Magnetic Sphincter Augmentation for Moderate to Severe Gastroesophageal Reflux Disease

(CPT Code 43284)

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Key Findings

This report reviews the evidence for the effectiveness and safety of magnetic sphincter augmentation devices (MSADs), as well as the clinical practice guidelines and payer policies related to this intervention.

- A recent Current Procedural Terminology (CPT) code addition (43284) provides a billing code for MSAD.
- The only MSAD approved for use in the U.S. is the LINX Reflux Management System, manufactured by Torax Medical. Torax Medical is the sponsor of nearly all of the studies related to this device. The U.S. Food and Drug Administration (FDA) conditionally approved the LINX device in 2012 and is awaiting completion of one of two required post-market studies.
- There are no published randomized controlled trials (RCTs) or controlled clinical trials on the use of MSAD compared to other treatments for moderate to severe gastroesophageal reflux disease (GERD).
- There is very low strength of evidence regarding both the effectiveness and safety of MSAD. Only one prospective, comparative registry study is available to contribute evidence about the efficacy of MSAD, but baseline differences between populations that received MSAD and populations that underwent laparoscopic fundoplication limits confidence in its findings.
- Several single-arm prospective studies are available to help assess the safety of MSAD, but the overall strength of evidence for these outcomes is also very low because of the risk of bias in these studies and the relative paucity of long-term follow-up data for sufficient numbers of participants.
- Of two poor methodological quality clinical practice guidelines, one (Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), 2013) recommends the LINX device as an option for patients with refractory GERD, and the other (Katz, Gerson, & Vela, 2013) makes no recommendation about its use.
- A search of private and public payer policies found no payers that covered MSAD; the majority of private payers stated that it was considered investigational. Most state Medicaid programs searched for this report do not have a pertinent coverage policy, and Washington lists it as a non-covered service. No Medicare national coverage determination (NCD) or local coverage determination (LCD) has covered the procedure.
- Ongoing and completed studies involving MSAD are listed in the ClinicalTrials.gov registry. One crossover RCT comparing the LINX device to high-dose proton pump inhibitor therapy is listed as having been completed, but no study results are posted or available in a publication. None of the other ongoing studies appear to be comparative.

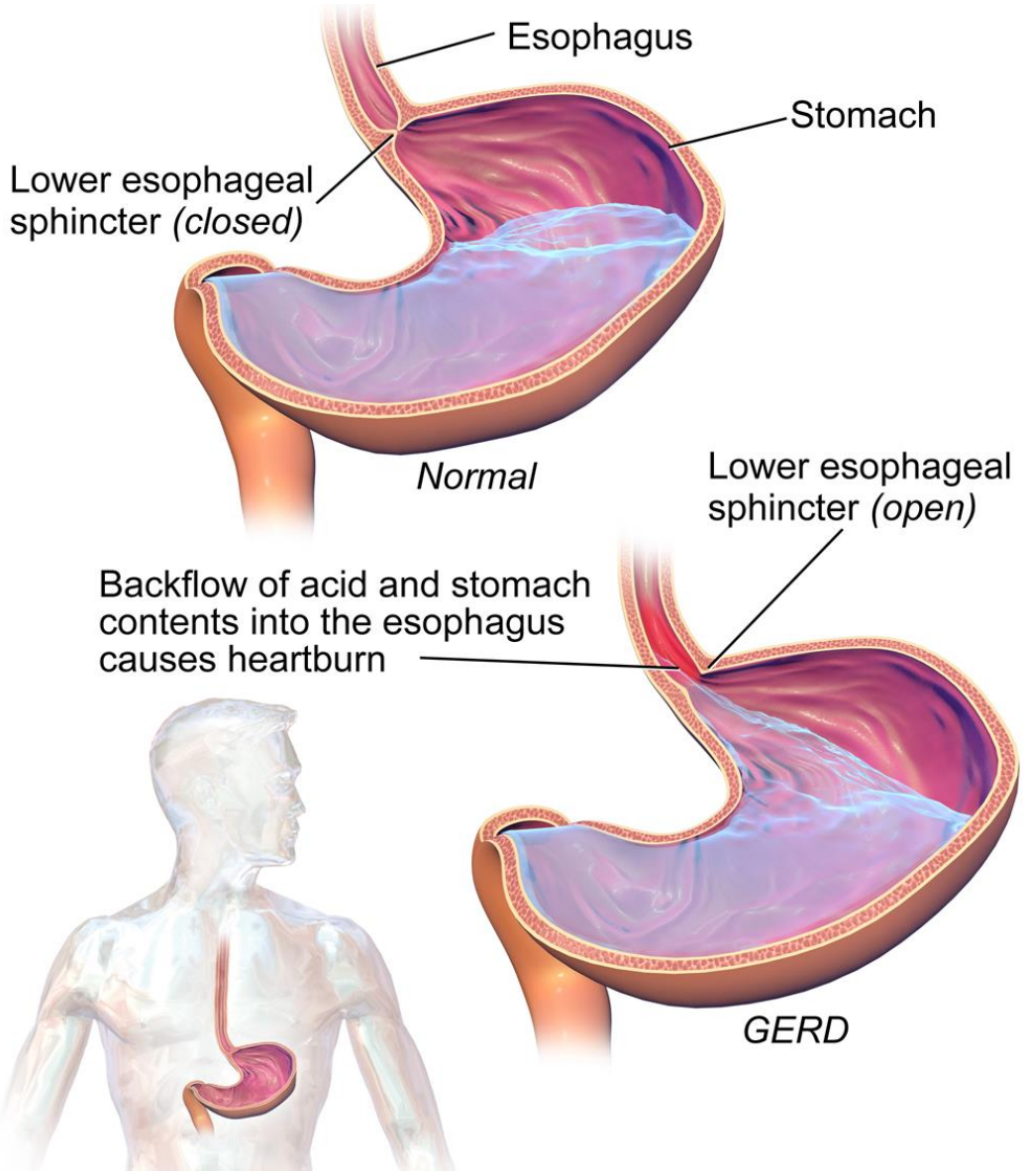
Background

Clinical Overview

- Gastroesophageal reflux, also known as heartburn or acid reflux, occurs when stomach contents rise into the esophagus (National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK], 2014). Acid reflux is common in adults (National Institute of Diabetes and Digestive and Kidney Diseases, 2014). However, individuals with gastroesophageal reflux that occurs more than twice a week may be diagnosed with GERD, a longer-lasting and more serious condition that can cause other complications such as esophagitis, esophageal stricture, respiratory problems, and Barrett's esophagus (NIDDK, 2014). The American College of Gastroenterology defines GERD as "symptoms or complications resulting from the reflux of gastric contents into the esophagus or beyond, into the oral cavity (including larynx) or lung" (American College of Gastroenterology, 2013).
- The primary cause of GERD is a weak or relaxed esophageal sphincter that allows stomach acid to enter the esophagus when it should be closed, and these conditions affect the strength and behavior of the esophageal sphincter (see Figure 1) (NIDDK, 2014). Individuals who are overweight, obese, or pregnant; take certain medications (e.g., asthma medicine, calcium channel blockers, antihistamines, pain medication, sedatives, antidepressants); use tobacco; or are exposed to secondhand smoke are more susceptible to developing GERD (NIDDK, 2014).
- GERD can be controlled through diet and lifestyle modifications, over-the-counter and prescription medications, and surgery (NIDDK, 2014). Surgical interventions include fundoplication and various endoscopic procedures (NIDDK, 2014). Fundoplication is the most common intervention for GERD and involves stitching the top of the stomach around the base of the esophagus to increase pressure around the lower end of the esophagus (NIDDK, 2014). Endoscopic procedures can be used to tighten the esophageal sphincter muscle, such as endoscopically sewing small stiches or using radiofrequency to create small lesions in the muscle (NIDDK, 2014).
- The use of an MSAD is a new surgical treatment for GERD in which a ring of titanium magnetic beads are laparoscopically placed around the lower esophagus to support the lower esophageal sphincter (Erdos & Stanek, 2016). The magnetic bond between beads keeps the lower esophageal sphincter closed. The act of swallowing food and liquid temporarily breaks the magnetic bond between the beads, and after the liquid or food bolus passes the sphincter into the stomach, the beads re-bond, closing the sphincter (Erdos & Stanek, 2016). See Figure 2 for an illustration of MSAD.
- The LINX Reflux Management System is currently the only MSAD available on the market (Erdos & Stanek, 2016). The LINX device received a four-year approval by the FDA in 2012 for treatment of people with GERD (as defined by abnormal pH testing) who have chronic GERD symptoms despite maximum medical therapy (FDA, 2012). The FDA required an extended five-year follow-up of participants who had been enrolled in approval studies and completion

