazi 2020a).

Readmission was described in 19 patients within 90 days after the procedure, including 14 patients with small hiatal hernias, 2 patients with large hiatal hernias,

and 3 patients with paraesophageal hernias (p=0.049) in the non-randomised comparative study of 350 patients (Ayazi 2020b).

Dysphagia needing hospital admission was reported in 7 patients in the case series of 553 patients (Ayazi 2020a).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events that they have heard about) and about theoretical adverse events (events that they think might possibly occur, even if they have never happened).

For this procedure, professional experts did not list any additional anecdotal or theoretical adverse events.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to laparoscopic insertion of a magnetic ring for GORD. The following databases were searched, covering the period from their start to 17 August 2022: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria were applied to the abstracts identified by the literature search. If selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded if no clinical outcomes were reported, or if the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with GORD.
Intervention/test	Laparoscopic insertion of a magnetic ring.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.

List of studies included in the IP overview

This IP overview is based on 13,713 patients from 3 systematic reviews and meta-analyses (Zhuang 2021; Guidozzi 2019; Aiolfi 2018), 1 RCT (Bell 2019, 2020), 3 non-randomised comparative studies (Bonavina 2020; Gerrari 2021; Ayazi 2020), and 2 case series (Ayazi 2019; Ferrari 2020). This overview also includes a review of the MAUDE database and the Ethicon's complaint database of 27,779 patients implanted with LINX devices.

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on laparoscopic insertion of a magnetic ring for GORD

Study 1 Zhuang QJ (2021)

Study details

Study type	Systematic review and meta-analysis
Country	Not reported for individual studies
Publication period	2013 to 2020
Study population and number	n=1,138 (15 studies) patients with refractory GORD
Age and sex	Mean age ranged from 42 to 62 years; 52.6% male
Patient selection criteria	Inclusion criteria: (1) single-arm studies evaluating the efficacy and safety of magnetic sphincter augmentation (MSA) in treating refractory GORD, or comparative studies comparing MSA with PPI or LNF; (2) patients with typical GORD symptoms whose GORD partially responded to PPI and who had pathological reflux confirmed by oesophageal reflux monitoring; (3) included at least 20 patients in the study; and (4) reported postoperative PPI use or GORD-HRQL explicitly as an outcome measure. Exclusion criteria: (1) studies evaluating patients with specific phenotypes of GORD as predominant study patients, such as those evaluating MSA efficacy among patients with large hiatus hernia, Barrett's oesophagus or erosive esophagitis; (2) poorly described diagnostic criteria, unsuitable interventions or outcomes; (3) duplications (for duplicate publications, the one with the largest number of patients was included); (4) studies for which the full text could not be obtained; and (5) reviews, editorials, commentaries, case report or case series, or studies on animals.
Technique	Laparoscopic insertion of a magnetic ring, PPI or LNF
Follow up	5 years
Conflict of interest/source of funding	None

Analysis

Study design issues: This systematic review and meta-analysis evaluated the therapeutic effect and safety of MSA in refractory GORD and compared MSA efficacy with PPI or LNF. Primary outcome was the rate of postoperative PPI use, and secondary outcomes included postoperative GORD-HRQL, normalisation of acid exposure time and incidence of procedure-related adverse events.

The favourable outcome of antireflux surgery included a complete and long-lasting alleviation of symptoms, absence of postoperative adverse events and retaining the ability to belch. Symptom relief was defined as

complete cessation of PPI and an at least 50% reduction in the GORD-HRQL score compared with their baseline data.

Two authors screened the literatures and extracted the data independently. Any disagreement was revolved by discussion with a third author. For publications that shared the same patient cohort, only those with the most complete follow-up data were extracted for the meta-analysis. Data extraction was done

Study population issues: Of the 15 included studies, there were 10 single-arm studies, 1 RCT (shared the same patient population with different follow-up duration) and 3 cohort studies. Among 10 single-arm studies, there were 8 studies of fair quality and 2 studies of high quality using the methodological index for non-randomised studies. For the comparative studies between MSA and LNF, 2 studies were at low risk of bias and 1 study at high risk using the Newcastle–Ottawa Scale. The study comparing MSA with PPI was of fair quality using the Jadad scale.

Other issues: The efficacy of MSA might be affected by selection bias, patients with less advanced GORD tend to choose MSA while those with severe GORD would turn to fundoplication. Significant heterogeneity was found in analyses of postoperative dysphagia, dilation and reserved ability to belch, and the heterogeneity was probably because of the use of inconsistent assessment criteria.

Key efficacy findings

Number of patients analysed: 1,138 (15 studies)

Pooled rate of postoperative PPI use:

- Within 1 year: 13.0% (95% CI 9.9% to 17.4%; Cochrane Q P = 0.12, I^2 = 43%; 6 studies, n=631)
- Within 2 years: 13.8% (95% CI 8.3% to 20.6%; Cochrane Q P=0.89, I^2=0%; 2 studies, n=125)
- Within 5 years: 19.4% (95% CI 9.9% to 35.9%; Cochrane Q P=0.13, I^2=55%; 2 studies, n=117)

When combining those who completely ceased PPI and those with a 50% reduction in PPI dosage as the ‘treatment-responsive’ group, the pooled rate of postoperative PPI use was 9.9% (95% CI 7.4% to 12.3%).

Pooled rate of GORD-HRQL improvement (at least 50% reduction in GORD-HRQL):

- Within 1 year: 88% (95% CI 83% to 93%, Cochrane Q P=0.11, I^2= 55%; 3 studies, n=370)
- Within 5 years: 85% (95% CI 78% to 91%, Cochrane Q P=0.52, I^2=0%; 2 studies, n=117)

The total pooled rate of GORD-HRQL improvement was 88% (95% CI 84% to 92%; Cochrane Q P=0.17, I^2=40%; 4 studies, n=395).

Pooled rated of normalisation in acid exposure time: 75% in 1 year after MSA (95% CI 68% to 82%; Cochrane Q P=0.29, I^2=19%; 3 studies).

Ability to belch: nearly all patients reported the retention of their belching ability (3 studies).

Comparison between MSA and double-dose PPI: 1 RCT

- Complete cessation of PPI: 91% compared with 0%
- Symptom alleviation (improvement in GORD-HRQL): 81% compared with 8%

Comparison between MSA and LNF:

- Daily PPI use after surgery: 148 patients in the MSA group and 146 patients in the LNF group (RR 1.55, 95% CI 0.49 to 4.94, p=0.46, Cochrane Q P=0.27, I^2=19%; 2 studies)
- GORD-HRQL score: 180 compared with 152 patients (WMD 0.20, 95%CI -1.60 to 2.00, p=0.83; Cochrane Q P=0.79, I^2=0%; 3 studies)
- Gas-bloat syndrome: 148 compared with 146 patients (RR 0.69, 95% CI 0.51 to 0.93, p=0.01; Cochrane Q P=0.39, I^2=0%; 2 studies)
- Ability to belch: 170 compared with 152 patients (RR 1.48, 95% CI 0.76 to 2.86, p=0.25; Cochrane Q P<0.00001, I^2=92%; 3 studies).

Key safety findings

Postoperative dysphagia was reported in 7 studies:

- Pooled incidence of postoperative dysphagia: 29% in 1 year after MSA (95% CI 13% to 46%; Cochrane Q P<0.00001, I^2=96%; 6 studies, n=543).
- Only one study reported that 3.6% to 5.6% of patients complained of dysphagia 1 year after MSA.

Pooled rate of dilation in 1 year: 7.4% (95% CI 2.9% to 13.7%; Cochrane Q P=0.0005, I^2=80%; 5 studies, n=543).

Implant removal in 5-year follow up: n=15 (5 studies, n=543; 14 patients had their implants removed because of persistent dysphasia, chest pain or unresolved GORD symptoms; and 1 reported implant erosion and the device was removed eventually).

Comparison between MSA and double-dose PPI: 1 RCT

- MSA: transient dysphagia, 28%; ongoing dysphagia, 4%

Comparison between MSA and LNF:

- Postoperative dysphagia: 146 compared with 120 patients (RR 1.21, 95% CI 0.92 to 1.60, p=0.18; Cochrane Q P=0.89, I^2=0%; 2 studies)
- LNF: retroesophageal abscesses, n=2 (these 2 patients needed further surgical drainage)

Study 2 Guidozzi N (2019)

Study details

Study type	Systematic review and meta-analysis
Country	Not reported for individual studies
Publication period	Up to 2019
Study population and number	n=12,697 (19 studies; MSA, n=12,230; fundoplication, n=467) Patients with GORD
Age and sex	Not reported
Patient selection criteria	Inclusion criteria: publications were included if they were cohort or comparative studies investigating MSA for treating GORD including more than 20 patients. Comparative studies were included in a pooled analysis that compared MSA with fundoplication (partial or total) for treating GORD. Exclusion criteria: studies were excluded if they included less than 20 patients receiving MSA, or for comparative studies if MSA was not compared with fundoplication.
Technique	Laparoscopic insertion of a LINX device Laparoscopic fundoplication
Follow up	6 to 44 months when reported
Conflict of interest/source of funding	Financial support: one author was supported by the National Institute for Health Research. The views expressed were those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health. Conflicts of interest: none.

Analysis

Study design issues: This systematic review and meta-analysis primarily compared clinical outcomes of laparoscopic fundoplication with the insertion of a LINX device in managing GORD associated symptoms and complications. The secondary objective was to evaluate the current literature published on the LINX device in substantial case series, in order to identify the true rate of complications, specifically focusing on erosion caused by the device. Two authors examined the abstracts of the articles to determine their suitability for inclusion in the pooled analysis.

Study population issues: The systematic review identified 6 cohort studies that directly compared MSA with fundoplication, comprising of 1,099 patients, 632 having MSA and 467 having fundoplication. This systematic review also included 13 single-arm cohort studies, comprising of 11,598 patients, evaluating clinical outcomes from MSA.

Other issues: A random-effects model was used to correct for the heterogeneity of the analysed data, however, there remained several other limitations. MSA studies might potentially underreport complications associated with device implantation, leading to publication bias. Many MSA studies and comparative studies had relatively small recruitment populations, leading to numerous underpowered studies. Reporting bias was also a limitation to consider, because insertion of the MSA device is a novel procedure, which some surgeons might be

technically invested in, driving promising outcomes. Meta-analysis of data on reoperation rates was based upon comparative studies with limited follow up, and might be expected to change over time with more extended follow up. There was also significant variation in the follow-up protocols and specifically length of follow up between individual studies.

Key efficacy findings

Number of patients analysed: 12,697 (19 studies)

13 single-arm cohort studies (n=11,598)

Postoperative PPI therapy: 13.2% (138/1,043)

6 cohort studies (n=1,099): MSA compared with fundoplication

Pooled OR of postoperative PPI therapy: 1.08 (95% CI 0.40 to 2.95; p=0.877; 5 studies)

Heterogeneity: Cochran Q=14.27; p=0.007, I^2=72%

WMD of postoperative GORD-HRQOL score: 0.34 (95% CI −0.70 to 1.37; p=0.525; 3 studies)

Heterogeneity: Cochran Q=6.79; p=0.033, I^2=70.6%

Pooled OR of postoperative gas bloating: 0.34 (95% CI 0.16 to 0.71; p=0.004; 5 studies)

Heterogeneity: Cochran Q=10.76; p=0.029, I^2=62.8%

Pooled OR of ability to belch: 12.34 (95% CI 6.43 to 23.7; p<0.001; 4 studies)

Heterogeneity: Cochran Q=1.46; p=0.669, I^2=0%

Key safety findings

13 single-arm cohort studies (n=11,598)

Postoperative dilation: 7.8% (164/2,112)

Device removal or reoperation: 3.3% (69/2,098)

Overall rate of oesophageal erosion: 0.3% (31/11,530)

6 cohort studies (n=1,099): MSA compared with fundoplication

Pooled OR of postoperative dysphagia: 0.94 (95% CI 0.57 to 1.55; p=0.822; 4 studies)

Heterogeneity: Cochran Q=3.77; p=0.288, I^2=20.4%

Pooled OR of needing for reoperation: 1.23 (95% CI 0.26 to 5.8; p=0.797; 4 studies)

Heterogeneity: Cochran Q=5.83; p=0.12, I^2=48.5%

Study 3 Aiolfi A (2018)

Study details

Study type	Systematic review and meta-analysis
Country	US (n=5) and Europe (n=2)
Publication period	2014 to 2017
Study population and number	n=1,211 (7 studies; 686 MSA and 525 fundoplication) patients with GORD
Age and sex	Mean age ranged from 39.3 to 54 years; 51.1% male
Patient selection criteria	Inclusion criteria: studies comparing laparoscopic MSA with laparoscopic partial or total fundoplication.
Technique	Laparoscopic insertion of a magnetic ring: LINX® (Thorax Medical) MSA device Fundoplication: total (Nissen) or partial (Toupet) fundoplication
Follow up	Follow up: 6 to 12 months
Conflict of interest/source of funding	None

Analysis

Study design issues: This systematic review and meta-analysis compared early outcomes of MSA and fundoplication. This study was done according to the PRISMA statement. Three authors independently extracted data from eligible studies. Disagreements between authors were resolved by consensus; if no agreement could be reached, a fourth senior author, made the decision. Three investigators independently assessed the methodological quality of the papers using the Newcastle–Ottawa Scale.

Study population issues: Across the 7 studies, the sample size ranged from 24 to 415. There were no randomised controlled studies. All reports were observational, cohort studies. There was one prospective and one propensity score matched study. Each study reached a Newcastle–Ottawa Scale score of 6 or 7 (median 6.8), suggesting a good quality level.

Of the 1,211 patients, the mean BMI ranged from 23.9 to 30; the mean hernia size ranged from 1 to 2 cm; esophagitis grade B or above was present in 15.4% of patients and Barrett oesophagus in 16.2%. The operative time ranged from 42 to 73 minutes in the MSA group and from 76 to 118 minutes in the fundoplication group.

Other issues: The heterogeneity of PPI suspension rate, postoperative gas/bloat symptoms and ability to vomit was moderate in the meta-analysis. Possible sources of heterogeneity might be related to different types of fundoplication, definition and perception of postoperative symptoms, the lack of validated guidelines on PPI dose and timing of PPI suspension.

Key efficacy findings

Number of patients analysed: 1,211 (7 studies)

Regurgitation (2 studies): Comparing with preoperative baseline, a statistically significant improvement was noted for both procedures.

Hospital length of stay: MSA, 13 to 48 hours; fundoplication, 26 to 48 hours.

Estimated pooled mean difference for postoperative GORD-HRQL: −0.48 (95% CI -1.05 to 0.09; p=0.101; 6 studies, n=1,083)

Heterogeneity: I^2=0.0%; 95% CI 0.0 to 42.3%; p=0.82

Estimated pooled OR of PPI suspension: 0.81 (95% CI 0.42 to 1.58; p=0.548; 6 studies, n=1,098).

Heterogeneity: I^2=63.9%; 95% CI 12.7 to 85.1%; p=0.016

Estimated pooled OR of gas/bloat symptoms: 0.39 (95% CI 0.25 to 0.61; p<0.001; 5 studies, n=1,042)

Heterogeneity: I^2=49.6%; 95% CI 0.0 to 81.5%; p=0.09

Estimated pooled OR for the ability to vomit: 10.10 (95% CI 5.33 to 19.15; p<0.001; 6 studies, n=1,048)

Heterogeneity: I^2=44%; 95% CI 0.0 to 78.0%; p=0.112

Estimated pooled OR for the ability to belch: 5.53 (95% CI 3.73 to 8.19; p<0.001; 7 studies, n=1,107)

Heterogeneity: I^2=8.2%; 95% CI 0.0 to 73.2%; p=0.365

Key safety findings

Overall postoperative morbidity: MSA, 0 to 3%; fundoplication, 0 to 7%. There was no mortality.

Endoscopic dilation needed: MSA, 9.3%; fundoplication, 6.6%

Estimated pooled OR of endoscopic dilation: 1.56 (95% CI 0.61 to 3.95; p=0.119; 5 studies, n=535).