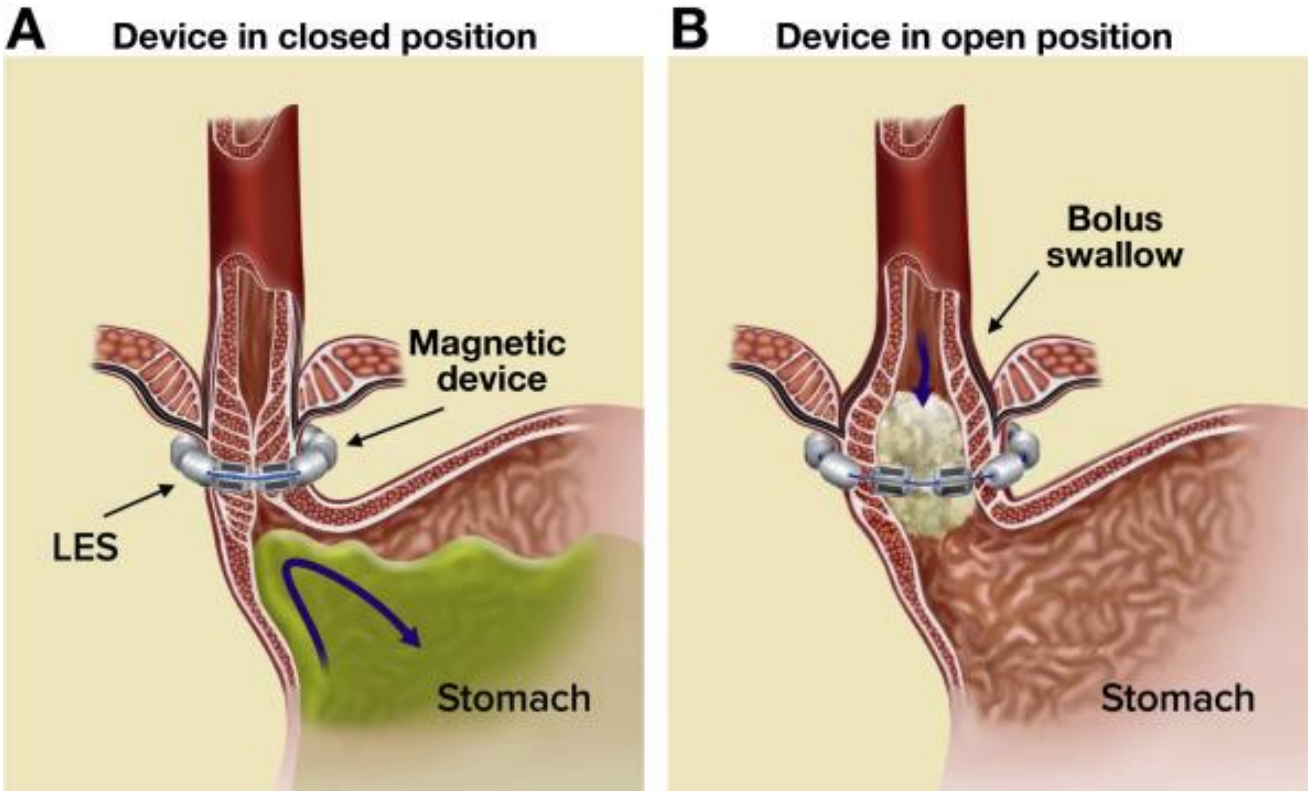
of a new five-year study enrolling at least 200 participants in at least 10 centers with no previous experience implanting the device (FDA, 2012). The first follow-up study has been completed; the second study (ClinicalTrials.gov, 2017) is listed as still active, but not recruiting, and has results expected no earlier than June 2018. A list of completed and ongoing studies is in Appendix C.

Figure 1. Overview of Gastroesophageal Reflux Disease



Source. Blaus, 2015

Figure 2. Magnetic Sphincter Augmentation Devices



Source. Ganz et al., 2016

Prevalence

Approximately 20% of the U.S. adult population is affected by GERD (NIDDK, 2014).

PICO

Population: Individuals with GERD (as defined by abnormal pH testing) who continue to have chronic GERD symptoms despite maximum medical therapy for the treatment of reflux

Interventions: Laparoscopic surgical esophageal sphincter augmentation procedure; placement of sphincter augmentation device (i.e., magnetic band); including cruroplasty when performed (CPT code 43284 replaces 0392T)

Comparators: Open or laparoscopic Nissen fundoplication; other minimally invasive procedures; maximal medical and lifestyle therapies

Efficacy and Effectiveness Outcomes: Function; quality of life; pain; prevention and/or healing of Barrett's metaplasia, adenocarcinoma, and other types of esophageal damage such as esophagitis and strictures; cost and cost-effectiveness

Harm Outcomes: Procedure or device-related adverse events; utilization of other subsequent procedures (e.g., endoscopy procedures)

Methods

Center for Evidence-based Policy (Center) researchers searched Center core evidence sources for systematic reviews (with or without meta-analysis), and technology assessments on MSAD, including the LINX device, published within the last 10 years and clinical practice guidelines published within the last five years. To ensure that the most recent data were included, Center researchers also searched Ovid MEDLINE from inception through June 22, 2017, for systematic reviews and individual studies on the use of MSADs. Center researchers also checked the search results against studies listed on the manufacturer's (Torax, Inc.) and the FDA's websites and scanned reference lists of studies undergoing full-text review for additional eligible studies.

Center researchers evaluated the methodological quality of eligible systematic reviews, individual studies, and clinical practice guidelines reviewed in this report using the quality assessment tools included with the New York State Department of Health dossier process (available on the New York State Department of Health website). Center researchers also searched Medicare, several state Medicaid programs, and private payers for coverage policies on the use of MSADs for the treatment of GERD. See Appendix A for a full list of payers searched.

Center researchers excluded systematic reviews if all of the included studies were summarized by a more comprehensive systematic review, a systematic review of a higher methodological quality, and/or a more recently published systematic review. Center researchers included RCTs, controlled clinical trials, and prospective nonrandomized studies, and excluded studies without a relevant comparison group for effectiveness outcomes. Single arm, non-comparative studies were included for outcomes involving safety, adverse events, and other harms. Only publications in English were retrieved and evaluated for inclusion. Studies involving MSADs that are not currently approved for use in the U.S. were excluded. Patient-important outcomes that have relevance for New York State Department of Health were predetermined in the topic scope development, and studies reporting other outcomes were not included. Exclusion criteria were selected prior to review of the studies, and study methods were assessed prior to review of outcomes to eliminate bias. See Appendix A for a full description of methods.

Studies often report on the statistical significance of findings, but it is not always clear how relevant an intermediate or surrogate outcome or a statistically significant finding is in clinical practice. There is some disagreement in the literature about what are considered clinically meaningful outcomes and changes for outcomes related to treatment of moderate to severe GERD. Included studies used a health-related quality-of-life scale specific to GERD (GERD-HRQL), which measures the degree to which 11 GERD symptoms are bothersome to the patient (Velanovich, 2007). The maximum score (indicating more severe symptoms) is 50, and the

minimum score (indicating no symptoms) is zero (Velanovich, 2007). However, Center researchers were unable to identify any studies that described a minimally important clinical difference associated with this scale.