Heterogeneity: I^2=35%; 95% CI 0.0 to 75.6%; p=0.19

Reoperation:

- MSA, n=13 (12 device removals [1 for erosion] and 1 crural release)
- Fundoplication, n=11 (5 herniation of the fundic wrap, 3 persistent GORD, 2 retroesophageal abscess and 1 crural release)

Estimated pooled OR of reoperation: 0.54 (95% CI 0.22 to 1.34; p=0.183; 3 studies, n=1,187)

Heterogeneity: I^2=0.0%; 95% CI 0.0 to 4.1%; p=0.814

Study 4 Bell R (2019, 2020)

Study details

Study type	Randomised controlled trial (CALIBER; NCT02505945)
Country	US (21 sites)
Recruitment period	2015 to 2017
Study population and number	n=134 (laparoscopic insertion of a magnetic ring, n=47; twice-daily PPIs, n=87) Patients with GORD
Age and sex	Median 46 (range 21 to 76) years; 58% MALE
Patient selection criteria	Inclusion criteria: patients aged at least 21 years, with moderate-to-severe regurgitation symptoms while having once-daily PPIs for at least 8 weeks and actively seeking alternative, surgical treatment, and with objective confirmation of GORD. Patients also had body mass index <35 kg/m^2, abnormal pH testing results, normal oesophageal motility, hiatal hernia of <3 cm by endoscopy, and absence of Barrett's oesophagus or Los Angeles Classification Grade C or D esophagitis.
Technique	Laparoscopic insertion of a magnetic ring BID PPIs: twice-daily omeprazole, 20 mg, 30 minutes before breakfast and 30 minutes before dinner.
Follow up	12 months
Conflict of interest/source of funding	Conflicts of interest: Reginald Bell, F. Paul Buckley III, Jon Gould, Leena Khaitan, Shanu Kothari, and John Lipham receive honoraria from Ethicon for teaching services. The remaining authors disclose no conflicts. Funding: editorial support for this study was provided by Ethicon, Inc.

Analysis

Follow-up issues: Of the 152 enrolled patients, 3 patients withdrew before having the MSA procedure, and 1 patient failed to start twice-daily PPI therapy. During the follow-up period, in the twice-daily PPI therapy group, 4 patients lost to follow up and 9 patients discontinued the intervention (8 patients voluntarily withdrew and 1 patient discontinued because of adverse event). One patient who had twice-daily PPI therapy was excluded from analysis because the patient completed 6-month testing off of allocated intervention. In total, 134 patients were included in the 6-month analysis. Between 6 and 12 months, 9 patients were lost to follow up (2 patients in the MSA arm and 7 patients in the MSA crossover arm and step-down PPI arm).

Study design issues: This randomised, controlled, prospective, double-arm, crossover study compared the effects of MSA with twice-daily PPI therapy in patients with GORD (moderate-to-severe regurgitation despite once-daily PPI therapy). The primary end point was the percent of patients in both treatment arms who had elimination of moderate-to-severe regurgitation. Secondary endpoints included: (1) change from baseline scores (while on PPIs) in the GORD-HRQL questionnaire and RDQ, and percentage of patients achieving ≥50% decrease in GORD-HRQL score from baseline; (2) differences between treatment arms in oesophageal reflux parameters (number of reflux episodes and percentage of time with pH <4); and (3) PPI use.

The sample size needed for statistical significance was calculated a priori, with the assumptions that the success rate in the MSA group would be at least 70%, and the difference in success rates between the MSA and twice-daily PPI groups would be at least 30%, with a power calculation of 85%. Given these assumptions, a minimum of 108 patients randomised and followed to 6 months was needed for statistical significance. Additional participants were randomised (n=152) to ensure that a minimum of 50 participants was randomised to MSA and to ensure the sample size requirement of 108 participants, with final end-point data, was met.

Enrolled patients were randomly assigned 2:1 to either twice-daily PPI therapy (n=102) or laparoscopic MSA (primary MSA cohort) (n=50). Patients assigned to the MSA group had laparoscopic MSA by a study investigator trained and experienced in MSA. Postoperatively, patients were instructed to have a soft mechanical diet, including small bites of food regularly, to minimise capsular contracture around the MSA device, and patients were monitored by routine postoperative methods.

At 6 months, eligible patients in the twice-daily PPI arm could cross over to receive a laparoscopic MSA (MSA crossover cohort) if both moderate-severe regurgitation persisted, and impedance-pH testing showed persistent excess reflux burden. Those that did not qualify for crossover were placed on a reduced 20-mg daily dose of omeprazole (step-down cohort).

As a result, 79 patients in the twice-daily PPI arm completed 6-month impedance or pH testing per protocol (85 were completed, but 6 tests were deemed invalid, or the patient was not taking medication as assigned). Of the 79 patients, 31 patients met all crossover requirements and 48 were placed on a reduced dose of 20-mg omeprazole daily as the step-down arm. All patients then had additional evaluation at 12 months, including standardised quality of life surveys, RDQ and GORD-HRQL, as well as specific questions about bloating, diarrhoea, flatulence, and medication use.

Study population issues: At baseline, demographic variables and baseline disease characteristics between both treatment arms were similar, with the exception of the DeMeester scores (MSA, 40.3 [IQR 28.1 to 53.0]; twice-daily PPI, 30.9 [IQR 24.3 to 39.5]), which were significantly higher in the patients assigned to the MSA. The population was 88% white, 5% Hispanic, 3% African American, 3% Asian, and 1% reported other. The average length of PPI use for all patients was 8.4 years. The RCT was included in Zhuang (2021).

Key efficacy findings

Number of patients analysed: 134

Outcomes at 6 months (laparoscopic MSA, n=47; twice-daily PPI, n=87):

Foregut symptom questionnaire – MSA compared with twice-daily PPI:

Relief from moderate-to-severe regurgitation: 89% (42/47, including 79% reported no regurgitation and 10.6% mild regurgitation) compared with 10% (10/101, including 3% reported no regurgitation and 7% mild regurgitation), p<0.001

ITT: 84% (42/50) compared with 10% (10/102), p<0.001

RDQ regurgitation score:

- MSA: mean score improved from 4.2 at baseline to 1.6 at 6 months (1=no symptoms, 6=severe)
- Twice-daily PPI: mean score was 4.4 at baseline and 4.3 at 6 months

GORD-HRQL:

- ≥50% improvement in GORD-HRQL score: 81% (38/47) in the MSA group compared with 8% (7/87) in the BID PPI group, p<0.001
- MSA: mean GORD-HRQL score decreased from 24 at baseline while having treatment with PPIs to 6 at 6 months while not having treatment with PPIs
- Twice-daily PPI: mean GORD-HRQL score was 25 at baseline taking once-daily PPI to 24 at 6 months
- Difference between groups: p<0.002

Satisfaction with current condition: 81% (38/47) compared with 2% (2/87)

Discontinued PPI use: 91% (43/47) in the MSA arm at 6 months

Oesophageal reflux parameters: MSA compared with twice-daily PPI

- Normal number of reflux episodes (<57): 91% (40/44) compared with 58% (46/79), p<0.001
- Normal DeMeester score (<14.7): 89% (39/44) compared with 71% (56/79), p=0.059
- Mean DeMeester score: 8 compared with 18, p=0.059
- Normal acid exposures by percentage of time with pH<4: 89% (39/44) compared with 75% (59/79), p=0.065
- Mean oesophageal acid exposure (percentage of time with pH <4): 2% compared with 5%, p=0.065

Outcomes at 12 months: (MSA, n=44; laparoscopic MSA crossover, n=31; step-down PPI, n=49)

MSA crossover cohort at study completion (6 months postimplantation)

Relief of moderate-severe regurgitation: 94% (29/31) with 68% (21/31) reporting elimination of all regurgitation.

Median RDQ regurgitation scores: improved from 4 (IQR 3.25 to 4.75) off PPI and 3.5 (IQR 2.5 to 4) on PPI at baseline to 0 (IQR 0 to 1.125; p<0.001) at 6 months postimplantation.

Median GORD-HRQL: improved from 26 (IQR, 21 to 30) off PPI and 21 (IQR 18 to 27) on PPI at baseline to 4 (IQR 1 to 7) after MSA implantation (p<0.001).

>50% improvement in baseline GORD-HRQL on PPIs: 80.6% (25/31).

Median RDQ heartburn scores: improved from 3.5 (IQR 2.25 to 4.5) off PPI, 2.38 (IQR 1.5 to 3.6) on PPI to 0 (IQR 0 to 0.5; p<0.001).

Median DeMeester pH score: improved to 6 (IQR 2.2 to 17.6) postoperatively from 31.7 (IQR 25.2 to 36.8) preoperatively (p<0.001).

Normal DeMeester score: 70% (21/30) at 6 months postimplantation.

Step-down PPI cohort at study completion

Relief of moderate-severe regurgitation: 17% (8/48) with 1 of 48 reporting complete regurgitation resolution.

Median RDQ regurgitation, heartburn and GORD-HRQL scores: no statistically significant change from baseline (exact data not reported).

Median DeMeester score tested on daily PPIs remained elevated at 16.7 (IQR 1.9 to 164) and was normal in 54%.

Treatment results based on final treatment arm (MSA or PPI)

Resolution of moderate-severe regurgitation:

- MSA patients: 96% (72/75)
- Total MSA patients: 93% (71/78)
- Primary MSA patients: 98% (43/44)
- Twice-daily PPIs patients: 11%
- Step-down PPI patients: 19% (8/43) p<0.001 compared with MSA

Complete elimination of regurgitation: MSA, 73% (51/75); step-down PPI, 2%; p<0.001

Median RDQ score:

- MSA: 0 (IQR 0 to 0.5) at 12 months post-MSA implantation
- PPI: no significant improvement happened (exact data not reported)

GORD-HRQL: baseline, 30±10 off PPIs and 24±10 on daily PPIs; 6 months, 6; 12 months, 5; p<0.001

Successful change of ≥50% from baseline score on PPIs: 6 months, 81% (61/75); 12 months 93% (41/44); p<0.001

Dysphagia scores ≥3 (bothersome every day or worse): baseline, 27% of patients off PPIs, 15% of patients on PPIs; 6 months, 11% (8/75); 12 months (3/44); p=0.0184

Frequent or continuous bloating: baseline, 58% of patients off PPIs, 55% of patients on PPIs; 6 months, 15% (11/75); 12 months, 27% (12/44); p=0.0416.

No change was seen in the patient who had medical treatment.

PPIs discontinuation: MSA, 91% (68/75) at study completion

Median total oesophageal acid exposure at study completion:

- all MSA patients: baseline, 10.7% (IQR 7.7% to 13.9%); study completion, 1.3% (IQR, 0.4% to 5.3%), p<0.001
- primary MSA patients: baseline, 11.5% (IQR 7.9% to 14.8%) to 1.3% (IQR 0.2% to 5.3%); p<0.001

DeMeester scores in all MSA patients: baseline, 40.5 (IQR 25.7 to 49.5); study completion, 5.3 (IQR 1.2 to 18.5); normalisation, 70% (48/69)

Endoscopic evaluation: esophagitis in patients with confirmed abnormal oesophageal acid exposure was present at baseline in 35% (42/119) of the patients who completed 12-month evaluation (off PPI x 7 days), in 5 of 72 (7%) MSA patients at follow up, and persisted in 8 of 47 (17%) patients maintained on single-dose PPI.

Key safety findings

Laparoscopic MSA group – adverse events at 6 months:

Dysphagia: 32% (n=15), rated mild in 19% (n=9), moderate in 9% (n=4) and severe in 4% (n=2)

- Transient dysphagia (minimal or resolved by 6 months): n=13
- Ongoing dysphagia: n=2

Intervention needed for postoperative dysphagia:

- medication (oral corticosteroids): n=3
- endoscopic dilation: n=3
- surgical intervention (laparoscopic hiatal hernia repair): n=1

Other adverse events in both groups were minor and did not fit any particular pattern; details were not reported.

Laparoscopic MSA group – adverse events at 12 months:

Dysphagia: 39.6% (n=19) in MSA patients and 33.3% (n=10) in MSA crossover patients

No serious perioperative adverse events happened in any arm of the study.

Study 5 Bonavina L (2020)

Study details

Study type	Non-randomised comparative study (registry; NCT01624506)
Country	Austria, Germany, Italy and UK (22 centres)
Recruitment period	2009 to 2014
Study population and number	n=631 (MSA, n=465; fundoplication, n=166) patients with GORD
Age and sex	MSA: mean 46.6 years; 63.7% male Fundoplication: mean 56.3 years; 49.4% male
Patient selection criteria	Inclusion criteria: patients had a diagnosis of GORD confirmed by abnormal oesophageal acid exposure on a prolonged pH or pH impedance study and chronic reflux symptoms despite the daily use of medical therapy with PPIs. Patients with severe GORD were also included: large hiatal hernia (>3 cm diameter of the oesophageal hiatus), Barrett's oesophagus, motility disorder, and/or Grade C or D esophagitis by Los Angeles classification. Patients without advanced GORD characteristics were considered to have moderate GORD (abnormal oesophageal pH, reflux symptoms despite medication). Exclusion criteria: Patients had known conditions that would make it unlikely for them to complete the 3-year follow up (for example, life expectancy less than 3 years).
Technique	Laparoscopic insertion of a magnetic ring: The MSA device (LINX system) was placed using the minimal dissection technique. Fundoplication: Nissen fundoplication, 62%; Toupet fundoplication, 31%; other/unspecified fundoplication procedure, 7%
Follow up	3 years
Conflict of interest/source of funding	LB and TH received consulting fees from Torax Medical Inc. In the past. SS received a research grant from Torax Medical Inc. Ms. DeMarchi was an employee of Ethicon. LB, SS and TH declared no current conflict of interest. This work was sponsored and partially funded by Torax Medical, Inc.

Analysis

Study design issues: This prospective, multicentre, observational registry evaluated the long-term safety and effectiveness outcomes of MSA and fundoplication in clinical practice

Study population issues: At baseline, statistically significant differences in patient's characteristics were detailed in the table below. The proportion of patients with moderate or severe GORD was 90.8% and 9.2%, respectively, in the MSA group and was 18.1% and 81.9% in the fundoplication group. The median GORD-HRQL score was 22.0 in the MSA group and 23.0 in the fundoplication group (p=0.0620).

Measure	MSA (n=465)	Fundoplication (n=166)	P value
Age, years (mean±SD)	46.6±13.6	56.3±12.6	<0.0001
BMI (kg/m^2) (mean±SD)	25.7±3.7	27.81±4.0	<0.0001
Oesophagitis, % of patients			0.0130
None	53.0%	40.9%	
Grade A	31.7%	29.6%	
Grade B	13.5%	16.4%	
Grade C	1.1%	8.2%	
Grade D	0.7%	5.0%	
Barrett's oesophagus, % of patients	1.7%	12.7%	<0.0001
Hiatal hernia size, % of patients			<0.0001
None	19.7%	7.5%	
1 to 3 cm	78.9%	44.4%	
>3 cm	1.4%	48.1%	

Other issues: Two groups were not comparable in some baseline characteristics, suggesting the results were confounded. Also, the procedure to implant MSA has evolved to include full crural and gastroesophageal junction dissection as opposed to the minimal dissection used in this study. The timeframe for this study would determine if the procedural modifications were relevant to the outcomes in this study population. The current procedure theoretically might provide better outcomes for patients as compared with those done under the "minimal dissection" protocol as the hiatal hernia was often addressed.

Key efficacy findings

Number of patients analysed: 631

Procedure time and hospital stay: MSA, n=459; fundoplication, n=163

- Mean procedure time, minutes: MSA, 43.2±19.7 minutes; fundoplication, 79.7±47.7 minutes
- Length of stay <24 hours: MSA, 36.1%; fundoplication, 11.4%
- Length of stay >48 hours: MSA, 50.8%; fundoplication, 72.3%

238 of 465 patients were German patients, have longer stay built into reimbursement.

Clinical effectiveness of MSA and fundoplication pre- and postsurgery

Measure	MSA	Fundoplication
Satisfaction with current condition (from GORD-HRQL)		
Baseline	4.6% (21/460; 95% CI 2.7% to 6.5%)	3.7% (6/164; 95% CI 0.8% to 6.5%)
12 months	75.3% (326/433; 95% CI 71.2% to 79.4%)	77.2% (122/158; 95% CI 70.7% to 83.8%)
24 months	78.9% (254/322; 95% CI 74.4% to 83.3%)	83.3% (90/108; 95% CI 76.3% to 90.4%)
36 months	78.2% (230/294; 95% CI 73.5% to 82.9%)	76.5% (65/85; 95% CI 67.5% to 85.5%)

Measure	MSA	Fundoplication
GORD interfering with sleep		
Baseline	73.3% (333/454; 95% CI 69.3% to 77.4%)	78.0% (128/164; 95% CI 71.7% to 84.4%)
12 months	11.9% (50/419; 95% CI 8.8% to 15.0%)	9.6% (15/157; 95% CI 5.0% to 14.2%)
24 months	11.7% (37/315; 95% CI 8.2% to 15.3%)	5.5% (6/109; 95% CI 1.2% to 9.8%)
36 months	9.0% (26/290; 95% CI 5.7% to 12.3%)	10.7% (9/84; 95% CI 4.1% to 17.3%)
Ability to belch		
Baseline	96.7% (441/456; 95% CI 95.1% to 98.3%)	93.9% (154/164; 95% CI 90.2% to 97.6%)
12 months	96.7% (406/420; 95% CI 94.9% to 98.4%)	88.5% (138/156; 95% CI 83.4% to 93.5%)
24 months	97.2% (308/317; 95% CI 95.3% to 99.0%)	92.5% (99/107; 95% CI 87.5% to 97.5%)
36 months	97.6% (284/291; 95% CI 95.8% to 99.4%)	91.7% (77/84; 95% CI 85.8% to 97.6%)
Ability to vomit		
Baseline	96.6% (343/355; 95% CI 94.8% to 98.4%)	92.0% (115/125; 95% CI 87.2% to 96.8%)
12 months	89.7% (191/213; 95% CI 85.6% to 93.8%)	55.8% (29/52; 95% CI 42.3% to 69.3%)
24 months	85.8% (133/155; 95% CI 80.3% to 91.3%)	52.6% (20/38; 95% CI 36.7% to 68.5%)
36 months	91.2% (134/147; 95% CI 86.6% to 95.8%)	68.0% (17/25; 95% CI 49.8% to 86.2%)
Use of PPIs		
Baseline	97.8% (453/463; 95% CI 95.6% to100%)	95.8% (158/165; 95% CI 91.6% to 100%)
12 months	18.9% (81/428; 95% CI 15.2% to 22.6%)	19.7% (31/157; 95% CI 13.5% to 26.0%)
24 months	21.4% (74/346; 95% CI 17.1% to 25.7%)	18.1% (21/116; 95% CI 11.1% to 25.1%)
36 months	24.2% (76/314; 95% CI 19.5% to 28.9%)	19.5% (17/87; 95% CI 11.2% to 27.9%)
Willingness to have surgery again		
12 months	89.5% (366/409; 95% CI 86.5% to 92.5%)	91.1% (143/157; 95% CI 86.6% to 95.5%)
24 months	90.6% (281/310; 95% CI 87.4% to 93.9%)	94.4% (102/108; 95% CI 90.1% to 98.8%)
36 months	93.1% (270/290; 95% CI 90.2% to 96.0%)	94.0% (79/84; 95% CI 89.0% to 99.1%)

GORD-HRQL scores and change from baseline

Measure	MSA		Fundoplication	
	Mean GORD-HRQL±SD Median (min, max)	Mean GORD-HRQL±SD Median (min, max; 95% CL) p value	Mean GORD-HRQL±SD Median (min, max)	Mean GORD-HRQL±SD Median (min, max; 95% CL) p value
Baseline	n=457 22.0±9.1 22.0 (0.0, 47.0)		n=163 23.6±9.8 23.0 (3.0, 47.0)	

Measure	MSA		Fundoplication	
Paired baseline/month 12	n=414 21.9±9.0 22.5 (0.0, 46.0)		n=152 23.4±9.9 23.0 (3.0, 47.0)	
Month 12	n=418 5.2±6.4 3.0 (0.0, 42.0)	n=414 -16.7±10.0 -17.0 (-41.0, 21.0; 95% CL -17.6 to -15.7) p<0.001	n=154 4.9±7.2 3.0 (0.0, 48.0)	n=152 -18.5±11.5 -19.5 (-45.0, 20.0; 95% CL -20.3 to -16.6) p<0.001
Pared baseline/month 24	n=296 21.6±9.2 22.0 (0.0, 41.0)		n=103 23.9±10.1 24.0 (3.0, 47.0)	
Month 24	n=300 4.9±6.1 2.0 (0.0, 35.0)	n=296 -16.7±10.6 -17.0 (-39.0, 28.0; 95% CL -17.9 to -15.5) p<0.001	n=105 3.9±4.4 3.0 (0.0, 19.0)	n=103 -20.0±10.0 -20.0 (-45.0, 0.0; 95% CL -22.0 to -18.1) p<0.001
Paired baseline/month 36	n=278 21.3±9.3 22.0 (0.0, 41.0)		n=80 22.5±9.7 22.5 (3.0, 47.0)	
Month 36	n=283 4.6±6.0 3.0 (0.0, 39.0)	n=278 -16.6±10.2 -18.0 (-41.0 to 12.0; 95% CL -17.8 to -15.4) p<0.001	n=82 4.9±7.1 3.0 (0.0 to 45.0)	n=80 -17.8±10.6 -18.0 (-39.0, 17.0; 95% CL -20.1 to -15.4) p<0.001

Dysphagia results from MSA and Fundoplication over study duration

Timepoint	MSA	Fundoplication	Q7 p value
Baseline			
Score	1.0±1.3	1.3±1.5	0.0227
% Q7>3.0	15.7%	24.4%	0.0174
12 months			
Score	0.8±1.1	0.6±1.1	-
% Q7>3.0	8.8%	7.6%	
24 months			
Score	0.6±0.9	0.4±0.9	-

Timepoint	MSA	Fundoplication	Q7 p value
% Q7>3.0	4.4%	4.6%	
36 months			
Score	0.5±0.9	0.4±1.1	-
% Q7>3.0	3.8%	4.8%	

Key safety findings

Intraoperative complication rate: MSA (n=459), 1.8%; fundoplication (n=163), 1.2%

Procedure-related complication rate: MSA (n=459), 2.0%; fundoplication (n=163), 1.8%

Healthcare needed with MSA and fundoplication

Measure	MSA (n=459)	Fundoplication (n=163)
Outpatient clinic visits		
12 months	18.9%	15.3%
24 months	14.7%	12.9%
36 months	10.5%	8.0%
Return to clinic for GORD symptoms		
12 months	58.5%	54.2%
24 months	80.4%	86.7%
36 months	87.9%	100%
Return to clinic because of procedural complaint/complication		
12 months	39.3%	41.7%
24 months	19.2%	20.0%
36 months	15.2%	0.0%
Surgical intervention		
12 months	1.6%	1.9%
24 months	1.2%	0.0%
36 months	0.6%	0.0%
Device removal		
12 months	1.5% (n=7)	NA
24 months	2.0% (n=9)	NA
36 months	2.4% (n=11)	NA

Surgical intervention: The intervention for the MSA group was the removal of the device for dysphagia (45%), ongoing GORD (18%), vomiting/regurgitation (18%), gastric pain (9.5%) and need for MRI (9.5%). There were no complications noted during the removal procedures. Two patients had fundoplication at the time of the device removal. The interventions for the fundoplication group were revision of a Nissen wrap because of

ongoing GORD, reherniation and a sigmoid resection secondary to diverticulitis. No complications or ongoing sequelae were reported.

Study 6 Ayazi S (2020a)

Study details

Study type	Case series (retrospective)
Country	US (single centre)
Recruitment period	2013 to 2018
Study population and number	n=553 patients with GORD
Age and sex	Mean 54.7 years; 38.2% (211/553) male
Patient selection criteria	Inclusion criteria: patients with GORD or laryngopharyngeal reflux symptoms despite being prescribed maximal antisecretory therapy who were 18 years or older were included. Objective evidence of reflux disease was based on increased oesophageal acid exposure on pH monitoring or a positive impedance-pH result. Exclusion criteria: patients with a history of oesophageal or gastric surgical procedure; significant oesophageal dysmotility; gross anatomic abnormality, such as oesophageal stricture; or a known allergy to titanium.
Technique	Laparoscopic insertion of a magnetic ring: the implant procedure was done laparoscopically and consisted of complete posterior mediastinal oesophageal mobilisation with restoration of intra-abdominal oesophageal length (≥3 cm) and interrupted posterior crural closure (without pledgets or mesh). The LINX device placement was at the level of the gastro-oesophageal junction with the posterior vagus nerve trunk located on the outside of the magnetic ring. A “minimal dissection” technique was used in patients with little to no hiatal hernia during the beginning of the procedure employment.
Follow up	Mean 10.3 months
Conflict of interest/source of funding	Disclosures outside the scope of this work: one author (BJ) was a paid consultant to Medtronic and Johnson & Johnson.

Analysis

Follow-up issues: Patients were assessed at 2 weeks, 6 weeks, 6 months, and 12 months after the procedure.

Study design issues: This study evaluated the outcomes of MSA in patients with GORD and determined the factors predicting favourable outcomes. Disease-related quality of life measures included GORD-HRQL and RSI.

Patients were assessed for resolution of their reflux symptoms, use of antisecretory medications, and procedure-related complications. Length of hospital stay, need for readmission within 90 days after operation, and need for postoperative dilation and device removal were also recorded.

A 50% improvement in the GORD-HRQL total score compared with baseline on antisecretory therapy was considered clinically significant. Favourable outcomes were defined as freedom from PPIs and ≥50%

improvement in GORD-HRQL total score. Persistent dysphagia was defined as a postoperative dysphagia score >3 on GORD-HRQL “difficulty swallowing” item at 3 months or later after MSA.

Study population issues: At baseline, 46.1% of patients had oesophagitis and 88.1% had hernia (≤3 cm, 67.5%; ≥3 cm, 14.8%; paraesophageal hernia, 5.8%); and the mean DeMeester score was 33.9±29.4.

Key efficacy findings

Number of patients analysed: 553

Patient satisfaction with the procedure: 86.7%

Free of PPI use: 92.7%

≥50% improvement in GORD-HRQL total score: 84%

Comparison of pertinent components of GORD-HRQL and RSI before and after operation

Measurement	Before operation	After operation	P value
GORD-HRQL scoring, mean±SD			
Heartburn score	14.7±8.7	3.1±5.8	<0.001
Regurgitation score	12.7±9.0	2.6±5.0	<0.001
Total score	33.8±18.7	7.2±9.0	<0.001
RSI scoring			
Difficulty swallowing score, mean±SD	1.7±1.6	1.0±1.3	<0.001
Difficulty swallowing score ≥3	33.7%	15.8%	<0.001
Total score, mean±SD	22.2±10.9	8.7±8.7	<0.001
LOS resting characteristic (n=109)			
Resting pressure, mmHg	23.1±14.3	27.7±14.1	0.009
Overall length, cm	2.9±0.8	3.2±0.9	0.003
Intra-abdominal length, cm	1.0±1.0	1.7±1.2	0.001
Composite pH score	32.9±31.9	12.3±25.9	<0.001

Objective and subjective outcomes across groups stratified by LINX size

Post measure	Small (sizes 13 and 14; n=327)	Medium (size 15; n=138)	Large (sizes 16 and 17; n=85)	P value
GORD-HRQL total score, mean±SD	9.0±11.1	6.0±7.7	5.7±8.3	0.0034
Favourable surgical outcome	77.4%	85.3%	80.0%	0.3521
Persistent dysphagia	20.2%	12.3%	11.9%	0.0991
DeMeester score, mean±SD	7.2±10.2	18.8±33.2	21.0±42.8	<0.0001
Normalisation of DeMeester score	82.4%	69.1%	65.7%	0.0349

Proportion of patients having a favourable outcome: 80%

Proportion of patients having normalisation of their oesophageal acid exposure: 76.1%

Independent predictors of favourable outcome after MSA using multivariable logistic model

Variable	Parameter (SE)	OR (95% CI)	P value
Age (<45 years)	1.43 (0.66)	4.17 (1.14 to 15.23)	0.0305
Sex (male)	0.91 (0.42)	2.49 (1.09 to 5.66)	0.0301
GORD-HRQL total score (>15)	2.01 (0.41)	7.47 (3.32 to 16.81)	<0.0001
Abnormal DeMeester score (>14.7)	0.93 (0.41)	2.55 (1.14 to 5.68)	0.0225

Discharged home on the day of operation: 93% (n=514)

At least 1 overnight stay: 7% (n=39), with a mean of 1.5±1.0 nights

Key safety findings

Major complications: n=2 (0.4%)

- CO_2 retention needing reintubation: n=1
- mediastinal abscess needing drainage and intravenous antibiotic: n=1

Minor complications: n=49 (8.9%)

- poor postoperative pain control: n=4
- significant nausea during immediate postoperative period: n=5
- hypoxia needing supplemental oxygenation: n=7

- lethargy: n=3
- abdominal pain needing additional evaluation: n=5
- bothersome nausea or vomiting needing emergency department visit: n=11
- dysphagia needing hospital admission: n=7
- abdominal wall hematoma at gastric pacer insertion site: n=1
- deep vein thrombosis: n=1
- urinary retention: n=1
- cardiac arrhythmia: n=1
- dyspnoea needing additional workup: n=2
- aspiration pneumonia: n=1

There was 1 death from causes unrelated to placement of the LINX device.

Postoperative endoscopic dilation: n=169 (99 patients needed 1, and 70 needed more than 1)

Indications for dilation:

- dysphagia: n=129 (23.3%)
- chest pain: n=14 (2.5%)
- both dysphagia and chest pain: n=26 (4.7%)

Device removal: n=37 (6.7%)

Reasons for device removal:

- troublesome dysphagia or chest pain not responding to dilation: n=20 (3.6%) Of these patients, 1 patient had pseudoachalsia not responding to dilation and 1 patient needed explanation 2 days after device implantation because of acute dysphagia
- recurrence of hernia and migration of the device: n=3
- recurrence of hernia and mediastinal abscess: n=1
- worsening typical reflux symptoms, n=4
- worsening atypical reflux symptoms, n=3
- possible titanium allergy, n=1
- unexplained leukocytosis: n=1
- need for subsequent operation: n=2
    - esophagectomy for oesophageal adenocarcinoma: n=1
    - gastrectomy for severe gastroparesis: n=1
- removal indicated by device malfunction: n=2

- disconnected device: n=2

Readmission:

- Readmission within 30 days from operation: 4.2% (n=23)
- Readmission between 30 and 90 days from operation: 1.4% (n=8)
- One patient was readmitted 3 times, 2 patients needed 2 readmissions, and the remaining patients were readmitted only once after the procedure.

Study 7 Ferrari D (2020)

Study details

Study type	Case series (retrospective)
Country	Italy (single centre)
Recruitment period	2007 to 2014
Study population and number	n=124 patients with GORD
Age and sex	Mean 44 years; 66.9% (88/124) male
Patient selection criteria	Initial inclusion criteria: persistent reflux symptoms despite optimal PPI therapy, abnormal oesophageal acid exposure confirmed by ambulatory oesophageal pH monitoring, hiatus hernia <3 cm, esophagitis < grade B, body mass index <35 kg/m^2, and absence of specific motility disorders. With further clinical experience and research, the criteria have been expanded to include patients with larger hiatus hernia, short Barrett's oesophagus, and mild oesophageal dysmotility. Exclusion criteria: patients with recurrent GORD after failed fundoplication or other surgical/endoscopic procedures at the esophagogastric junction, and to those with known history of nickel allergy or eating disorders.
Technique	Laparoscopic insertion of a magnetic ring: the MSA device was implanted via laparoscopy. Under general anaesthesia, the esophago-gastric junction was exposed after incision of the peritoneal reflection. The posterior vagus nerve was identified and separated from the oesophagus for a length of about 1 cm. No short gastric vessels were divided. The oesophageal circumference was measured with an appropriate magnetic sizer inserted through the retroesophageal tunnel. A minimal or formal posterior crural repair was done depending on the size of the hiatal defect and the degree of hiatus hernia.
Follow up	Median 9 years (IQR 2)
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Two patients died during the follow up for unrelated reasons (exact year not reported).