Evidence Review

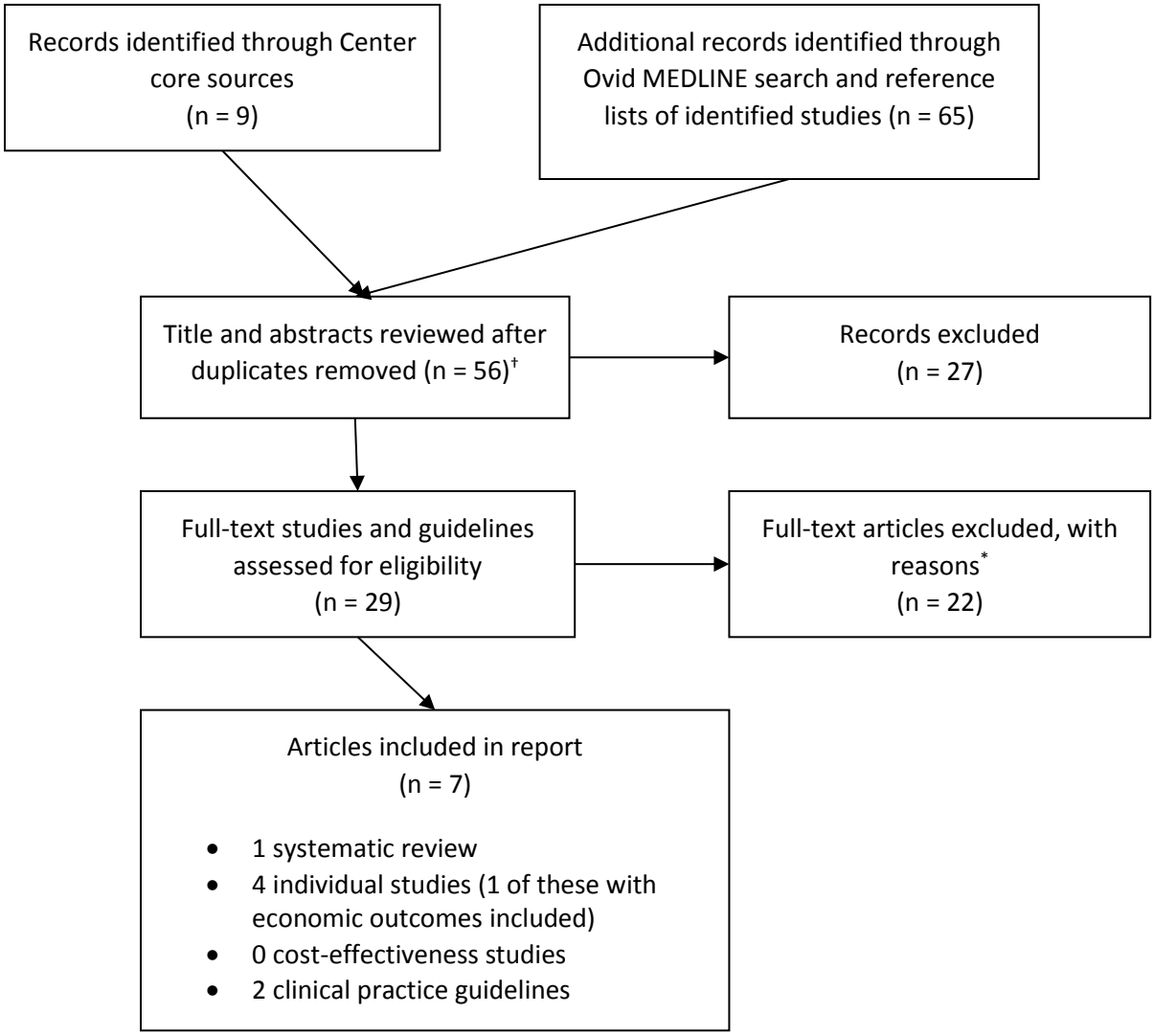
Findings

Center researchers identified one recent systematic review and four additional individual studies relevant to the effectiveness, safety, and economic outcomes of MSAD for people with moderate to severe GERD that is not responsive to medical management. The Ovid MEDLINE database search identified 65 citations, some of which were also identified through the Center core source search. After removal of duplicate citations within the MEDLINE search results and between the core source and MEDLINE searches, Center researchers evaluated 56 studies for possible inclusion. Figure 3 outlines the number of citations identified by each search and the total number of studies included in this evidence synthesis. The search strategies and list of studies reviewed in full, including reasons for exclusion, are detailed in Appendices A and B, respectively.

Overview of Evidence Sources

Center researchers summarized the evidence as reported by the included systematic review and four additional individual studies. There were six individual studies identified in the included systematic review. Center researchers did not review the individual studies included in the systematic review unless necessary for clarification of information reported in the systematic review. Table 1 provides an overview of findings from the included systematic review and four additional individual studies.

Figure 3. Search Results



† Some duplication of articles between Center core source search results and Ovid MEDLINE search results.

* Exclusion rationale provided in Appendix B.

Systematic Reviews

Erdos and Stanek (2016)

Erdos and Stanek (2016) conducted a good methodological quality health technology assessment for the Austrian Ministry of Health to support its decision about including MSADs in the Austrian catalog of benefits. The systematic review defined the population to include adults with a chronic (greater than six months) history of GERD diagnosed based on abnormal ambulatory pH study, endoscopic esophagitis, moderate to severe or refractory GERD symptoms, and at least partial response to a therapeutic trial of a proton pump inhibitor (Erdos & Stanek, 2016). Interventions evaluated included MSAD inserted laparoscopically (LINX Reflux Management System) and comparators were considered to be standard surgical treatments, including Nissen fundoplication and partial or Toupet fundoplication (Erdos & Stanek, 2016). Outcomes of interest included a primary clinical efficacy endpoint of GERD HRQL, and intermediate outcomes included heartburn, daily regurgitation, dysphagia, excessive bloating, extra-esophageal symptoms, and discontinuation of antireflux medications (Erdos & Stanek, 2016). Safety outcomes included dysphagia, excessive bloating, inability to belch or vomit, device migration, device erosion, device malfunction, device removal, rehospitalization, and reoperation (Erdos & Stanek, 2016).

Randomized controlled trials and prospective nonrandomized controlled trials were eligible for inclusion for efficacy outcomes, and for safety outcomes the authors included prospective single-arm studies such as registries and case series (Erdos & Stanek, 2016). There were no randomized or nonrandomized clinical trials available for inclusion (Erdos & Stanek, 2016). The systematic review included a comprehensive database literature search through mid-December 2015, as well as citation tracking, hand searching, and contact with industry representatives up to mid-February 2016 (Erdos & Stanek, 2016). The searches identified 273 unduplicated citations, and six studies were included in the final review (one prospective registry study with a control group for efficacy outcomes and five case series for safety outcomes) (Erdos & Stanek, 2016).

The registry study that Erdos and Stanek (2016) identified in their systematic review included four efficacy outcomes (Riegler et al., 2015). Center researchers' Ovid MEDLINE search identified each of the five case series studies that Erdos and Stanek (2016) identified for safety outcomes (Bonavina, Saino, Bona, Sironi, & Lazzari, 2013a; Ganz et al., 2016; Reynolds et al., 2014; Schwameis et al., 2014; Smith, DeVault, & Buchanan, 2014). The population characteristics for each study are detailed in Table 1.

Individual Studies

Saino, Bonavina, Lipham, Dunn, and Ganz (2015)

Saino et al. (2015) conducted a poor methodological quality prospective single-arm case series that reported outcomes at five years for 33 of 44 patients who had an MSAD implanted between 2007 and 2008 at four clinical sites in the U.S. and Europe (countries not specified). This study is non-comparative and is included for outcomes related to adverse events only.

Ganz et al. (2013)

Ganz et al. (2013) conducted a poor methodological quality prospective single-arm case series that reported outcomes for 96 of 100 enrolled subjects at Year 3 of a five-year study period. The MSAD was implanted during the first nine months of 2009 in 13 U.S. centers and one center in the Netherlands (Ganz et al., 2013). Reported outcomes included serious adverse events, device removal, rehospitalization, subsequent dilation procedures, proton pump inhibitor use, and GERD symptoms (Ganz et al., 2013). This study is non-comparative and is included for outcomes related to adverse events only.

Lipham, Taiganides, Louie, Ganz, and DeMeester (2015)

Lipham et al. (2015) reported safety outcomes compiled from multiple data sources for the first 1,084 patients who had the LINX MSAD implanted between 2007 and 2013 at 82 institutions in the U.S. and Europe. Data sources included the FDA database for device-related complications (the Manufacturer and User Facility Device Experience [MAUDE] database), information from the manufacturer, and published literature. This study was rated by Center researchers as having poor methodological quality. Reported safety outcomes included perioperative complications; device migration, removal, or failure; readmission; subsequent dilation procedures; and reported symptoms (Lipham et al., 2015).

Reynolds et al. (2016)

Reynolds et al. (2016) conducted a poor methodological quality retrospective cohort study of hospital charges related to MSAD versus laparoscopic Nissen fundoplication from a single U.S. hospital procedure database. The study reported total charges and charges in five categories (billable supplies, drugs, laboratory/radiology, operating room services, anesthesia), and room and board (Reynolds et al., 2016). The authors reported operating room time and length of stay (Reynolds et al., 2016). Costs could not be determined because of multiple factors that influenced what was actually paid; thus, billed charges were reported by the authors (Reynolds et al., 2016). This article also reported some clinical outcomes, including quality of life, symptoms, subsequent dilation procedures, and proton pump inhibitor use at one year of follow-up (Reynolds et al., 2016).

Quality and Limitations

Center researchers rated the systematic review by Erdos and Stanek (2016) as having good methodological quality. The search and inclusion criteria were rigorous and intended to limit bias. Center researchers assessed the methodological quality of the included systematic review and not the individual studies included within the review, with one exception. The Erdos and Staneck (2016) systematic review included a single study that reported on effectiveness outcomes (Riegler et al. 2015). Center researchers independently assessed the methodological quality of the Riegler et al. (2015) study. This rating is included in Table 1. All other individual studies included in the systematic review were assessed by the respective review authors.

Center researchers assessed the methodological study quality of studies not included in the systematic review using standard quality assessment methods (see Appendix A for further details). Center researchers rated all of the additional included studies as poor methodological quality (Ganz et al., 2013; Lipham et al., 2015; Reynolds et al., 2016; Saino et al., 2015).

There are several common biases across the included studies. The MSAD has never been subjected to investigation in a randomized or nonrandomized clinical trial. Efficacy data were from registries only, and safety data were found in single-arm and registry studies with a high risk of bias. Nearly all data were from studies conducted by investigators with direct or indirect funding from the manufacturer, and the manufacturer funded the majority of studies. There is a high probability of overlap of participants and data across various publications in the field. It is unclear whether subjects in the single-arm studies or registries were enrolled consecutively, and subjects in the one comparative registry study included in the eligible systematic review (Erdos & Stanek, 2016) were clearly different in terms of baseline disease state (Riegler et al., 2015). Because of inadequate reporting in the single-arm studies, it was unclear whether subjects entered the study at similar points in their disease. There were high losses to follow-up in many of the studies. Length of follow-up was generally adequate to determine immediate and postoperative complications and moderate-term outcomes (one to five years after insertion), but might not be adequate to determine either longer-term outcomes or important clinical outcomes such as development or progression of esophageal metaplasia or cancer.

Summary of the Evidence

Evidence is summarized in Table 1 by comparator and then by outcomes of effectiveness and harms. Individual study quality discussed in the context of the included systematic review is taken directly from review authors and is not the Center's original assessment of the study, unless otherwise noted. Table 1 provides a high-level summary of the evidence listed by systematic review and included studies.

Table 1. Overview of Included Studies

Citation, Study Details	# of Studies (k) Population (n) *Individual Study Quality*[a]	Study Summary and Findings	Comments
Systematic Reviews with Meta-analyses			
Center researchers did not identify any systematic reviews with meta-analyses on this topic.			
Systematic Reviews (without Meta-analyses)			
Erdos and Stanek (2016) Search Dates Inception to December 2015, other searches to February 2016 Eligible Study Designs RCTs, CCTs, prospective comparative observational studies (efficacy outcomes) and prospective non-comparative studies (harms only) Location Studies from Austria, Germany, Italy, and the U.K. were included in the SR	k = 6 studies (5 for harms only) Total n > 600 (249 for efficacy and safety outcomes and 356 for safety outcomes only); potential overlap of subjects across studies included in systematic review *SR's quality assessment of individual studies:* Systematic reviews: low risk of bias for prospective comparative registry study (Riegler, 2015) and high risk of bias for all others	Comparators MSAD vs. LNF (for efficacy outcomes only) MSAD without comparator group (for safety outcomes) Outcomes (outcomes are from the Riegler et al. (2015) registry study unless otherwise noted and no statistical testing for comparisons provided in SR unless noted) *GERD HRQL scores from baseline to 1-year follow-up* MSAD 20 to 3 points LNF 23 to 3.5 points *Patient satisfaction at 1-year follow-up* MSAD 91.8% LNF 86.7% *Discontinued PPI therapy at 1-year follow-up* MSAD 81.8% vs. LNF 63% *Improvement in heartburn (baseline to 1-year follow-up)* MSAD 30.8% to 3.5%	Narrative summary only with no meta-analysis due to inclusion of only one registry study for effectiveness outcomes. Single-arm studies were included for harms outcomes and these types of studies are not amenable to meta-analysis. There were differences between the MSAD and LNF groups for inclusion criteria and patient characteristics in the Riegler et al. (2015) registry study, reflecting that LNF patients were at a more severe stage of GERD (e.g., hiatal hernia size >3 cm 45.7% in LNF group and 1.6% in MSAD group; Barrett's esophagus 19.1% in LNF

Methodological Quality Good		LNF 40% to 8.5% *Improvement in regurgitation symptoms (baseline to 1-year follow-up)* MSAD 60% to 13% LNF 58.2% to 3.1% *Extra-esophageal symptoms (e.g., cough, asthma, hoarseness, etc.) (baseline to 1-year follow-up)* MSAD 63.9% to 22.3% LNF 53.3% to 17.4% *Dysphagia at 1 year of follow-up* MSAD 7% vs. LNF 10.6% *Procedure or device-related adverse events* *Intraoperative complications* MSAD 1.49% vs. LNF 2.13% *Postoperative excessive bloating* MSAD 10% vs. LNF 31.9% *Inability to belch* MSAD 1.6% vs. LNF 10.1% *Inability to vomit* MSAD 8.7% vs. LNF 56.6% *Esophageal erosion, device migration, and device malfunction*	group versus 1% in MSAD group; grade C esophagitis 8.5% in LNF group versus 1% in MSAD group). The mean BMI score, duration of GERD diagnosis, and number of years of PPI therapy were similar for the MSAD and LNF groups. Authors' conclusions: "Overall, the strength of evidence is moderate for efficacy and very low to moderate for safety outcomes" (p. 42). Note: Center researchers rated the strength of evidence as very low for all outcomes evaluated, given the risk of bias and other limitations of the underlying studies. Center researchers independently rated the methodological quality of the Riegler et al. (2015) registry study as poor. There was significant risk of bias in patient selection, individuals identified for follow-up, and

Citation, Study Details	# of Studies (k) Population (n) *Individual Study Quality*[a]	Study Summary and Findings	Comments
		Three studies reported on esophageal erosion, two studies reported on device migration, and one study reported on device malfunction. No events were reported in any of the studies on these adverse events. *Removal of MSAD (reported in registry study)* 4 of 202 were removed at 1 year of follow-up *Removal of MSAD (reported in 5 single-arm studies: 2 with follow-up <1 year; 3 with follow-up of 1 to 5 years)* 0% removed at < 1 year 4% removed at 1 year 3% removed at 3 years 7% removed at 5 years *Reoperation at 1 year of follow-up* MSAD 4% (for device removal) vs. LNF 6.4% (for persistent GERD and herniation of the fundic wrap) *Hospital readmission at 1 year of follow-up* MSAD 5.4% vs. LNF 4.3%	conflict of interest. The study was funded by the manufacturer and several of the study authors received consulting fees from the manufacturer.
Single-Arm, Non-comparative Studies			
Saino et al. (2015)	n = 44 (33 [75%] had data from 5-year follow-up) All subjects had abnormal ambulatory esophageal pH	<u>Comparators</u> None <u>Outcomes (included for harms only)</u> *Procedure or device-related adverse events*	Single-arm small study with a high risk of bias due to design and high losses to follow-up, but does give information on harms