Study design issues: This study reported the long-term outcomes of patients followed for a minimum of 6 years. GORD-HRQL, use of PPI, and oesophageal pH monitoring parameters were compared with patients' own preoperative data. Favourable outcome of the MSA procedure was defined as ≥50% improvement in GORD-HRQL total score and PPI discontinuation. GORD-HRQL, use of PPI, and oesophageal acid exposure were compared with baseline.

In terms of surgical approach, over the study period and starting from 2014, modifications of the surgical technique occurred. First, formal mediastinal dissection became routine practice; second, a new generation MSA device was introduced for use in magnetic resonance up to 1.5 T; third, a new generation sizer device for measuring the oesophageal circumference was introduced.

Study population issues: Although 211 patients with GORD having laparoscopic MSA were followed up for less than 6 years, this study reported the long-term (6 to 12 years) safety and efficacy outcomes in 124 patients. Of the 124 patients, 21 patients had esophagitis (grade A, n=11; grade B, n=9; grade C, n=1), 4 patients had Barrett's oesophagus, and 106 patients had hiatal hernia (1 cm in length, n=37; 2 cm in length, n=44, 3 cm in length, n=20; ≥4 cm in length, n=5).

Key efficacy findings

Number of patients analysed: 124

Average percent reduction (±SD) of total GORD-HRQL score:

- year 6: 77%±32%
- year 7: 80%±29%
- year 8: 82%±25%
- year 9: 86%±22%
- year 10: 92%±10%
- year 11: 97%±4%
- year 12: 95%±8%

No oesophageal symptom (grade 0 to 1): 74.2% (n=92)

Mean total GORD-HRQL score: baseline, 19.9; final follow up, 4.01; $p<0.001$

Proportion of patients who met the criteria of favourable long-term outcome: 89%

Clinically significant improvement in GORD-HRQL is also reflected by the reported patient satisfaction, which occurred in 92.7% of patients.

Grade 2 to 4 regurgitation: baseline, 59.6%; final follow up, 9.6%; $p<0.01$

Daily use of PPIs: complete reduction, 79%; at least 50% reduction, 89.5%

Upper gastrointestinal endoscopy after 6 years of follow up:

- Hiatus hernia: 6.5% (n=7)
- Grade A oesophagitis, 4.7% (n=5)
- Incomplete intestinal metaplasia, 2.8% (n=3)

Hill grade (n=45): at the latest endoscopic follow up, 41 patients (91%) retained their preoperative Hill grade I or improved, 3 (7%) remained stable, and in 1 (2%) patient the Hill grade worsened ($p<0.01$)

Oesophageal pH measurements (mean±SD) off PPIs

Measure	Baseline (n=124)	6 to 12 years (n=91)	P value
Total time (%)			
pH<4	9.7±6.4	4.2±4.9	<0.001
Upright	9.7±7.8	4.6±4.9	<0.001
Supine	8.3±9.6	3.3±7.4	<0.001
Reflux episodes			
Total number	92.2±92.2	71.5±67.7	0.125
Number lasting >5 minutes	6.1±6.0	4.3±5.8	0.036
Longest (minutes)	32.9±34.2	19.6±31.5	0.005
DeMeester score	40.7±26.5	16.3±18.8	<0.001

Oesophageal pH testing off PPI therapy showed that the mean percentage of time that pH was <4 decreased from 9.7% at baseline to 4.2% at latest follow up (p<0.001).

Eighty-nine percent of patients who completed oesophageal pH monitoring at 6- to 12 years follow up had either normal oesophageal acid exposure or had at least a 50% reduction compared with baseline.

Proportion of patients with a successful clinical outcome: 81%

Long-term results in 32 patients with follow up more than 10 years:

- GORD-HRQL score: median 2
- Dysphagia: 0
- Ability to belch: n=32 (100%)
- Ability to vomit: n=29 (90.6%)
- Occasional PPI use: n=7 (21.8%)
- Daily PPI use: n=3 (9.4%)
- Overall patient satisfaction: n=30 (93.8%)

Predictors of long-term clinical success:

Univariate analysis: age at intervention <40 years, preoperative GORD-HRQL total score >15, duration of symptoms, regurgitation, atypical symptoms and absence of generalised anxiety disorder were statistically significant as independent predictors of clinical success.

Multivariate analysis: independent predictive variables of successful outcome were confirmed to be age <40 years (OR 4.17) and GORD-HRQL score >15 (OR 4.09).

Key safety findings

Laparoscopic device removal: 9.2% (n=31) the most common one-stage remedial procedure was a laparoscopic Toupet fundoplication (n=18).

Main reasons for MSA device removal

	<6 years (n=28)	6 to 12 years (n=3)
Erosion	6	0
Regurgitation	6	0
Heartburn	5	1
Dysphagia	5	1
“Foreign body” sensation	2	0
Odynophagia	1	0
Pharyngodinia	1	0
Chronic cough	1	0
Need of magnetic resonance study	1	1

Study 8 Ferrari D (2021)

Study details

Study type	Non-randomised comparative study (retrospective)
Country	Italy (single centre)
Recruitment period	Not reported
Study population and number	n=336 (non-severe GORD, n=234; severe GORD, n=102) patients with GORD
Age and sex	Non-severe GORD: mean 45.2 years, 69.3% male Severe GORD: mean 46.2 years, 62.8% male
Patient selection criteria	Inclusion criteria: age between 18 and 65 years and a minimum postoperative follow up of 6 months. Inclusion criteria for the severe GORD group: LOS basal pressure <5 mmHg or distal oesophageal amplitude <30 mmHg on oesophageal manometry, biopsy-proven Barrett's metaplasia, presence of stricture or grade C to D esophagitis on upper gastrointestinal endoscopy, and/or DeMeester score >50 on ambulatory oesophageal pH monitoring. Exclusion criteria: previous esophagogastric surgery and documented allergy to titanium or nickel.
Technique	Laparoscopic insertion of a magnetic ring: under general anaesthesia, the gastroesophageal junction was dissected, the posterior vagus nerve was identified and separated from the oesophageal wall, and the oesophagus was encircled with a Penrose drain. No short gastric vessels were divided. In patients with hiatal hernia >3 cm, mediastinal dissection and posterior crural repair were routinely done. The oesophageal circumference is measured with a magnetic sizer device. The correct size of MSA was decided by increasing 2 or 3 beads from the point of sizer release. Finally, the LINX device was inserted through the retroesophageal tunnel and locked anteriorly.
Follow up	Severe GORD: median 24 months (IQR 75), mean 49.6 months Non-severe GORD: median 32 months (IQR 84), mean 50.8 months
Conflict of interest/source of funding	Conflict of Interest: the research was done in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. Funding: this study was supported by A.I.R.ES. (Associazione Italiana Ricerca ESofago).

Analysis

Follow-up issues: Patients were followed up at 2 weeks, 6 months and then each year after the operation.

Study design issues: This study evaluates the short- and long-term effectiveness of MSA in patients with severe GORD compared with patients with mild-to-moderate disease. Postoperative assessments included

GORD-HRQL, FOSS, upper gastrointestinal endoscopy, barium swallow study, oesophageal manometry and oesophageal pH monitoring. A FOSS score >1 identified severe postoperative dysphagia.

Study population issues: At baseline, demographic characteristics were similar between the 2 groups. However, patients with severe GORD had a statistically significantly higher rate of preoperative dysphagia (severe GORD, 12%; non-severe GORD, 6%; p=0.0460), higher scores of GORD-HRQL questionnaire (severe GORD, 21.0±7.5; non-severe GORD, 19.2±7.7; p=0.0479), higher PPI use (severe GORD, 86%; non-severe GORD, 71%; p=0.0034), and higher DeMeester score (severe GORD, 58.3±33.5; non-severe GORD, 26.2±12; p<0.0001). The main preoperative reasons accounting for disease severity were DeMeester score >50 (49% of patients), biopsy-proven Barrett's metaplasia (33.3%), and LOS basal pressure <5 mmHg (27.5%).

Key efficacy findings

- Number of patients analysed: 336

Intraoperative and clinical course of patients with severe or non-severe GORD

	Non-severe GORD (n=234)	Severe GORD (n=102)	P value
Duration of intervention, minutes	61.4±30	61.1±24.5	0.9292
Number of beads	13.9±1.3	14.1±1.4	0.2062
Crural repair	40.2% (n=94)	49% (n=50)	0.1345
Length hospital stay, days	1.4±0.7	1.2±0.6	0.0125

Postoperative outcomes in patients having MSA for severe or non-severe GORD

	Non-severe GORD (n=234)	Severe GORD (n=102)	P value
Follow up, months	50.8±44.2	49.6±43.7	0.8185
GORD-HRQL score	3.8±5.7	3.9±4.8	0.8870
Use of PPI	13.2% (n=31)	15.6% (n=16)	0.5597
LOS resting pressure, mmHg	24.3±10.4	21.4±12.3	0.0271
LOS overall length, cm	3.2±1.3	3.1±1.4	0.5270
LOS abdominal length, cm	1.4±1.4	1.4±1.5	1.000
DEA, mmHg	82.4±44.4	66.8±28.9	0.0011
Acid exposure time	3.6±4.4%	4.5±4.4%	0.0856
DeMeester score	13.4±15.9	17±16.3	0.0591
DeMeester >14.7	27.8% (n=20)	41.7% (n=15)	0.1476

Overall, 122 patients had oesophageal manometry at a median of 12 months (IQR = 30) after surgery, and 108 patients had postoperative oesophageal pH monitoring at a median of 28 months (IQR 51) after surgery.

Key safety findings

Postoperative complications in patients having MSA for severe or non-severe GORD

	Non-severe GORD (n=234)	Severe GORD (n=102)	P value
Follow up, months	50.8±44.2	49.6±43.7	0.8185
Occasional postoperative dysphagia	14.1 (n=33)	25.4% (n=26)	0.0124
Recurrent hiatal hernia	2.6% (n=6)	3.9% (n=4)	0.5209
Endoscopic dilation	2.1% (n=5)	2.9% (n=3)	0.6562
Device removal	10.2% (n=24)	7.8% (n=8)	0.4903

Study 9 Ayazi S (2020b)

Study details

Study type	Non-randomised comparative study (retrospective)
Country	US (single centre)
Recruitment period	2013 to 2017
Study population and number	n=350 (no hiatal hernia, n=65; small hiatal hernia, n=205, large hiatal hernia, n=58; paraesophageal hernia, n=22) patients with GORD
Age and sex	Mean 53.5 years; 40.3% (141/350) male
Patient selection criteria	Inclusion criteria: symptomatic GORD patients 18 years or older with persistent GORD or laryngopharyngeal reflux symptoms despite maximal antisecretory therapy and objective evidence of reflux disease based on increased oesophageal acid exposure on pH monitoring or a positive impedance-pH. Exclusion criteria: patients with a previous history of oesophageal or gastric surgery, gross anatomic abnormalities such as oesophageal stricture, significant oesophageal dysmotility or a known allergy to titanium.
Technique	Laparoscopic insertion of a magnetic ring: this procedure was done laparoscopically and consisted of complete posterior mediastinal oesophageal mobilisation with restoration of intra-abdominal oesophageal length (≥ 3 cm), interrupted posterior crural closure (without pledgets or mesh) and device placement at the level of the gastro-oesophageal junction with the posterior vagus nerve trunk located on the outside of the magnetic ring (LINX device).
Follow up	Mean 13.6 months (SD 10.4)
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were followed up at 2 weeks, 6 weeks, 3 months and then yearly after surgery.

Study design issues: This study compared the outcome of MSA across the spectrum of hiatal hernias commonly encountered in patients with GORD and reviewed the pattern of hiatal hernia recurrence. Patients were divided into 4 groups based on hiatal hernia status: no hiatal hernia, small hiatal hernia (< 3 cm), large hiatal hernia (≥ 3 cm), and paraesophageal hernia. Patient satisfaction, GORD-HRQL and RSI data, freedom from PPI, need for postoperative dilation, length of hospitalisation, 90-day readmission rate, need for device removal, and hiatal hernia recurrence were compared between groups.

Study population issues: At baseline, 285 of the 350 patients were found to have a hiatal hernia. Patients with a large or paraesophageal hernia were statistically significantly older compared with those with a small or no hernia (60.4 [SD 10.7] compared with 51.5 [SD 14], p<0.0001). There was also a higher percentage of women

among those with large or paraesophageal hernia (70% compared with 56.7%, p=0.037). The total sample of 350 patients was likely to be covered in Ayazi (2020a).

Key efficacy findings

- Number of patients analysed: 350

Subjective and objective outcome measures 1 year after MSA

Measurement	% (n)	No hiatal hernia, % (n)	Small hiatal hernia, % (n)	Large hiatal hernia, % (n)	Paraesophageal hernia, % (n)	p value
Total	100% (n=350)	18.6% (n=65)	58.6% (n=205)	16.6% (n=58)	6.2% (n=22)	N/A
Satisfaction from surgery	n=277					
No	11.2% (n=31)	13.3% (n=6)	12.1% (n=20)	7.8% (n=4)	6.2% (n=10	0.73
Yes	88.8% (n=246)	86.7% (n=39)	87.9% (n=145)	92.2% (n=47)	93.8% (n=15)	
GORD-HRQL total score clinical improvement	n=280					
No	20.7% (n=58)	20.9% (n=9)	22.2% (n=38)	18.0% (n=9)	12.5% (n=2)	0.77
Yes	79.3% (n=222)	79.1% (n=34)	77.8% (n=133)	82.0% (n=41)	87.5% (n=14)	
Normalisation of acid exposure	n=193					
DeMeester score <14.7	74.1% (n=143)	71.1% (n=27)	79.3% (n=88)	65.6% (n=21)	58.3% (n=7)	0.21
Freedom from PPI use	n=282					
Yes	91.8% (n=259)	93.2% (n=41)	91.8% (n=156)	90.4% (n=47)	93.8% (n=15)	0.96
No	8.2% (n=23)	6.8% (n=3)	8.2% (n=14)	9.6% (n=5)	6.2% (n=1)	

There was an improvement in the overall prevalence of dysphagia when compared with baseline (11.7 compared with 35%, p<0.001).

Of the patients that returned for high-resolution manometry (n=95) at 1-year after MSA, there was no difference in oesophageal function (peristalsis or pressure) when compared with preoperative values.

Key safety findings

Hospital stay and complication and readmission rates (within 90 days)

Measurement	% (n)	No hiatal hernia, % (n)	Small hiatal hernia, % (n)	Large hiatal hernia, % (n)	Paraesophageal hernia, % (n)	p value
Total	100% (n=350)	18.6% (n=65)	58.6% (n=205)	16.6% (n=58)	6.2% (n=22)	
Hospitalisation						
Same day discharge	92.3% (n=323)	93.9% (n=61)	95.6% (n=196)	84.5% (n=49)	77.3% (n=17)	0.002
≥1 day hospital stay	7.7% (n=27)	6.1% (n=4)	4.4% (n=9)	15.5% (n=9)	22.7% (n=5)	
Readmission within 90 days	5.4% (n=19)	0.0% (n=0)	6.8% (n=14)	3.5% (n=2)	13.7% (n=3)	0.049
Major complications	0.6% (n=2)	0.0% (n=0)	0.0% (n=0)	3.4% (n=2)	0.0% (n=0)	
Minor complications	10.6% (n=37)	3.1% (n=2)	11.2% (n=23)	10.4% (n=6)	27.3% (n=6)	
Overall complications	11.1% (n=39)	3.1% (n=2)	11.2% (n=23)	13.8% (n=8)	27.3% (n=6)	0.015
Hiatal hernia recurrence on upper endoscopy	n=24	n/a	n=20	n=1	n=3	

Major complications included CO_2 retention requiring reintubation (n=1) and mediastinal abscess requiring drainage and intravenous antibiotic (n=1).