Citation, Study Details	# of Studies (k) Population (n) *Individual Study Quality*[a]	Study Summary and Findings	Comments
Study Length 5-year follow-up (MSAD placed February 2007 to October 2008) Location 4 clinical sites, 2 in U.S. and 2 in Europe (not otherwise specified) Study Funding Torax Medical Methodological Quality Poor	monitoring, typical GERD symptoms and daily use of PPIs. Age range 18-75 years Patients excluded: Large hiatal hernia (>3cm); Grade B or higher esophagitis; BMI >35 kg/m^2; Barrett's esophagus; motility disorders; gross esophageal anatomic abnormalities. Contraindications: known allergy to titanium, stainless steel, nickel, or ferrous materials	"There were no reports of death, device erosions, device migrations, device malfunction, or late-occurring device complications. No new safety risks were identified related to the implant procedure or device." (p. 790) "The rate of serious adverse events (SAEs) related to the device and/or implant procedure was 6.8% (3/44). All SAEs occurred and resolved within the first year after implant. " (p. 790) *Use of subsequent procedures: Removal of MSAD* 6.8% (3/44) removed (1 for persistent dysphagia; 1 for ongoing reflux symptoms requiring Nissen fundoplication; 1 in order to have an MRI)	outcomes at 5 years for those who could be tracked.
Ganz et al. (2013) Study Length 3 year follow-up	n = 100 (85 completed follow-up at 3 years) All subjects had abnormal ambulatory pH monitoring Subject characteristics: 52% male; median age 53	Comparators None Outcomes (included for harms only) *Procedure or device-related adverse events* Pain: 25/100 (25%)	Relatively small, single-arm study with substantial methodological limitations that is included for harms outcomes only. Unclear whether losses to follow-up

Citation, Study Details	# of Studies (k) Population (n) *Individual Study Quality*[a]	Study Summary and Findings	Comments
Location 13 Centers in the U.S., 1 in the Netherlands Study Funding Torax Medical Methodological Quality Poor	years (range 18-75); median BMI 28 kg/m^2 (range 20-35); median duration of PPI treatment 5 years (range <1 to 20);	Inability to belch or vomit: 6/100 (6%) Bloating: 14/100 (14%) Dysphagia: 68/100 (68%, 5% were categorized as severe dysphagia) Other reported adverse events included odynophagia (8/100); hiccups (8/100); nausea (7/100); decreased appetite (4/100); and several other categories that occurred in 2 or fewer patients (flatulence, belching, weight loss, food impaction, globus sensation, irritable bowel syndrome or dyspepsia, regurgitation of sticky mucus, uncomfortable feeling in chest, vomiting, persistent GERD symptoms). *Use of subsequent procedures: Removal of MSAD* 6 of 100 (6%) removed at 3 years (3 for dysphagia, 1 for pain, 1 for vomiting, 1 for persistent GERD symptoms)	were considered in outcome reporting.
Lipham et al. (2015) Study Length Devices implanted between February 27, 2007 and July 1, 2013	n = 1048 patients with implants during study period (144 during pre-market studies; 332 enrolled in post-market registry or study; 572 implanted outside of a	Comparators None Outcomes (included for harms only) *Procedure or device-related adverse events* Perioperative complications: 0.1% Device erosion: 0.1% Device migration: 0%	Although this study is to be commended for trying to determine complications related to MSAD implantation across time and geographical boundaries, it was not possible to follow all people who received MSAD and calculate the true number of

Citation, Study Details	# of Studies (k) Population (n) *Individual Study Quality*[a]	Study Summary and Findings	Comments
Location Implants placed at 82 institutions in the U.S. and Europe (countries not specified) Study Funding Torax Medical Methodological Quality Poor	post-market registry or study) Total of 111 events occurring in 82 patients at 26 centers analyzed Mean implant duration 274 days	Device malfunction: 0% *Use of subsequent procedures* *Removal of MSAD* 3.4% (23 for dysphagia; 7 for GERD symptoms; 3 for pain; 1 for vomiting; 1 to have an MRI; 1 for erosion). Removals <= and > 90 days post-implantation similar (17 vs. 19). *Esophageal dilation* 59 (5.6%) *Hospital readmission* 1.3% (13 at <=90 days and 1 at >90 days post-implantation) Reasons for readmission: dysphagia (8); pain (4); nausea and vomiting (2)	denominator events, thereby likely underestimating the adverse event rates. The authors did locate 111 events collected from clinical literature (32); FDA MAUDE database (20); and manufacturer's database (59). This study does highlight potential complications, but without complete tracking of people who received MSAD devices, it does not offer data to support true complication rates, only a potential range of complications that can occur. The majority of data came from persons who had implants in place for less than one year, and so it offers little information about longer-term adverse events.
Reynolds et al. (2016) Study Length Patients had procedures between	N = 119 (52 MSAD, 67 LNF)	Comparators MSAD vs. LNF Outcomes (included for economic outcomes only) *Cost/cost-effectiveness (Data reported for charges only)*	This retrospective cohort study is included because it was the only study identified in the search that addressed economic outcomes. Other

Citation, Study Details	# of Studies (k) Population (n) *Individual Study Quality*[a]	Study Summary and Findings	Comments
January 2010 and June 2013. Charges are derived from the index hospitalization, representing initial and periprocedural charges only. Location Two institutions in Los Angeles, CA Study Funding Torax Medical Methodological Quality Poor	Patient characteristics (MSAD vs. LNF): Mean age: 53 vs. 53 Male: 61.5% vs. 46.2% (p = 0.04) Mean BMI in kg/m^2: 26 vs. 27 Preoperative GERD HRQL score: 17 vs. 19 Hiatal hernia: 67% vs. 75% Barrett's esophagus: 31% vs. 27% No difference between groups that was statistically significant except for gender.	Total mean charges +/- SD (MSAD vs. LNF): $48,491 +/- $16,481 vs. $50,111 +/- $17,376 *Components of total charges* Total billable supplies: $24,552 +/- $8,143 vs. $17,118 +/- $6,187 Pharmacy/drugs: $2,243 +/- $2,791 vs. $5,453 +/- $4,196 Laboratories/tests/radiology: $1,358 +/- $1,891 vs. $2,758 +/- $2,744 Operating room services: $15,849 +/- $4,398 vs. $18,664 +/- $5,170 Anesthesia: $2,782 +/- $1,429 vs. $3,224 +/- $1,519 Room and board: $2,619 +/- $2,226 vs. $4,235 +/- $3,006 *Other resource utilization outcomes* Operating room time (minutes +/- SD): 66 +/- 23 vs. 82 +/- 18 Length of stay (hours +/- SD): 17 +/- 10 vs. 38 +/- 14	reported outcomes are not included because the study design did not meet full inclusion criteria. MSAD and LNF surgeries were performed by a single surgeon (the first author of the paper). This increases internal validity of the charges estimates, but may decrease the generalizability of these estimates.

Abbreviations. CCT: controlled clinical trial; HRQL: health-related quality of life; LNF: laparoscopic Nissen fundoplication; MAUDE: Manufacturer and User Facility Device Experience; MRI: magnetic resonance imaging; PPI: proton pump inhibitor; SAE: serious adverse event; SD: standard deviation; SR: systematic review.