Minor complications included poor postoperative pain control (n=2), significant nausea during immediate postoperative period (n=3), hypoxia requiring supplemental oxygenation (n=6), lethargy (n=2), abdominal pain needing further evaluation (n=5), persistent nausea and vomiting (n=8), abdominal wall hematoma at gastric pacer insertion site (n=1), DVT (n=1), urinary retention (n=1), and dyspnoea needing further workup (n=2).

Hiatal hernia recurrence: recurrence rate increased in a stepwise fashion with an increase in preoperative hiatal hernia size (0%, 10.1%, 16.6% and 20%, p=0.032). Patients with a minimal dissection had a higher hiatal hernia recurrence rate compared with those with a full dissection (21% compared with 7.9%, p=0.033). Of 24 patients found to have hiatal hernia recurrence on endoscopy, 7 needed reoperation. Patient with minimal dissection was more likely to need reoperation compared with those with a full dissection (10.5% compared with 1.5%, p=0.0133).

Rate of dysphagia, need for dilation or device removal

Measurement	% (n)	No hiatal hernia, % (n)	Small hiatal hernia, % (n)	Large hiatal hernia, % (n)	Paraesophageal hernia, % (n)	p value

Dysphagia	15.3% (n=41)	15.8% (n=6)	15.7% (n=31)	5.8% (n=3)	5.9% (n=1)	0.08
Need for endoscopic dilation	23.4% (n=82)	20.0% (n=13)	26.3% (n=54)	24.1% (n=14)	4.5% (n=1)	0.12
Device removal	5.1% (n=18)	6.1% (n=4)	6.4% (n=13)	1.7% (n=1)	0.0% (n=0)	0.28

All the removals were for persistent dysphagia or oesophageal spasm unresponsive to endoscopic dilation. There were no device erosions in this study.

Study 10 DeMarchi J (2021)

Study details

Study type	Review of the MAUDE database and the Ethicon's complaint database
Country	US (350 centres), outside the US (90 centres)
Recruitment period	2013 to 2020
Study population and number	n=27,779 patients implanted with LINX devices
Age and sex	Not reported
Patient selection criteria	Not reported
Technique	Laparoscopic insertion of a magnetic ring: LINX device implantation
Follow up	>5 years
Conflict of interest/source of funding	All the authors were employed by Ethicon Inc.

Analysis

Study design issues: This study described the safety profile of the LINX® device. The MAUDE database and Ethicon's complaint database were queried for all device removals. The end point was based on the time from implant to explant in months. Incomplete data were apparent in both databases.

This analysis included patients from the geographies in which the clasp-closure MSA device was commercially available, beginning in 2013. It did not include the original device design that was secured by sutures nor the size 12-bead device. Neither of those device options are commercially available today.

Study population issues: Based on implant duration, 31.8% (n=8,836) of patients had less than 1 year after implantation, 46.7% (n=12,961) had 1 to 3 years, 14.6% (n=4,060) had 3 to 5 years, and 6.9% (n=1,922) had more than 5 years.

Key efficacy findings

Number of patients analysed: 27,779

Key safety findings

Reasons for device removal and mean time to removal

Reasons for removal	Number of removals	Percentage of total removals	Mean time to removal, months (±SD)
Dysphagia	292	47.9%	10.9±11.9

Reasons for removal	Number of removals	Percentage of total removals	Mean time to removal, months (±SD)
Persistent GORD	125	20.5%	20.5±13.0
Erosion	27	4.4%	25.0±12.9
Abdominal pain/pain	46	7.6%	15.8±14.3
Discontinuous device*	17	2.8%	33.7±6.0
Need for MRI	11	1.8%	28.6±13.2
Vomiting	16	2.6%	7.4±8.2
Gastroparesis	4	0.7%	20.7±18.5
Device migration	3	0.5%	12.6±17.7
Other/unknown	68	11.2%	6.8±6.4
Total removals	609	100.0%	14.6±13.4

*Discontinuous devices were the result of a manufacturing issue that resulted in a voluntary recall in 2018.

The overall 7-year cumulative risk of explant was 4.81% (95% CI 4.31% to 5.36%).

The cumulative risk of erosion at 7 years was 0.28% (95% CI: 0.17% to 0.46%).

Device size and removal rate:

- 13 beads: 3.5%
- 14 beads: 2.4%
- 15 beads: 1.7%
- 16 beads: 1.5%
- 17 beads: 1.3%

Device size was significantly related (Chi-square p value < 0.0001) to the likelihood of an explant, with the smallest size having the highest explant rate.

Validity and generalisability of the studies

- When reported, studies were done in various countries and data relating to the UK context (Bonavina 2020) were included.
- There was 1 RCT (low risk of bias) which compared laparoscopic MSA with PPIs.
- When comparing laparoscopic insertion of a magnetic ring with fundoplication, Zhuang (2021) included Nissen fundoplication, and Guidozzi (2019), Aiolfi (2018) and Bonavina (2020) included both total and partial fundoplication.
- The longest follow up was a median of 9 years (Ferrari 2020). Two studies reported outcomes at 5 years or more (Zhuang 2021; DeMarchi 2021) and the remaining studies reported outcomes between 6 and 50 months.
- There was variation in the population included, such as hiatal hernia size, GORD severity, oesophagitis severity, and presence of Barrett's oesophagus. There was some patient overlap between the studies.
- There was variation in the procedural technique depending on the presence of hiatal hernia, the size of the hiatal defect, and the degree of hiatus hernia.
- Device has evolved over time and different generations of the LINX Reflux Management System were used.
- Length of hospital stay might be affected by different healthcare systems, such as in Germany, patients had longer stay built into reimbursement as shown in Bonavina (2020).

Existing assessments of this procedure

In 2022, the American Gastroenterological Association published the clinical practice update on the personalised approach to the evaluation and management of GERD: expert review. This expert review recommended that 'in patients with proven GERD, laparoscopic fundoplication and MSA are effective surgical options, and transoral incisionless fundoplication is an effective endoscopic option in carefully selected patients'. The recommendation relating to laparoscopic MSA was based on 1 RCT (Bell 2019, 2022).

In 2022, Austrian Institute for Health Technology Assessment (AIHTA) GmbH published the decision support document. AIHTA recommended that 'due to the methodological shortcomings of the available evidence and the lack of controlled evidence, especially between different surgical approaches, the inclusion of either of the three investigated devices [Magnetic sphincter augmentation device (LINX®), non-active silicone implant (RefluxStop™), and electrical stimulation therapy device (EndoStim® LES stimulator)] in the catalogue of benefits is currently not recommended.' The recommendation relating to laparoscopic MSA for GORD was based on 1 RCT (Bell 2019, 2020), 2 single-arm studies (Bonavina 2013; Ganz 2015) and 1 registry-based study (Riegler 2015; Bonavina 2021).

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Electrical stimulation of the lower oesophageal sphincter for treating gastro-oesophageal reflux disease. NICE interventional procedure guidance 540 (2015). Available from https://www.nice.org.uk/guidance/ipg540
- Endoscopic radiofrequency ablation for gastro-oesophageal reflux disease. NICE interventional procedure guidance 461 (2013). Available from https://www.nice.org.uk/guidance/ipg461
- Endoluminal gastroplication for gastro-oesophageal reflux disease. NICE interventional procedure guidance 404 (2011). Available from https://www.nice.org.uk/guidance/ipg404
- Endoscopic augmentation of the lower oesophageal sphincter using hydrogel implants for the treatment of gastro-oesophageal reflux disease. NICE interventional procedure guidance 222 (2007). Available from https://www.nice.org.uk/guidance/ipg222
- Endoscopic injection of bulking agents for gastro-oesophageal reflux disease. NICE interventional procedure guidance 55 (2004). Available from https://www.nice.org.uk/guidance/ipg55

NICE guidelines

- Gastro-oesophageal reflux disease in children and young people: diagnosis and management NICE guideline NG1 (2015). Available from https://www.nice.org.uk/guidance/ng1

- Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. NICE clinical guideline CG184 (updated in 2019). Available from https://www.nice.org.uk/guidance/cg184

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, when comments are considered voluminous, or publication would be unlawful or inappropriate.

Five professional expert questionnaires for laparoscopic insertion of a magnetic ring for gastro-oesophageal reflux disease were submitted and can be found on the NICE website.

Patient opinions

One patient organisation submission for laparoscopic insertion of a magnetic ring for GORD was received and can be found on the NICE website. For patient commentators' opinions, 2 completed questionnaires were received.

Company engagement

A structured information request was sent to 1 company who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

Ongoing trials:

- A Post-Approval Study of the LINX® Reflux Management System (NCT01940185); observational cohort study; US; estimated enrolment n=200; estimated study completion date October 2025.
- LINX Reflux Management System or Fundoplication Clinical Study in Patients with Hiatal Hernia >3 cm (NCT04695171); observational cohort study (patient

registry); US; estimated enrolment n=450; estimated study completion date January 2028.

- RETHINK REFLUX Registry (NCT04253392); observation study (patient registry); US, Austria, Germany, Italy, Singapore, UK; estimated enrolment n=500; estimated study completion date July 2032.
- Registry of Outcomes from AntiReflux Surgery (ROARS) (NCT02923362); observation cohort study (patient registry); US; estimated enrolment n=2,500; estimated study completion date May 2025.

References

1. Zhuang QJ, Tan ND, Chen SF et al. (2021) Magnetic sphincter augmentation in treating refractory gastroesophageal reflux disease: A systematic review and meta-analysis. Journal of digestive diseases 22(12): 695-705
2. Guidozzi N, Wiggins T, Ahmed AR et al. (2019) Laparoscopic magnetic sphincter augmentation versus fundoplication for gastroesophageal reflux disease: systematic review and pooled analysis. Diseases of the esophagus: official journal of the International Society for Diseases of the Esophagus 32(9)
3. Aiolfi A, Asti E, Bernardi D et al. (2018) Early results of magnetic sphincter augmentation versus fundoplication for gastroesophageal reflux disease: Systematic review and meta-analysis. International journal of surgery (London, England) 52: 82-8
4. Bell R, Lipham J, Louie B et al. (2019) Laparoscopic magnetic sphincter augmentation versus double-dose proton pump inhibitors for management of moderate-to-severe regurgitation in GERD: a randomized controlled trial. Gastrointestinal endoscopy 89(1): 14-22e1

   Bell R, Lipham J, Louie BE et al. (2020) Magnetic sphincter augmentation superior to proton pump inhibitors for regurgitation in a 1-year randomized trial. Clinical Gastroenterology and Hepatology 18(8): 1736
5. Bonavina L, Horbach T, Schoppmann SF et al. (2020) Three-year clinical experience with magnetic sphincter augmentation and laparoscopic fundoplication. Surgical Endoscopy
6. Ayazi S, Zheng P, Zaidi AH et al. (2020a) Clinical outcomes and predictors of favorable result after laparoscopic magnetic sphincter augmentation: single-institution experience with more than 500 patients. Journal of the American College of Surgeons 230(5): 733-43
7. Ferrari D, Asti E, Lazzari V et al. (2020) Six to 12-year outcomes of magnetic sphincter augmentation for gastroesophageal reflux disease. Scientific reports 10(1): 13753
8. Ferrari D, Siboni S, Riva CG et al. (2021) Magnetic sphincter augmentation outcomes in severe gastroesophageal reflux disease. Frontiers in Medicine 8: 645592
9. DeMarchi J, Schwiers M, Soberman M et al. (2021) Evolution of a novel technology for gastroesophageal reflux disease: a safety perspective of magnetic sphincter augmentation. Diseases of the esophagus: official journal of the International Society for Diseases of the Esophagus 34(11)

10. Ayazi S, Chowdhury N, Zaidi AH et al. (2020b) Magnetic sphincter augmentation (MSA) in patients with hiatal hernia: clinical outcome and patterns of recurrence. Surgical Endoscopy 34(4): 1835-46
11. Yadlapati R, Gyawali CP and Pandolfino JE (2022) AGA clinical practice update on the personalized approach to the evaluation and management of gastroesophageal reflux disease. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association
12. Strohmaier C and Erdos J (2022) Lower esophageal sphincter devices for laparoscopic surgery in patients with gastroesophageal reflux disease (GERD). AIHTA Decision Support Documents No. 134; Year. Vienna: Austrian Institute for Health Technology Assessment GmbH.

Literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	17/08/2022	1946 to August 16, 2022
MEDLINE In-Process (Ovid)	17/08/2022	August 16, 2022
MEDLINE Epubs ahead of print (Ovid)	17/08/2022	1946 to August 16, 2022
EMBASE (Ovid)	17/08/2022	1974 to 2022 August 16
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	17/08/2022	Issue 8 of 12, August 2022
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	17/08/2022	Issue 7 of 12, July 2022
International HTA database (INAHTA)	17/08/2022	n/a

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Literature search strategy

1 exp Gastroesophageal Reflux/
2 ((gastro-esophag* or gastro-oesophag* or gastro?esophag* or oesophag* or esophag*) adj4 reflux*).tw.
3 Esophageal Motility Disorders/
4 ((oesophag* or esophag*) adj4 (motilit* or dysmotilit* or disorder*)).tw.
5 (gord or gerd).tw.
6 Heartburn/
7 ((heart adj1 burn) or heartburn or pyros?s or (water adj1 brash) or waterbrash or (acid adj1 brash) or acidbrash).tw.
8 Barrett Esophagus/
9 (barrett* adj4 (esophag* or oesophag* or dysplas* or syndrom*)).tw.
10 Esophageal Sphincter, Lower/
11 (lower adj4 (gastro-esophag* or gastro-oesophag* or gastro?esophag* or oesophag* or esophag*) adj4 sphincter*).tw.
12 (gastric adj4 (reflux* or regurgitat* or acid* or juice*)).tw.
13 ((acid or bile) adj4 (reflux* or indigest* or flow-back or flowback or back-flow or backflow)).tw.
14 Dyspepsia/
15 dyspepsi*.tw.
16 Hernia, Hiatal/
17 ((oesophag* or esophag* or para?esophag* or hiat*) adj4 hernia*).tw.
18 or/1-17
19 "Prostheses and Implants"/
20 Prosthesis Implantation/
21 prosthe*.tw.
22 (titanium or bead* or band* or linx or bracelet* or ring*).tw.
23 (sphincter adj2 augment*).tw.

24 or/19-23
25 Magnets/
26 magnet*.tw.
27 MSA.tw.
28 or/25-27
29 24 and 28
30 18 and 29
31 LINX.tw.
32 30 or 31
33 animals/ not humans/
34 32 not 33
35 limit 34 to english language

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Alicuben ET, Bell RCW, Jobe BA et al. (2018) Worldwide experience with erosion of the magnetic sphincter augmentation device. Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract 22(8): 1442-7	Review of the MAUDE database n=9,453 (erosion, n=29)	Erosion of the LINX device is an important but rare complication to recognise that has been safely managed via minimally invasive approaches without long-term consequences.	Recent review (DeMarchi 2021) is included in the key evidence.
Alicuben ET, Tatum JM, Bildzukewicz N et al. (2019) Regression of intestinal metaplasia following magnetic sphincter augmentation device placement. Surgical endoscopy 33(2): 576-9	Case series n=86	MSA is effective in achieving regression of intestinal metaplasia. Longer-term follow up is needed to assess durability of effect and make meaningful comparisons to fundoplication.	This study examined the possible progression and the anticipated regression rate of intestinal metaplasia after MSA for GORD and patients with intestinal metaplasia were not initially considered candidates for this procedure.
Antiporda M, Jackson C, Smith CD et al. (2019) Short-term	Case series n=98	Laparoscopic MSA is associated with excellent outcomes	Studies with larger samples or better designs are

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
outcomes predict long-term satisfaction in patients undergoing laparoscopic magnetic sphincter augmentation. Journal of laparoendoscopic & advanced surgical techniques. Part A 29(2): 198-202		with decrease in GORD-HRQL scores in short term that are durable to longer term follow up, and with low rates of new-onset dysphagia.	included in the key evidence.
Asti E, Bonitta G, Lovece A et al. (2016) Longitudinal comparison of quality of life in patients undergoing laparoscopic Toupet fundoplication versus magnetic sphincter augmentation: Observational cohort study with propensity score analysis. Medicine (Baltimore): 95(30): e4366.	Non-randomised comparative study n=238 (MSA, n=103; LTF, n=135)	The results show that LTF and LINX provide similar disease-specific quality of life over time in patients with early stage GORD.	This study was included in Guidozzi (2019).
Asti E, Siboni S, Lazzari V et al. (2017) Removal of the magnetic sphincter augmentation device: surgical technique and results of a single-center cohort study. Annals of surgery 265(5): 941-5	Case series n=164	Laparoscopic removal of the LINX device can be safely done as a 1-stage procedure and in conjunction with fundoplication even in patients presenting with device erosion.	Studies with larger samples or better designs are included in the key evidence.
Asti E, Aiolfi A, Lazzari V et al. (2018) Magnetic sphincter augmentation for gastroesophageal reflux disease: review of clinical studies.	Review	The procedure has proven to be highly effective in improving typical reflux symptoms, reducing the use of proton-pump	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Updates in surgery 70(3): 323-30		inhibitors, and decreasing oesophageal acid exposure. The device can be easily removed if necessary. Most removals have occurred within 2 years after implant and have been managed non-emergently, with no complications or long-term consequences.	
Ayazi S, Schwameis K, Zheng P et al. (2021) The impact of magnetic sphincter augmentation (MSA) on esophagogastric junction (EGJ) and esophageal body physiology and manometric characteristics. Annals of surgery	Case series n=100	MSA results in improvement in the LOS manometric characteristics. Although the device results in an increased outflow resistance at the EGJ, the compensatory increase in the force of oesophageal contraction will result in unaltered oesophageal peristaltic progression and bolus clearance.	Studies with larger samples or better designs are included in the key evidence.
Ayazi S, Zaidi AH, Zheng P. et al. (2020) Comparison of surgical payer costs and implication on the healthcare expenses between laparoscopic magnetic sphincter	Non-randomised comparative study n=1,226 (MSA, n=195; LNF, n=1,131)	When compared with LNF, MSA results in a reduction of disease-related expenses for the payer in the year after surgery. While	Limited efficacy and safety data were reported.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
augmentation (MSA) and laparoscopic Nissen fundoplication (LNF) in a large healthcare system. Surgical Endoscopy 34(5): 2279-86		MSA is associated with a higher procedural payer cost compared with LNF, payer costs may offset due to reduction in the expenses after surgery.	
Ayazi S, Schwameis K, Zheng P et al. (2021) The impact of magnetic sphincter augmentation (MSA) on esophagogastric junction (EGJ) and esophageal body physiology and manometric characteristics. Annals of surgery	Case series n=100	MSA results in improvement in the LOS manometric characteristics. Although the device results in an increased outflow resistance at the EGJ, the compensatory increase in the force of oesophageal contraction will result in unaltered oesophageal peristaltic progression and bolus clearance.	Studies with larger samples or better designs are included in the key evidence.
Ayazi S, Zheng P, Zaidi A H et al. (2020) Magnetic sphincter augmentation and postoperative dysphagia: characterization, clinical risk factors, and management. Journal of gastrointestinal surgery: official journal of the Society for Surgery of the	Case series n=380	In a large cohort of patients who had MSA, authors report 15.5% rate of persistent postoperative dysphagia. The overall response rate to dilation therapy is 67%, and the efficacy of dilation with each subsequent procedure reduces. Patients with	Studies with larger samples or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Alimentary Tract 24(1): 39-49		normal hiatal anatomy, significant preoperative dysphagia, and less than 80% peristaltic contractions of the smooth muscle portion of the oesophagus should be counselled that they have an increased risk for persistent postoperative dysphagia.	
Baison GN, Jackson AS, Wilshire CL et al. (2022) The impact of ineffective esophageal motility on patients undergoing magnetic sphincter augmentation. Annals of surgery	Non-randomised comparative study n=210 (105 patient with ineffective oesophageal motility and 105 matched controls)	Patients with ineffective oesophageal motility having MSA show improved quality of life and reduction in acid exposure. Key differences in ineffective oesophageal motility patients include lower rates of objective GORD resolution, lower resolution of existing dysphagia, higher rates of new onset dysphagia and need for dilation. GORD patients with ineffective oesophageal motility should be	Studies with larger samples or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		counselled about these possibilities.	
Bell RCW (2020) Management of regurgitation in patients with gastroesophageal reflux disease. Current opinion in gastroenterology 36(4): 336-43	Review	Precision care of regurgitation should recognise the low-therapeutic impact of acid control, while antireflux procedures are very successful.	Review article
Bologheanu M, Matic A, Feka J et al. (2022) Severe dysphagia is rare after magnetic sphincter augmentation. World journal of surgery 46(9): 2243-50	Case series n=357	Dysphagia requiring endoscopic or surgical intervention was rare after MSA in a large case series. LINX® devices with a size >13 were shown to be an independent risk factor for developing postoperative dysphagia.	Studies with larger samples or better designs are included in the key evidence.
Bona D, Saino G, Mini E et al. (2021) Magnetic sphincter augmentation device removal: surgical technique and results at medium-term follow-up. Langenbeck's archives of surgery 406(7): 2545-51	Case series n=5	The MSA device can be safely explanted through a single-stage laparoscopic procedure. Tailoring a fundoplication, according to preoperative patient symptoms and intraoperative findings, seems feasible and safe with a promising trend toward	Small sample

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		improved symptoms and quality of life.	
Bonavina L, Fisichella PM, Gavini S et al. (2020) Clinical course of gastroesophageal reflux disease and impact of treatment in symptomatic young patients. Annals of the New York Academy of Sciences	Review	In patients with early-stage disease, when the LOS function is still preserved and before endoscopically visible Barrett's oesophagus develops, novel laparoscopic procedures, such as magnetic and electric sphincter augmentation, may have a greater role than conventional surgical therapy.	Review article
Bonavina L, Boyle N and Schoppmann SF (2021) The role of magnetic sphincter augmentation in the treatment of gastroesophageal reflux disease. Current opinion in gastroenterology 37(4): 384-9	Review	MSA has a favourable side-effect profile and is highly effective in reducing typical reflux symptoms, medication dependency, and oesophageal acid exposure. Excellent outcomes have been confirmed over a 12-year follow up, showing that the operation has the potential to prevent GORD progression. Further studies are needed to confirm the cost-	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		effectiveness of this procedure in patients with more advanced disease-stage and prior gastric surgery. A randomised control trial comparing MSA with fundoplication could raise the level of evidence and the strength of recommendation.	
Bonavina L, Saino G, Bona D et al. (2013) One hundred consecutive patients treated with magnetic sphincter augmentation for gastroesophageal reflux disease: 6 years of clinical experience from a single center. J Am Coll Surg 217(4): 577-85	Case series n=100	MSA for GORD in clinical practice provides safe and long-term reduction of oesophageal acid exposure, substantial symptom improvement, and elimination of daily PPI use.	This study was included in Zhuang (2021).
Bortolotti M (2021) Magnetic challenge against gastroesophageal reflux. World Journal of Gastroenterology 27(48): 8227-41	Review	considering the available studies, it can be said that the MSA system achieves a GER control roughly similar to that of fundoplication with the advantage of less gas bloating and a greater ability to vomit and belch. On the other hand, it has the disadvantage of more prolonged	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		and severe dysphagia, needing endoscopic dilatation more frequently and, in some cases, device removal. The latter may also be necessary for some other severe complications, which are infrequent, such as mucosal erosions and device penetration through the oesophageal wall.	
Bridges LC, Shillinglaw JP, Smith BE et al. (2022) Augmentation of the esophageal sphincter using LINX. American Surgeon	Case series n=106	The results showed that there was no difference in DeMeester scores, size of device or BMI in patients requiring LINX removal compared to those not removed or postoperative EGD with dilation rates. Patients who needed LINX removal had higher GORD HRQL scores both preoperatively (median 34 vs 28) and postoperatively at all visits compared to those patients who did not undergo removal (p=0.032).	Studies with larger samples or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		Manometry and DeMeester scores were not associated with LINX removal suggesting a less invasive GORD HRQL questionnaire may be a better predictor of patients who will succeed with LINX surgery.	
Broderick RC, Smith CD, Cheverie JN et al. (2020) Magnetic sphincter augmentation: a viable rescue therapy for symptomatic reflux following bariatric surgery. Surgical Endoscopy 34(7): 3211-5	Case series n=13	LINX placement is a safe, effective treatment option for surgical management of refractory GORD after bariatric surgery. It can relieve symptoms and obviate the requirement of high-dose medical management. Magnetic LOS augmentation should be another tool in the surgeon's toolbox for managing reflux after bariatric surgery in select patients.	Small sample
Buckley FP, Bell RCW, Freeman K et al. (2018) Favorable results from a prospective evaluation of 200 patients with large hiatal hernias	Case series n=200	This prospective study of 200 patients with >3 cm hernias having MSA with hiatoplasty resulted in favourable	This study was included in Guidozzi (2019)

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
undergoing LINX magnetic sphincter augmentation. Surg Endosc. 32(4):1762-8		outcomes with a median of 9 months of follow up. Comparing this to published reports of MSA in patients with <3 cm hernias, the safety and clinical efficacy of MSA are independent of initial hernia size.	
Chen MY, Huang DY, Wu A et al. (2017) Efficacy of magnetic sphincter augmentation versus Nissen fundoplication for gastroesophageal reflux disease in short term: a meta-analysis. Canadian journal of gastroenterology & hepatology 2017: 9596342	Meta-analysis n=5 studies	MSA can be recommended as an alternative treatment for GORD according to their short-term studies, especially in main-features of gas-bloating, due to shorter operative time and less complication of gas or bloating.	All studies in this meta-analysis were included in Aiolfi (2018) and Zhuang (2021)
Clapp B, Dodoo C, Harper B et al. (2021) Magnetic sphincter augmentation at the time of bariatric surgery: an analysis of the MBSAQIP. Surgery for obesity and related diseases: official journal of the American Society for Bariatric Surgery 17(3): 555-61	Non-randomised comparative study n=319,580 (MSA, n=24; non-MSA, 319,556)	MSA is safe in the short term in metabolic and bariatric surgery. There is no difference in major morbidity or mortality and operative times are similar in MSA patients. The long-term efficacy of this practice is unknown.	Sample for MSA was small. This study examined the short-term outcomes of patients that had metabolic and bariatric surgery concomitantly with MSA
Czosnyka NM, Buckley FP, Doggett SL et al. (2017) Outcomes of magnetic	Case series n=102	MSA is a safe and effective treatment for GORD, with significant	Studies with larger samples or better designs are

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
sphincter augmentation - A community hospital perspective. American journal of surgery 213(6): 1019-23		improvement in quality of life. GORD-HRQL, medication reduction, operative times, and dysphagia rates were similar to other reports, showing the reproducibility of MSA. Lower dilation rates may be due to refinements in technique and postoperative dietary management.	included in the key evidence.
Dunn C, Bildzukewicz N and Lipham J (2020) Magnetic sphincter augmentation for gastroesophageal reflux disease. Gastrointestinal Endoscopy Clinics of North America 30(2): 325-42	Review	MSA with LINX is an effective surgical treatment of reflux disease. Intermediate-term outcomes have shown safety and efficacy of the LINX device compared with both laparoscopic fundoplication and medical therapy. New research has expanded on indications for MSA, including after failure of single PPI therapy rather than twice-daily therapy, in patients with Barrett's oesophagus, and	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		in patients with large hiatal hernias.	
Fuchs KH, Varga G, Papp A et al. (2022) Results in antireflux surgery, an analysis of case-controlled cohorts versus multicenter studies and meta-analyses. Chirurgia (Bucharest, Romania: 1990) 117(2): 134-42	Review	It can be concluded that special efforts in patient management in high volume centres and a vast experience may substantially contribute to excellent results for several antireflux techniques, which may reach a level of quality above results of registries and meta-analyses.	Review article
Ganz RA (2017) A modern magnetic implant for gastroesophageal reflux disease. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association 15(9): 1326-37	Review	MSA is proven to be effective and safe in treating GORD and should be considered a surgical option for patients dissatisfied with medical management and considering surgical therapy, particularly for those seeking a fundic-sparing operation, and with reflux parameters consistent with study cohorts.	Review article
Ganz RA, Edmundowicz SA, Taiganides PA et al. (2016) Long-term	Case series n=100	Augmentation of the LOS with a magnetic device provides significant	This study was included in Zhuang (2021).

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
outcomes of patients receiving a magnetic sphincter augmentation device for gastroesophageal reflux. Clin Gastroenterol Hepatol: 14(5): 671-7		and sustained control of reflux, with minimal side effects or complications. No new safety risks emerged over a 5-year follow-up period. These findings validate the long-term safety and efficacy of the MSA device for patients with GORD.	
Ganz RA, Peters JH, Horgan S et al. (2013) Esophageal sphincter device for gastroesophageal reflux disease. N Engl J Med 368(8): 719-27	Case series n=100	The results showed that exposure to oesophageal acid decreased, reflux symptoms improved, and use of PPIs decreased. Follow-up studies are needed to assess long-term safety.	This study was included in Zhuang (2021).
Gyawali CP and Fass R (2018) Management of gastroesophageal reflux disease. Gastroenterology 154(2): 302-18	Review	MSA may be a viable alternative to ARS for patients with well-documented reflux disease, particularly patients with regurgitation, in the absence of significant structural disruption at the EGJ, or oesophageal body motor dysfunction. However, the long-term	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		consequences of having an implanted titanium bracelet need to be better understood.	
Halpern SH, Gupta A, Jawitz OK et al. (2021) Safety and efficacy of an implantable device for management of gastroesophageal reflux in lung transplant recipients. Journal of Thoracic Disease 13(4): 2116-27	Case series n=17	Use of the LINX MSA device in a cohort of lung transplant recipients was associated with similar short-term safety compared with traditional fundoplication, however assessment of efficacy was limited. Further investigation is needed to characterise the long-term efficacy of LINX implantation after LTx.	Small sample
Hawasli A, Sadoun M, Meguid A et al. (2019) Laparoscopic placement of the LINX system in management of severe reflux after sleeve gastrectomy. American Journal of Surgery 217(3): 496-9	Case series n=13	The LINX® system may be used as an alternative to RYGB conversion in managing refractory post-SG reflux.	Small sample
Hawasli A, Tarakji M and Tarboush M (2017) Laparoscopic management of severe reflux after sleeve gastrectomy using the LINX R	Case report n=1	Laparoscopic placement of the LINX® system to correct severe reflux after sleeve gastrectomy is a safe alternative	Single case report

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
system: Technique and one year follow up case report. International journal of surgery case reports 30: 148-51		procedure to conversion to a Roux-en-y gastric bypass.	
Hillman L, Yadlapati R, Whitsett M et al. (2017) Review of antireflux procedures for proton pump inhibitor nonresponsive gastroesophageal reflux disease. Diseases of the esophagus: official journal of the International Society for Diseases of the Esophagus 30(9): 1-14	Review	Laparoscopic fundoplication remains the most proven therapeutic approach. Newer antireflux procedures such as MSA and transoral incisionless fundoplication offer alternatives with varying degrees of success, durability, and side effect profiles that may better suit individual patients. Larger head-to-head comparison trials are needed to better characterise the difference in symptom response and side effect profiles.	Review article
Huynh P, Konda V, Sanguansataya S et al. (2020) mind the gap: current treatment alternatives for GERD patients failing medical treatment and not ready for a fundoplication. Surgical laparoscopy, endoscopy &	Review	This literature review compares 3 rival procedures to treat “gap” patients for GORD with 4 common endpoints. MSA appears to have the most reproducible and linear outcomes	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
percutaneous techniques 31(2): 264-76		but is the most invasive of the 3 procedures. MSA outcomes most closely mirrors that of fundoplication.	
Irribarra MM, Blitz S, Wilshire CL et al. (2019) Does treatment of the hiatus influence the outcomes of magnetic sphincter augmentation for chronic GERD? Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract 23(6): 1104-12	Non-randomised comparative study n=197 (minimal dissection, n=81; crural closure, n=40; formal crural repair, n=42; extensive dissection without closure, n=34)	Hiatal dissection with restoration of oesophageal length and crural closure during MSA increases the likelihood of normalising acid exposure.	Studies with larger samples or better designs are included in the key evidence.
Ji H, Chandrasekhara V, Leggett CL (2020) Magnetic sphincter augmentation device malfunction. Gastrointestinal endoscopy	Case report n=1	It is unclear what led to device failure in this particular patient. Potential contributing factors include a hiatal hernia size >3 cm requiring intraoperative repair, and obesity. MSA device failure should be considered for patients with recurrent GORD symptoms and can be identified with x-ray or fluoroscopic imaging.	Single case report
Kirkham EN, Main BG, Jones KJB et al. (2020) Systematic	Systematic review	Most studies on MSA lacked information about	Meta-analysis was not conducted, and