Effectiveness: Outcome #1 Function and quality of life

Systematic Reviews

One systematic review reported quality of life scores derived from the GERD-HRQL instrument at one year after surgery from a single registry study (Riegler et al., 2015) of people who had MSAD implantation versus laparoscopic Nissen fundoplication (Erdos & Stanek, 2016). Although the laparoscopic Nissen fundoplication group had more severe GERD at baseline, both groups improved to a similar level (score of 3 in MSAD vs. score of 3.5 in laparoscopic Nissen fundoplication group) (Erdos & Stanek, 2016). Patient satisfaction was similarly high in both groups at one year (MSAD 91.8% vs. laparoscopic Nissen fundoplication 86.7%) (Erdos & Stanek, 2016). Heartburn, regurgitation, and extra-esophageal symptoms improved in both the MSAD and laparoscopic Nissen fundoplication groups: heartburn symptoms improved to a greater degree in the MSAD group and regurgitation and extra-esophageal symptoms showed greater improvement in the laparoscopic Nissen fundoplication group (Erdos & Stanek, 2016).

Several studies reported rates of discontinuation of proton pump inhibitor use at various time periods after procedures, but only one study (Riegler et al., 2015) included in the systematic review by Erdos and Stanek (2016) provided rates of proton pump inhibitor discontinuation in MSAD recipients compared to those who had laparoscopic Nissen fundoplication surgery. The review authors reported that 81.8% of the MSAD group had discontinued proton pump inhibitor use compared to 63% of the laparoscopic Nissen fundoplication group (Erdos & Stanek, 2016). For comparison, the two non-comparative observational studies that reported this outcome had similar estimates. Saino and colleagues (2015) reported that 87.8% of 33 MSAD recipients had discontinued proton pump inhibitor use at five years of follow-up; Ganz and colleagues (2013) reported that 87% had discontinued proton pump inhibitor use at three years of follow-up.

Individual Studies

No individual studies met inclusion criteria for effectiveness outcomes.

Effectiveness: Outcome #2 Prevention or healing of Barrett's metaplasia, adenocarcinoma, or other types of esophageal damage (e.g., esophagitis, strictures)

Systematic Reviews

This outcome was not reported in the included systematic review (Erdos & Stanek, 2016).

Individual Studies

No individual studies met inclusion criteria for effectiveness outcomes.

Harms: Outcome #1 Procedure-related adverse events

Systematic Reviews

Erdos and Stanek (2016) reported adverse outcomes from the Riegler (2015) registry study. Intraoperative complications were minimal, but higher among people in the laparoscopic Nissen

fundoplication group. Postoperative symptoms, including excessive bloating, inability to belch, and inability to vomit, were substantially higher among the laparoscopic Nissen fundoplication groups, although no statistical testing was conducted (Erdos & Stanek, 2016). Dysphagia, which is considered to be a risk of laparoscopic Nissen fundoplication procedures was, as expected, higher in the laparoscopic Nissen fundoplication group (10.6%), but was also reported to be 7% in the MSAD group. Esophageal erosion, device migration, and device malfunction were included as potential outcomes in several of the prospective, non-comparative observational studies within this systematic review (Erdos & Stanek, 2016), but no events were recorded. Of 202 patients, 4% had their devices removed for dysphagia, pain, or persistent GERD by one year of follow-up in the Riegler registry study (2015).

Individual Studies

Saino et al. (2015) reported that there were no deaths, device erosions, migrations, malfunctions or late MSAD complications in five years of follow-up for 44 patients who had the implant, but that 6.8% of patients experienced serious adverse events that occurred and were resolved within the first year after implantation.

Ganz et al. (2013) reported on a range of procedure- and device-related adverse outcomes at three years post-MSAD implantation in a cohort of 100 people. Pain was reported by 25% of the subjects and dysphagia by 68%, although severe dysphagia was only reported by 5% (Ganz et al., 2013). Bloating was reported by 14%, odynophagia and hiccups by 8%, nausea by 7%, and decreased appetite by 4% (Ganz et al., 2013). A range of other symptoms occurred in two or fewer subjects each (Ganz et al., 2013).

According to Lipham et al. (2015), there were 111 reported events among 82 subjects who had implants at 26 centers. The study authors reported that eight patients had a readmission for dysphagia, four for pain, and two each for nausea and vomiting (Lipham et al., 2015). One patient had respiratory arrest immediately after the implant procedure, but was able to be resuscitated (Lipham et al., 2015). Lipham and colleagues reported that one device erosion was recorded in the FDA's MAUDE database (2015).

Harms: Outcome #2 Use of subsequent procedures (e.g., device removal, dilation)

Systematic Reviews

In the Riegler et al. (2015) study included in the Erdos and Stanek (2016) systematic review, 4% of MSAD recipients had reoperation (for device removal) by one year of follow-up, and 6.4% of the laparoscopic Nissen fundoplication group had operations for indications of persistent GERD and/or herniation of the fundic wrap. Readmission occurred among 5.4% of the MSAD group and 4.3% of the laparoscopic Nissen fundoplication group by one year of follow-up (Erdos & Stanek, 2016). Across the non-comparative observational studies in this systematic review, device removals were reported at 0% at less than one year and increased to 7% by five years of follow-up (Erdos & Stanek, 2016).

Individual Studies

Three additional non-comparative individual studies reported device removals (Ganz et al., 2013; Lipham et al., 2015; Saino et al., 2015). Saino et al. (2015) reported 6.8% removed at five years of follow-up; Ganz et al. (2013) reported 6% removed at three years of follow-up, and Lipham et al. (2015) reported that 3.4% of subjects had removals (median total length of device implantation for all devices was 274 days, but total nor mean duration of device implantation before removal was reported). In addition, Saino et al. (2015) reported two cases in which the device was electively removed; one so that the patient could undergo magnetic resonance imaging; the second individual received Nissen fundoplication for ongoing reflux symptoms.

Lipham and colleagues reported that among the 111 recorded adverse events, 59 subjects (5.6%) required esophageal dilation and that the majority of these were performed prior to 90 days post-procedure (2015).

Harms: Outcome #3 Economic outcomes

Systematic Reviews

The one included systematic review did not report an economic outcome (Erdos & Stanek, 2016).

Individual Studies

Only the Reynolds retrospective observational cohort study reported any economic outcomes (Reynolds et al., 2016). Total mean charges (+/- standard deviation) were similar between the MSAD and laparoscopic Nissen fundoplication groups at $48,491 +/- $16,481 vs. $50,111 +/- $17,376 (Reynolds et al., 2016). The breakdown of total charge components is detailed in Table 1, along with a comparison of required operating room time and length of stay for each group. These surgeries occurred between 2010 and 2013 and charges are not presented in today's dollars. The authors stated that because of the differences in payer reimbursement, actual cost to the patient or insurer could not be determined (Reynolds et al., 2016). The charges reported reflect immediate and periprocedural charges only and do not account for any subsequent care required after hospital discharge (Reynolds et al., 2016).

Cost-Effectiveness

Center researchers did not identify any systematic reviews that included an economic analysis, but did identify one individual study (Reynolds et al., 2016) that reported hospital-related charges for the use of the LINX device compared to surgical Nissen fundoplication for the treatment of GERD. The individual economic study was rated as having poor methodological

quality by Center researchers. This study is described in the section above and included in Table 1.

Clinical Practice Guidelines

Center researchers identified two poor methodological quality clinical practice guidelines that address the use of the LINX Reflux Management System for GERD management (Katz et al., 2013; Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), 2013). The SAGES Technology and Value Assessment Committee, based on a review of five small case series (total n = 244), concluded that the LINX Reflux Management System is safe and effective to use for patients with medically refractory GERD that has not progressed to end-stage reflux disease, and recommended that LINX is a "reasonable treatment option for appropriately selected patients with GERD who meet indications for antireflux surgery" (SAGES, 2013, Expert Panel Recommendation). However, the committee cautioned that there is a high incidence of dysphagia with LINX use and additional research is needed to establish the comparative effectiveness of LINX with Nissen fundoplication (SAGES, 2013).