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
review of the introduction and evaluation of magnetic augmentation of the lower oesophageal sphincter for gastro-oesophageal reflux disease. The British journal of surgery 107(1): 44-55	n=39 studies	patient selection, governance, expertise, techniques and outcomes, or varied between studies. Currently, MSA is being used despite a lack of robust evidence for its effectiveness.	most studies were included in Aiolfi (2018), Zhuang (2021) or Guidozzi (2019).
Kuckelman JP, Barron MR and Martin MJ (2017) "The missing LINX" for gastroesophageal reflux disease: Operative techniques video for the LINX magnetic sphincter augmentation procedure. American journal of surgery 213(5): 984-7	Case series n=2	LINX placement offers a technically unique option that effectively provides a less invasive alternative for symptomatic reflux disease. This procedure is effective and safe in patients with significantly altered anatomy or previous foregut surgery when there is strict adherence to sound surgical technique and when crucial operative steps are accomplished.	Small sample and limited efficacy and safety data reported.
Kuckelman JP, Phillips CJ, Derickson MJ et al. (2018) Esophageal magnetic sphincter augmentation as a novel approach to post-bariatric surgery gastroesophageal reflux disease. Obesity	Non-randomised comparative study n=28	MSA is a technically simple operation that offers a safe and highly effective new option for all patients with GORD. This procedure appears to exhibit a similar	Studies with larger samples or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
surgery 28(10): 3080-3086		profile for patients who have previously had bariatric surgery, particularly sleeve gastrectomy. Prospective randomised studies will be necessary, but there is exciting potential for the role of MSA in providing surgeons a new and much needed tool in their armamentarium against refractory or de novo GORD after bariatric procedures.	
Kuckelman JP, Phillips CJ, Hardin MO et al. (2017) Standard vs expanded indications for esophageal magnetic sphincter augmentation for reflux disease. JAMA surgery 152(9): 890-891	Non-randomised comparative study n=31	Evidence found MSA to be safe and effective for GORD, with relatively low complication rates and acceptable degrees of improvement in subjective GORD symptoms and in G-QOL survey scores for all patients. Of greatest importance, results were equivalent even when using MSA for expanded indications, such as larger hiatal hernias, higher	Studies with larger samples or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		BMI, or prior foregut surgery.	
Laird J (2020) Magnetic sphincter augmentation device placement for treatment of gastroesophageal reflux. JAAPA: official journal of the American Academy of Physician Assistants 33(12): 30-2	Review	The MSA procedure showed the results in treating reflux and regurgitation, with reduction in PPI use comparable with that seen with fundoplication, but without the loss of ability to belch and vomit. The improvement in quality of life and the less-invasive nature of the procedure offer patients with GORD an alternative between medical management and more invasive surgeries. The MSA procedure should be considered a viable option for any antireflux surgical candidate.	Review article
Louie BE, Smith CD, Smith CC et al. (2019) Objective evidence of reflux control after magnetic sphincter augmentation: one year results from a post approval study. Annals of surgery 270(2): 302-308	Case series n=200	Safety and effectiveness of MSA has been shown outside of an investigational setting to further confirm MSA as treatment for GORD.	This study was included in Zhuang (2021)

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Louie BE, Farivar AS, Shultz D et al. (2014) Short-term outcomes using magnetic sphincter augmentation versus Nissen fundoplication for medically resistant gastroesophageal reflux disease. Annals of Thoracic Surgery 98: 498–505	Non-randomised comparative study n=66	MSA results in similar objective control of GORD, symptom resolution, and improved quality of life compared with LNF. MSA seems to restore a more physiologic sphincter that allows physiologic reflux, facilitates belching, and creates less bloating and flatulence. This device has the potential to allow individualised treatment of GORD and increase the surgical treatment of GORD.	Studies with larger samples or better designs are included in the key evidence.
Melloni M, Lazzari V, Asti E et al. (2018) Magnetic sphincter augmentation is an effective option for refractory duodeno-gastro-oesophageal reflux following Billroth II gastrectomy. BMJ case reports 2018	Case report n=1	MSA is a new and highly standardised surgical option for treating refractory GORD after partial gastrectomy and Billroth 2 reconstruction. Compared with the classic Roux-en-Y anastomosis, MSA can be done laparoscopically and can simultaneously correct acid and biliary reflux.	Single case report
Mermelstein J, Mermelstein AC and	Review	Data is limited to short-term case	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Chait MM (2018) Proton pump inhibitor-refractory gastroesophageal reflux disease: Challenges and solutions. Clinical and Experimental Gastroenterology 11: 119-34		series, but multiple prospective studies have shown the safety and efficacy of LINX in treating refractory GORD symptoms.	
Min MX and Ganz RA (2014) Update in procedural therapy for GERD - Magnetic sphincter augmentation, endoscopic transoral incisionless fundoplication vs laparoscopic Nissen fundoplication. Current Gastroenterology Reports 16(2): 374	Review	Collective data gathered from 4 studies published within the past year suggest that MSA, TIF and Nissen fundoplication share comparable effectiveness in pH monitoring and patient satisfaction, TIF may have a lower PPI cessation rate, and Nissen fundoplication needed longer recovery time and had a more serious adverse effects profile. Large, prospective, RCTs are needed to reliably compare the 3 procedures.	Review article
Ndubizu GU, Petrick AT and Horsley R (2020) Concurrent magnetic sphincter augmentation and hiatal hernia repair for refractory GERD after laparoscopic sleeve	Case report n=1	MSA can be considered in the management of refractory GORD after laparoscopic sleeve gastrectomy (LSG) in patients with normal	Single case report

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
gastrectomy. Surgery for Obesity and Related Diseases 16(1): 168-70		oesophageal motility. The procedure is relatively uncomplicated and appears to be safe with little variation in technique between post SG patients and those having MSA for primary GORD symptoms. While more studies are required to determine the efficacy of MSA after SG, it appears to be a promising alternative to conversion to RYGB in select patients with recalcitrant GORD after SG.	
Nicolau AE, Lobontiu A and Constantinoiu S (2018) New minimally invasive endoscopic and surgical therapies for gastroesophageal reflux disease (GERD). Chirurgia (Bucharest, Romania: 1990) 113(1): 70-82	Review	Laparoscopic procedures can address HH larger than 2 cm. They are technically easy less invasive and with reduced adverse events and post fundoplication syndromes in comparing with fundoplication. In case of recurrence, fundoplication can be done, so there are no bridges burnt.	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Nikolic M, Matic A, Feka J et al. (2021) Expanded indication for magnetic sphincter augmentation: outcomes in weakly acidic reflux compared to standard GERD patients. Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract	Non-randomised comparative study n=268 (weakly acidic reflux, n=67; acidic reflux, n=201)	MSA statistically significantly improves GORD-related symptoms and quality of life in patients with weakly acidic reflux with very low postoperative morbidity.	Studies with larger samples or better designs are included in the key evidence.
Nikolic M, Schwameis K, Paireder M et al. (2019) Tailored modern GERD therapy - steps towards the development of an aid to guide personalized anti-reflux surgery. Scientific reports 9(1): 19174	Non-randomised comparative study n=267 (MSA, n=73; electrical stimulation, n=25; Nissen fundoplication, n=169	The main differences and the deciding factors in the aid for choice of GORD therapy were found to be the preoperative DCI and subsequently the presence of ineffective oesophageal motility, hiatal hernia size and the patient's preference. The overall low postoperative dysphagia-rate and no statistically significant differences in symptom control and patient satisfaction rates between the 3 surgical treatments show that such a treatment decision	Studies with larger samples or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		aid is feasible in the short-term postoperative time and could be considered in surgical antireflux evaluation.	
O'Neill SM, Jalilvand AD, Colvin JS et al. (2022) S148: Long-term patient-reported outcomes of laparoscopic magnetic sphincter augmentation versus Nissen fundoplication: a 5-year follow-up study. Surgical Endoscopy	Non-randomised comparative study n=70 (MSA, n=25; LNF, n=45)	MSA appears to offer similar long-term improvement in disease-specific quality of life as LNF. For MSA, there was a trend toward reduced long-term bloating compared with LNF but need for reoperation and device removal may be associated with patient dissatisfaction.	Studies with larger samples or better designs are included in the key evidence.
Parmar AD, Tessler RA, Chang HY et al. (2017) Two-stage explantation of a magnetic lower esophageal sphincter augmentation device due to esophageal erosion. Journal of laparoendoscopic & advanced surgical techniques. Part A 27(8): 829-33	Case report n=1	This paper presented the first account of LINX explantation for oesophageal erosion in the US. It showed that a staged laparoendoscopic approach to LINX removal is feasible with minimal morbidity.	Single case report
Patel SH, Smith B, Polak R et al. (2022) Laparoscopic magnetic sphincter augmentation device placement for patients with medically-	Case series n=22	MSA device placement in patients with medically refractory GORD after sleeve gastrectomy is a safe and viable	Small sample

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
refractory gastroesophageal reflux after sleeve gastrectomy. Surgical Endoscopy		alternative to Roux-en-Y gastric bypass without conferring additional risks. We show an improvement in reflux symptoms after MSA device placement as evidenced by decreased post-operative GORD-HRQL scores, decreased anti-acid medication usage, and overall patient satisfaction with the procedure. Further prospective and comparative studies with longer term follow-up are needed to validate the use of MSA in patients who have undergone sleeve gastrectomy.	
Prakash D, Campbell B and Wajed S (2018) Introduction into the NHS of magnetic sphincter augmentation: an innovative surgical therapy for reflux - results and challenges. Annals of the Royal College of Surgeons of England 100(4): 251-6	Case series n=47	MSA is highly effective in treating uncomplicated GORD, with durable results and an excellent safety profile. This laparoscopic, minimally invasive procedure provides a good alternative for patients where surgical anatomy is unaltered.	Small sample

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Rabach L, Saad AR, Velanovich V (2019) How to choose among fundoplication, magnetic sphincter augmentation or transoral incisionless fundoplication. Current Opinion in Gastroenterology 35(4): 371-8	Review	Fundoplication remains the standard of care for patients with GORD complicated by hiatal hernias more than 2 cm, Barrett's oesophagus or grade C and D erosive esophagitis. For the patient with uncomplicated GORD, MSA appears to be a viable alternative that has greater technical standardisation and fewer postoperative side-effects than fundoplication. TIF remains an option for patients with refractory GORD who refuse surgical intervention.	Review article
Rausa E, Manfredi R, Kelly ME et al. (2021) Magnetic sphincter augmentation placement for recalcitrant gastroesophageal reflux disease following bariatric procedures: a systematic review and Bayesian meta-analysis. Journal of laparoendoscopic &	Systematic review and Bayesian meta-analysis n=3 studies (33 patients)	MSA for refractory GORD after bariatric surgery appears feasible. Prospective randomised controlled with standardised surgical technique and objective follow-up evaluation is needed to better	Small sample, with limited efficacy outcomes reported.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
advanced surgical techniques. Part A 31(9): 1034-9		assess short- and long-term efficacy.	
Rebecchi F, Allaix ME, Cinti L et al. (2018) Comparison of the outcome of laparoscopic procedures for GERD. Updates in surgery 70(3): 315-21	Review	laparoscopic fundoplication is the standard of care for treating GORD. During the last 10 years, many efforts have been done to develop a minimally invasive alternative to laparoscopic fundoplication with reduced less side effects. Both MSA and LOS Electrical Stimulation have been proven to be safe. However, there are no long-term and robust studies comparing these two novel techniques to the laparoscopic fundoplication.	Review article
Reynolds JL, Zehetner J, Nieh A et al. (2016) Charges, outcomes, and complications: a comparison of magnetic sphincter augmentation versus laparoscopic Nissen fundoplication for the treatment of GERD. Surg Endosc 30(8): 3225-30	Non-randomised comparative study n=119 (MSA, n=52; LNF, n=67)	The side effect profile of MSA is better than LNF as evidenced by less gas bloat and increase ability to belch and vomit. LNF and MSA are comparable in symptom control, safety, and overall hospital charges. The charge for the MSA device is offset by less	This study was included in Guidozzi (2019).

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		charges in other categories as a result of the shorter operative time and LOS.	
Reynolds JL, Zehetner J, Wu P et al. (2015) Laparoscopic magnetic sphincter augmentation vs laparoscopic Nissen fundoplication: a matched-pair analysis of 100 patients. Journal of the American College of Surgeons 221: 123-8	Non-randomised comparative study n=100	Analogous GORD patients had similar control of reflux symptoms after both MSA and LNF. The inabilities to belch and vomit were significantly fewer with MSA, along with a significantly lower incidence of severe gas-bloat symptoms. These results support the use of MSA as first-line therapy in patients with mild to moderate GORD.	Studies with larger samples or better designs are included in the key evidence.
Reynolds JL, Zehetner J, Bildzukewicz N et al. (2014) Magnetic sphincter augmentation with the LINX device for gastroesophageal reflux disease after U.S. Food and Drug Administration approval. Am Surg. 80(10): 1034-8	Case series n=67	MSA with LINX is a safe and effective alternative to fundoplication for treating GORD. The most common postoperative complaint is mild to moderate dysphagia, which usually resolves within 12 weeks.	Studies with larger samples or better designs are included in the key evidence.
Rettura F, Bronzini F, Campigotto M et al. (2021) Refractory gastroesophageal reflux disease: a management update.	Review	The most widely done invasive antireflux option remains laparoscopic antireflux surgery	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Frontiers in Medicine 8: 765061		(LARS), even if other, less invasive, interventions have been suggested in the last few decades, including endoscopic transoral incisionless fundoplication (TIF), MSA (LINX) or radiofrequency therapy (Stretta). Due to the different mechanisms underlying refractory GORD, the most effective strategy can vary, and it should be tailored to each patient.	
Richards WO and McRae C (2018) Comparative analysis of laparoscopic fundoplication and magnetic sphincter augmentation for the treatment of medically refractory GERD. The American surgeon 84(11): 1762-7	Non-randomised comparative study n=38 (MSA, n=32; fundoplication, n=6)	MSA and laparoscopic fundoplication both lead to a comparable decrease in HRQL score and an increase in patient satisfaction when compared with patient's preoperative symptoms with maximum PPI use. In addition, our study shows that MSA is a safe minimally invasive antireflux procedure without	This study was included in Zhuang (2021)

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		the negative side-effects, such as gas bloat, inability to belch, and inability to vomit, commonly associated with NF.	
Richter JE (2020) Laparoscopic magnetic sphincter augmentation: potential applications and safety are becoming more clear-but the story is not over. Clinical Gastroenterology and Hepatology 18(8): 1685-7	Editorial	To an admitted sceptic about new antireflux treatments, the available data about the symptomatic and physiological effectiveness, durability, and safety of MSA are very impressive. This procedure now deserves to be routinely done as an alternative surgical procedure to traditional fundoplication for patients with mild-moderate GORD.	Editorial
Riegler M, Schoppman SF, Bonavina L et al. (2015) Magnetic sphincter augmentation and fundoplication for GERD in clinical practice: one-year results of a multicenter, prospective observational study. Surgical Endoscopy 29: 1123–9	Non-randomised comparative study n=249 (MSA, n=202; fundoplication, n=47)	Both MSA device and fundoplication showed significant improvements in reflux control, with similar safety and reoperation rates. In the treatment continuum of antireflux surgery, MSA device should be considered as a first-line surgical option in	This study was included in Guidozzi (2019).

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		appropriately selected patients without Barrett's oesophagus or a large hiatal hernia in order to avoid unnecessary dissection and preserve the patient's native gastric anatomy.	
Riva CG, Siboni S, Sozzi M et al. (2020) High-resolution manometry findings after LINX procedure for gastro-esophageal reflux disease. Neurogastroenterology and Motility 32(3): e13750	Case series n=45	The Linx procedure had a remarkable effect on oesophageal motility in the short-term follow-up. It appears that the overall postoperative increase of IRP and IBP may justify the higher DCI values. Preoperative dysphagia was the only factor associated with postoperative dysphagia.	Small sample
Riva CG, Asti E, Lazzari V et al. (2019) Magnetic sphincter augmentation after gastric surgery. JSLS: Journal of the Society of Laparoendoscopic Surgeons 23(4)	Systematic review n=7 studies (35 patients)	MSA is a safe, simple, and standardized antireflux procedure. It is also feasible in patients with refractory GORD after gastric or bariatric surgery. Further prospective and comparative	This study investigated the effect of MSA for GORD after gastric/bariatric surgery, and systematic reviews with larger samples are included in the key evidence

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		studies are needed to validate the preliminary clinical experience in this subset of patients.	
Rogers BD, Valdovinos LR, Crowell MD et al. (2020) Number of reflux episodes on pH-impedance monitoring associates with improved symptom outcome and treatment satisfaction in gastro-oesophageal reflux disease (GERD) patients with regurgitation. Gut	Post hoc analysis of an RCT (NCT02505945) n=152	Reduction of reflux episodes on pH-impedance to physiological levels associates with improved outcomes, while pathological levels predict improvement with MSA in regurgitation predominant GORD.	Patients in this study were included in Bell (2020).
Rona KA, Reynolds J, Schwameis K et al. (2017) Efficacy of magnetic sphincter augmentation in patients with large hiatal hernias. Surgical endoscopy 31(5): 2096-102	Non-randomised comparative study n=192 (hiatal hernia<3 cm, n=140; large hiatal hernia, n=52)	MSA in patients with large hiatal hernias shows decreased postoperative PPI requirement and mean GORD-HRQL scores compared with patients with smaller hernias. The incidence of symptom resolution or improvement and the percentage of patients needing intervention for dysphagia are similar. Short-term outcomes of MSA are encouraging in patients with GORD and large hiatal hernias.	Studies with larger sample or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Rona KA, Tatum JM, Zehetner J et al. (2018) Hiatal hernia recurrence following magnetic sphincter augmentation and posterior cruroplasty: intermediate-term outcomes. Surgical endoscopy 32(7): 3374-9	Case series n=47	Concomitant MSA and hiatal hernia repair in patients with gastroesophageal reflux disease and a moderate-sized hiatal hernia shows durable subjective reflux control and an acceptable hiatal hernia recurrence rate at 1- to 2-year follow up.	Studies with larger sample or better designs are included in the key evidence.
Salvador R, Costantin, M, Capovilla G et al. (2017) Esophageal penetration of the magnetic sphincter augmentation device: history repeats itself. Journal of laparoendoscopic & advanced surgical techniques. Part A 27(8): 834-838	Case series n=2	Judging from the literature, MSAD implantation may be an effective way to control GORD, but the method can carry major complications, such as migration of the device into the oesophagus (as in the 2 cases reported here). Endoscopic removal of a device possibly penetrating inside the oesophagus is feasible and safe, and may later be followed up with a laparoscopic antireflux procedure without any particular difficulty.	Small sample

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Saino G, Bonavina L, Lipham JC et al. (2015) Magnetic sphincter augmentation for gastroesophageal reflux at 5 years: final results of a pilot study show long-term acid reduction and symptom improvement. J Laparoendosc Adv Surg Tech A 25(10): 787-92	Case series n=44	Based on long-term reduction in oesophageal acid, symptom improvement, and no late complications, this study shows the relative safety and efficacy of MSA for GORD.	This study was included in Zhuang (2021).
Schizas, D., Mastoraki, A., Papoutsi, E. et al. (2020) LINX reflux management system to bridge the "treatment gap" in gastroesophageal reflux disease: A systematic review of 35 studies. World Journal of Clinical Cases 8(2): 294-305	Systematic review n=20	The findings of our review suggest that MSA has the potential to bridge the treatment gap between maxed-out medical treatment and fundoplication. However, further studies with longer follow up are needed for a better elucidation of these results.	Meta-analysis was not carried out, and all studies were included in Aiolfi (2018), Zhuang (2021) or Guidozzi (2019)
Schwameis K, Ayazi S, Zaidi AH et al. (2020) Development of pseudoachalasia following magnetic sphincter augmentation (MSA) with restoration of peristalsis after endoscopic dilation. Clinical Journal of Gastroenterology	Case report n=1	This case report presents a patient with long-standing GORD symptoms that had MSA with complete resolution of his reflux symptoms. He did not have dysphagia before surgery and his preoperative manometry showed normal	Single case report

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		peristaltic progression of oesophageal contractions. He developed pseudoachalasia 14 months after surgery. Repeated endoscopic dilation resulted in resolution of dysphagia and complete restoration of peristaltic contractions.	
Schwameis K, Ayazi S, Zheng P et al. (2021) Efficacy of magnetic sphincter augmentation across the spectrum of GERD disease severity. Journal of the American College of Surgeons 232(3): 288-97	Non-randomised comparative study n=334 (mild-to-severe GORD, n=274; severe GORD, n=60)	MSA is an effective treatment in patients with severe GORD and leads to significant clinical improvement across the spectrum of disease severity, with few objective outcomes being superior in patients with mild-to-moderate reflux disease.	Studies with larger samples or better designs are included in the key evidence.
Schwameis K, Nikolic M, Morales Castellano DG et al. (2018) Crural closure improves outcomes of magnetic sphincter augmentation in GERD patients with hiatal hernia. Scientific reports 8(1): 7319	Case series n=68	MSA leads to significant symptom relief, increased quality of life and alimentary satisfaction with low perioperative morbidity. Cruroplasty tends to result in better reflux control and	Studies with larger samples or better designs are included in the key evidence.

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		symptom relief than exclusive MSA without increasing dysphagia rates.	
Schwameis K, Nikolic M, Morales Castellano DG et al. (2018) Results of magnetic sphincter augmentation for gastroesophageal reflux disease. World journal of surgery 42(10): 3263-3269	Case series n=68	Sphincter augmentation results in significantly reduced reflux symptoms, increased GORD-specific quality of life and excellent alimentary satisfaction with low perioperative morbidity. This procedure should be considered an excellent alternative to fundoplication in treating GORD.	This study was included in Zhuang (2021)
Siboni S, Ferrari D, Riva CG et al. (2021) Reference high-resolution manometry values after magnetic sphincter augmentation. Neurogastroenterology and Motility 33(10): e14139	Non-randomised comparative study n=84 (MSA without crural repair, n=31; MSA with crural repair, n=53)	This study provides HRM reference values for patients having successful MSA implantation. Crural repair appears to be a key component of LOS augmentation and is associated with improved clinical outcomes.	Studies with larger samples or better designs are included in the key evidence.
Sheu EG, Nau P, Nath B et al. (2015) A comparative trial of laparoscopic magnetic sphincter	Non-randomised comparative study n=24 (MSA, n=12; LNF, n=12)	MSA and LNF are both effective and safe treatments for GORD; however, severe dysphagia	This study was included in Guidozzi (2019).

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
augmentation and Nissen fundoplication. Surg Endosc: 29(3): 505-9		requiring endoscopic intervention is more common with MSA. Other adverse GI side effects may be less frequent after MSA. Consideration should be paid to these distinct postoperative symptom profiles when selecting a surgical therapy for reflux disease.	
Skubleny D, Switzer NJ, Dang J et al. (2017) LINX® magnetic esophageal sphincter augmentation versus Nissen fundoplication for gastroesophageal reflux disease: a systematic review and meta-analysis. Surgical endoscopy 31(8): 3078-84	Systematic review n=3 studies	MSA appears to be an effective treatment for GORD with short-term outcomes comparable with the more technically challenging and time consuming Nissen fundoplication. Long-term comparative outcome data past 1 year are needed in order to further understand the efficacy of MSA.	All studies in this systematic review were included in Aiolfi (2018)
Smith CD, Ganz RA, Lipham JC et al. (2017) Lower esophageal sphincter augmentation for gastroesophageal reflux disease: the safety of a modern	Review of MAUDE n=3,283	During a 4-year period in more than 3000 patients, no unanticipated MSAD complications have emerged, and there is no data to	Recent review (DeMarchi 2021) is included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
implant. Journal of laparoendoscopic & advanced surgical techniques. Part A 27(6): 586-91		suggest a trend of increased events over time. The presentation and management of device-related issues have been less complicated than revisions for laparoscopic fundoplication or other interventions for GORD. MSAD is considered safe for the widespread treatment of GORD.	
Smith CD, DeVault KR and Buchanan M (2014) Introduction of mechanical sphincter augmentation for gastroesophageal reflux disease into practice: early clinical outcomes and keys to successful adoption. J Am Coll Surg. 218(4): 776-81	Case series n=66	92% of patients are satisfied or neutral with their condition, and 83% are PPI free. The GORD-HRQL scores are similar to those of patients without GORD. There were no device ulcers or erosions and no devices explanted. Thirteen patients had additional testing for dysphagia or persistent symptoms.	This study was included in Zhuang (2021).
Stadlhuber RJ, Dubecz A, Meining A et al. (2015) Adenocarcinoma of the distal esophagus in a patient with a magnetic sphincter augmentation device:	Case report n=1	This case report shows the development of oesophageal cancer after laparoscopic implantation of a magnetic sphincter	Single case report included in the previous review.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
first of many to come? Annals of Thoracic Surgery 99: e147-8		device and highlights the need for further endoscopic surveillance of patients even after a successful antireflux procedure.	
Stanak M, Erdos J, Hawlik K et al. (2018) Novel surgical treatments for gastroesophageal reflux disease: systematic review of magnetic sphincter augmentation and electric stimulation therapy. Gastroenterology research 11(3): 161-73	Systematic review n=6 studies for MSAD	Clinical effectiveness and safety of both MSAD and EST are not sufficiently proven and are yet to be supported by high quality evidence from RCTs.	Most studies included in this systematic review were included in Aiolfi (2018) and Zhuang (2021)
Sterris JA, Dunn CP, Bildzukewicz NA et al. (2020) Magnetic sphincter augmentation versus fundoplication for gastroesophageal reflux disease: pros and cons. Current opinion in gastroenterology 36(4): 323-8	Review	MSA is a safe and efficacious procedure originally approved for patients with medically refractory, uncomplicated gastroesophageal reflux disease. The accumulating body of evidence suggests patients with intestinal metaplasia or hiatal hernias can safely and effectively have MSA, whereas further research will be required before	Review article

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		MSA is widely used for patients after bariatric surgery or for patients needing a transthoracic surgical approach. MSA is equivalent or superior to laparoscopic fundoplication in all surgical outcomes measured thus far.	
Strollo DC, Chan EG, Jaimes Vanegas N et al. (2019) Innovative and Contemporary Interventional Therapies for Esophageal Diseases. Journal of thoracic imaging 34(4): 217-35	Review	Patients with benign disorders of GORD and achalasia or with premalignant or early-stage oesophageal cancer may now be treated with minimally invasive or endoscopic techniques such LINX device, POEM, and EMR or RFA, respectively.	Review article
Tatum JM, Alicuben E, Bildzukewicz N et al. (2019) Minimal versus obligatory dissection of the diaphragmatic hiatus during magnetic sphincter augmentation surgery. Surgical endoscopy 33(3): 782-8	Non-randomised comparative study n=182 (minimal hiatal dissection, n=96; obligatory hiatal dissection, n=86)	Obligatory dissection of the hiatus with crural closure resulted in less recurrence of reflux symptoms and hiatal hernia, despite an increased proportion of patients with larger hiatal hernia and more complex anatomic disease	This study was included in Guidozzi (2019).

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		at the time of operation.	
Tatum JM, Alicuben E, Bildzukewicz N et al. (2019) Removing the magnetic sphincter augmentation device: operative management and outcomes. Surgical endoscopy 33(8): 2663-9	Case series n=435 (device removal, n=24)	MSA removal when necessary can be accomplished through minimally invasive means. Repeat LINX or fundoplication can be done after removal, however, may not be necessary in patients with removal for dysphagia.	This study focused on removing the MSA device, and studies with larger samples or better designs are included in the key evidence.
Tsai C, Steffen R, Kessler U et al. (2020) Postoperative dysphagia following magnetic sphincter augmentation for gastroesophageal reflux disease. Surgical Laparoscopy, Endoscopy and Percutaneous Techniques	Case series n=118	Postoperative dysphagia after MSA with routine posterior cruroplasty is a common transient condition, with some patients requiring dilation procedures. Patients who have atypical GORD symptoms preoperatively are more likely to require a dilation procedure for postoperative dysphagia. Most persistent dysphagia can be safely treated with 1 to 2 dilation procedures, which do not negatively affect patient quality of life.	Studies with larger samples or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Wahi JE, Le C, Yousef M et al. (2021) Robotic LINX placement: is it worth it? Journal of laparoendoscopic & advanced surgical techniques. Part A 31(5): 526-9	Non-randomised comparative study n=20 (laparoscopic LINX placement, n=10; robotic LINX place, n=10)	In comparison with laparoscopic LINX procedures, robotic LINX does not offer superior surgical outcomes in terms of postoperative PPI use, dysphagia or hospital length of stay. Robotic LINX procedures are associated with increased operative time and overall charges.	Small sample
Warren HF, Brown LM, Mihura M et al. (2018) Factors influencing the outcome of magnetic sphincter augmentation for chronic gastroesophageal reflux disease. Surgical endoscopy 32(1): 405-12	Case series n=170	MSA results in excellent/good outcomes in most patients but a higher BMI, structurally defective sphincter, and elevated LOS residual pressure may prevent this goal.	Studies with larger samples or better designs are included in the key evidence.
Warren HF, Louie BE, Farivar AS et al. (2017) Manometric changes to the lower oesophageal sphincter after magnetic sphincter augmentation in patients with chronic gastroesophageal reflux disease. Annals of surgery 266(1): 99-104	Case series n=121	MSA results in significant manometric improvement of the LOS without apparent deleterious effects on the oesophageal body. A manometrically defective LOS can be restored to normal sphincter, whereas a normal LOS remains stable.	Studies with larger samples or better designs are included in the key evidence.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Warren HF, Reynolds JL, Lipham JC et al. (2016) Multi-institutional outcomes using magnetic sphincter augmentation versus Nissen fundoplication for chronic gastroesophageal reflux disease. Surgical Endoscopy and Other Interventional Techniques 30: 3289–96	Non-randomised comparative study n=415 (MSA, n=201; Nissen fundoplication, n=214)	MSA for uncomplicated GORD achieves similar improvements in quality of life and symptomatic relief, with fewer side effects, but lower PPI elimination rates when compared with propensity-matched NF cases. In appropriate candidates, MSA is a valid alternative surgical treatment for GORD management.	This study was included in Zhuang (2021).
Yeung BPM and Fullarton G (2017) Endoscopic removal of an eroded magnetic sphincter augmentation device. Endoscopy 49(7): 718-9	Case report n=1	This study presented a single case of LINX erosion and its endoscopic removal. The patient was discharged with PPIs on postoperative day 1 after a normal oral contrast swallow study.	Single case report
Zadeh J, Andreoni A, Treitl D et al. (2018) Spotlight on the LINX™ reflux management system for the treatment of gastroesophageal reflux disease: Evidence and research. Medical	Review	The LINX device has been shown to not only be effective for managing GORD but also be as effective as fundoplication. The most common complication of	Review article

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Devices: Evidence and Research 11: 291-300		MSA is dysphagia. Erosion of the device into the oesophagus appears to be the most significant complication of the device after extended follow up. While very rare, the potentially severe consequences of this phenomenon suggest that the device should be used with some restraint and that patients should be made aware of this potential morbidity.	

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