In a guideline from the American College of Gastroenterology, Katz et al. (2013) briefly discussed a single trial on the use of the LINX Reflux Management System, but did not include reference to LINX in their summary recommendations. As part of the discussion text, the authors noted that "more data are required before widespread usage [of LINX] can be recommended" (Katz et al., 2013, p. 317).

Payer Policies

Center researchers searched for policies on the coverage of MSAD for the treatment of GERD from Aetna, Anthem, Blue Shield of Northeastern New York (BSNENY), Capital District Physicians' Health Plan, Centers for Medicare and Medicaid Services, Cigna, Emblem Health, Empire Blue Cross Blue Shield (BCBS), Excellus BCBS, Tufts Health Plan, UnitedHealthcare, and nine state Medicaid programs (CA, FL, MA, NJ, NY, OR, PA, TX, and WA).

A search of the CMS website identified five LCDs from Medicare rejecting coverage of MSAD. Of the nine state Medicaid programs searched, Center researchers did not identify coverage policies or inclusion of CPT code 43284 in fee schedules for eight states (CA, FL, MA, NJ, NY, OR, PA, and TX). Washington Medicaid's April 2017 fee schedule states that CPT code 43284 is not covered for all hospitals (Washington Health Care Authority, 2017). Of the 10 private payers searched, seven payers (Aetna, Anthem, BSNENY, Cigna, Empire BCBS, Excellus BCBS, and United Healthcare) do not cover MSAD for their populations; specific policy language from these payers is shown in Table 2 below. Center researchers were not able to identify publicly available coverage policies for three payers (Capital District Physicians' Health Plan, Emblem Health, and Tufts Health Plan).

Medicare Local Coverage Determinations

No NCD has addressed CPT code 43284, and five LCDs have rejected coverage of the code, according to the Center search. Specific language from the LCDs is included in Table 2 below. The companies issuing the LCDs and the regions they cover include the following:

- First Coast Service Options, Inc., *Local Coverage Determination: Noncovered services (L33777):* Florida, Puerto Rico, and Virgin Islands
- Noridian Healthcare Solutions, LLC, *Local Coverage Determination: Non Covered Services (L36219)*: California, Hawaii, Nevada, and U.S. Pacific territories (Noridian Healthcare Solutions, 2017b)
- Noridian Healthcare Solutions, LLC, *Local Coverage Determination: Non-covered Services (L35008)*: Alaska, Arizona, Idaho, Montana, North Dakota, Oregon, South Dakota, Utah, and Wyoming (Noridian Healthcare Solutions, 2017a)
- Novitas Solutions, Inc., *Local Coverage Determination: Services That Are Not Reasonable and Necessary (L35094):* Arkansas, Colorado, Delaware, District of Columbia, Louisiana, Maryland, Mississippi, New Jersey, New Mexico, Oklahoma, Pennsylvania, and Texas (Novitas Solutions Inc., 2017)
- Palmetto GBA, *Local Coverage Determination (LCD): Upper Gastrointestinal Endoscopy and Visualization (L34434):* North Carolina, South Carolina, Virginia, and West Virginia (Palmetto GBA, 2017)

Medicaid Coverage Policies

Center researchers did not identify coverage policies or fee schedule listings for eight of the nine Medicaid programs searched. The Washington Health Care Authority's April 2017 fee schedule states that CPT code 43284 is not covered (Washington Health Care Authority, 2017).

Private Payer Coverage Policies

Three of the 10 private payers searched for this report did not have publicly available coverage policies for MSAD. Seven payers have specific policy language rejecting coverage of MSAD. Specific policy language and links to policies for these payers are included in Table 2.

Table 2. Policy Language for Payers Regarding MSAD

Payer	Policy Language
Medicare	
First Coast Service Options, Inc. L33777—Noncovered services *(Revision effective date 5/1/2017)*	"The below list of noncovered services is not all inclusive … [CPT code] 43284." (First Coast Service Options Inc., 2017)
Noridian Healthcare Solutions, LLC L36219—Non Covered Services *(Revision effective date 1/18/2017)*	"The following services [including CPT 43284], as described below and billed with any CPT and or HCPCS code, are considered not proven effective or not medically reasonable and necessary and will be denied as such." (Noridian Healthcare Solutions, 2017b)
Noridian Healthcare Solutions, LLC L35008—Non-covered Services *(Revision effective date 1/18/2017)*	"The following services [including CPT 43284], as described below and billed with any CPT and or HCPCS code, are considered not proven effective or not medically reasonable and necessary and will be denied as such." (Noridian Healthcare Solutions, 2017a)
Novitas Solutions, Inc. L35094—Services That Are Not Reasonable and Necessary *Revision effective date 3/16/2017)*	"Specific services considered not reasonable and necessary, per the following previous Novitas evaluations … CPT codes 43284 (Placement of augmentation device in sphincter of esophagus using laparoscope) and 43285 (Removal of augmentation device from sphincter of esophagus) have replaced Category III codes 0392T (Repair of esophageal sphincter using an endoscope and placement of sphincter augmentation device) and 0393T (Removal of prosthesis of esophageal sphincter). 0392T and 0393T were considered not reasonable and necessary; therefore, services reported with CPT codes 43284 and 43285 will be considered not reasonable and necessary. (Position regarding 0392T and 0393T reaffirmed upon reconsideration in November 2015)." (Novitas Solutions Inc., 2017)
Palmetto GBA L34434—Upper Gastrointestinal Endoscopy and Visualization43284 *(Revision effective date 1/1/2017)*	"The following CPT codes are noncovered … 43284 and 43285." (Palmetto GBA, 2017)
Private Payers	
Aetna (*last review 4/14/2017)*	"Aetna considers the LINX Reflux Management System (a sphincter augmentation device) (Torax Medical, Shoreview, MN) experimental and investigational for the management of GERD and all other indications

Payer	Policy Language
	because it has not been established as an effective option for the treatment of GERD and other indications." (Aetna, 2017)
Anthem (*last review 11/3/2016*)	"Lower esophageal sphincter augmentation devices are considered investigational and not medically necessary for the treatment of gastroesophageal reflux disease (GERD) and for all other indications." (Anthem, 2016)
BSNENY *(last review 1/2017)*	"Endoscopic submucosal implantation of a prosthesis or injection of a bulking agent (e.g., polymethylmethacrylate beads, zirconium oxide spheres) is considered investigational as a treatment of gastroesophageal reflux disease." (Blue Shield Northeastern New York, 2017)
CDPHP	*Coverage policy not publicly available.*
Cigna (*effective 2/15/2017*)	"Cigna does not cover any of the following endoscopic anti-reflux procedures for gastroesophageal reflux disease (GERD), or any other indication, because each is considered experimental, investigational or unproven (list may not be all inclusive): • injection/implantation of biocompatible material (e.g., plexiglas or polymethylmethacrylate [PMMA], Durasphere™, Gatekeeper™ Reflux Repair System; LINX™ Reflux Management System)" (Cigna, 2017)
Emblem Health	*Coverage policy not publicly available.*
Empire BCBS (*effective 12/28/2016*)	"Lower esophageal sphincter augmentation devices are considered investigational and not medically necessary for the treatment of gastroesophageal reflux disease (GERD) and for all other indications." (Empire Blue Cross Blue Shield, 2016)
Excellus BCBS (*last review 12/15/2016*)	"Based upon our review and assessment of peer-reviewed literature, use of a magnetic esophageal ring (e.g., LINX™ Reflux Management System) in the treatment of gastroesophageal reflux disease (GERD) has not proven to be medically effective and is therefore considered investigational." (Excellus Blue Cross Blue Shield, 2016)
Tufts Health Plan	*Coverage policy not publicly available.*
UnitedHealthcare (*effective 1/1/2017)*	"The LINX™ Reflux Management System is unproven and not medically necessary for treating GERD. The safety and efficacy of this system has not been established in the peer-reviewed medical literature. Available studies are hampered by a number of limitations, including small study size, lack of statistical power, lack of controls or comparators, and lack of long-term follow-up." (United Healthcare, 2017)

Payer	Policy Language
State Medicaid	
California	*No coverage criteria identified.*
Florida	*No coverage criteria identified.*
Massachusetts	*No coverage criteria identified.*
New Jersey	*No coverage criteria identified.*
New York	*No coverage criteria identified.*
Oregon	*No coverage criteria identified.*
Pennsylvania	*No coverage criteria identified.*
Texas	*No coverage criteria identified.*
Washington *(effective 4/1/2017)*	Washington Health Care Authority's April 2017 outpatient fee schedule states that CPT code 43284 is not covered (Washington Health Care Authority, 2017).

Abbreviations. BSNENY: Blue Shield Northeastern New York; CDPHP: Capital District Physicians' Health Plan; CPT: current procedural terminology; GERD: gastrointestinal esophageal reflux disease; HCPCS: healthcare common procedure coding system.

Policy Summary

None of the payers searched for this report covered MSAD for GERD.

Conclusion

Although the LINX MSAD device has been approved for use in the U.S. since 2012, there is no high-quality evidence upon which to make a determination of its effectiveness or harms. Of note, no randomized or controlled clinical trials have been conducted, and virtually all studies have been funded by the manufacturer and conducted by investigators who have financial and other potential conflicts of interest. The one comparative, prospective study available that examines outcomes with MSAD compared to laparoscopic fundoplication has substantial baseline differences in the populations enrolled. Although subjects who had fundoplication surgery had more severe GERD disease, quality of life and satisfaction scores were good and similar for both groups.

There are questions about the longevity of the MSAD device, in that removals appeared to increase over time. Erdos and Stanek (2016) noted that one included observational study also showed evidence of heartburn symptom recurrence in Years 2 through 5 post-implantation. Although nearly 90% of subjects reported heartburn at baseline and this decreased to about 3% at Year 1 post-implantation, it had risen to nearly 12% by Year 5. This also highlights the lack of data on long-term, patient-important outcomes. It is difficult to compare the safety of MSAD directly to fundoplication surgery given the baseline differences in populations that received each procedure and the lack of longer-term follow-up. There are no data on comparison of MSAD to other treatments, including other endoscopic procedures or drug treatments. MSAD is likely to be relatively safe and could offer some advantages in terms of operative and recovery time, in addition to reversibility. Yet, without truly comparative, long-term data it is impossible to determine whether these initial advantages are offset by longer-term lack of effectiveness or adverse outcomes.

Although numerous clinical practice guideline address management of GERD, Center researchers found only two that specifically mentioned MSAD and the LINX device (Katz et al., 2013; Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), 2013). The SAGES Technology and Value Assessment Committee, recommended LINX for use in refractory GERD that had not progressed to end-stage disease, but also stated that further comparative research is needed to determine effectiveness (SAGES, 2013). The American College of Gastroenterology's guideline authors discuss the LINX device in their evidence review, but do not give a recommendation related to it (Katz et al., 2013). Both guidelines were of poor methodological quality. No payer that Center researchers included in a broad search of national and local payers, including private and public payers, covers MSAD. The majority of commercial payers reviewed have found that the device is investigational and do not cover it on that basis. No

Medicare area LCD reviewed has covered the procedure. Only one reviewed Medicaid program (Washington) specifically lists the CPT code as not covered; the others do not specifically address it.

Strength of Evidence

The Center uses the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group approach to enhance consistency in grading the strength of evidence. RCTs are initially categorized as having high strength of evidence and observational studies are categorized as having low strength of evidence. The strength rating is downgraded based on limitations including inconsistency of results, uncertainty of directness of measurement or population, imprecision or sparseness data, and high probability of reporting bias. The grade is increased from low for evidence from observational studies if there is a strong association (i.e., significant relative risk of >2 or <0.5 with no plausible confounders in two or more observational studies), a very strong association (i.e., significant relative risk of >5 or <0.2 based on direct evidence with no major threats to validity), or a dose-response gradient. The grade is also increased if all plausible confounders would have reduced the effect (GRADE Working Group, 2004). Table 3 provides an overview of the strength of evidence by outcome and associated rationale for the strength of evidence rating.

Table 3. Strength of Evidence for MSAD: Effectiveness, Harms, and Cost-Effectiveness

Outcome	Strength of Evidence Assessment	Rationale
Effectiveness		
Function and Quality of Life	Very Low	Evidence derives from only one prospective, comparative study with significant methodological limitations. Downgraded for risk of bias (primarily baseline differences in populations) and imprecision (paucity of data).
Pain	Very Low	Evidence derives from a solo single arm, non-comparative study. Downgraded for risk of bias.
Prevention or Healing of Barrett's Metaplasia, Adenocarcinoma, or Other Types of Esophageal Damage	No evidence	Center researchers did not identify any eligible studies that reported these patient-important outcomes.
Harms		
Procedure-Related Adverse Events	Very Low	Evidence derives from one systematic review containing one prospective comparative study, and several poor methodological quality non-comparative prospective observational studies, although estimates appear to be similar across these studies. Center researchers believe that individual subjects might have been reported in more than one of these studies, which could artificially increase the consistency of these estimates. Downgraded for risk of bias.
Use of Subsequent Procedures	Very Low	Evidence derives from one systematic review containing one prospective comparative study, and several poor methodological quality non-comparative prospective observational studies, although estimates appear to be similar across these studies. Center researchers believe that individual subjects might have been reported in more than one of these studies, which could artificially increase the consistency of these estimates. Downgraded for risk of bias.
Economic Outcomes	Very Low	Only one retrospective study with a high risk of bias reported charges for MSAD and laparoscopic Nissen fundoplication. Downgraded for risk of bias.
Cost-Effectiveness		
Center researchers did not identify any studies that addressed cost-effectiveness.		

Abbreviations. MSAD: magnetic sphincter augmentation device.

References

Aetna. (2017). *Gastroesophageal reflux disease (GERD): Treatment devices*. Retrieved from http://www.aetna.com/cpb/medical/data/200_299/0213.html

American College of Gastroenterology. (2013). *Diagnosis and mangement of gastroesophageal reflux disease*. Retrieved from http://gi.org/guideline/diagnosis-and-managemen-of-gastroesophageal-reflux-disease/

Anthem. (2016). *Lower esophageal sphincter augmentation devices for the treatment of gastroesophageal reflux disease (GERD)*. Retrieved from https://www.anthem.com/medicalpolicies/policies/mp_pw_c151320.htm

Asti, E., Bonitta, G., Lovece, A., Lazzari, V., & Bonavina, L. (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, 95*(30), e4366.

Asti, E., Siboni, S., Lazzari, V., Bonitta, G., Sironi, A., & Bonavina, L. (2017). Removal of the magnetic sphincter augmentation device: Surgical technique and results of a single-center cohort study. *Annals of Surgery, 265*(5), 941-945.

Blaus, B. (2015). *Gastroesophaeal reflux disease (GERD)*. Retrieved from https://commons.wikimedia.org/wiki/File:GERD.png

Blue Shield Northeastern New York. (2017). *Transesophageal endoscopic therapies for gastroesophageal reflux disease*. Retrieved from https://www.bsneny.com/content/dam/COMMON/Provider/Protocols/T/prov_prot_20138.pdf

Bonavina, L., DeMeester, T., Fockens, P., Dunn, D., Saino, G., Bona, D., . . . Ganz, R. A. (2010). Laparoscopic sphincter augmentation device eliminates reflux symptoms and normalizes esophageal acid exposure: One- and 2-year results of a feasibility trial. *Annals of Surgery, 252*(5), 857-862. doi: 10.1097/SLA.0b013e3181fd879b

Bonavina, L., Saino, G., Bona, D., Sironi, A., & Lazzari, V. (2013a). One hundred consecutive patients treated with magnetic sphincter augmentation for gastroesophageal reflux disease: 6 years of clinical experience from a single center. *Journal of the American College of Surgeons, 217*(4), 577-585. doi: http://dx.doi.org/10.1016/j.jamcollsurg.2013.04.039

Bonavina, L., Saino, G., Lipham, J. C., & Demeester, T. R. (2013b). LINX Reflux Management System in chronic gastroesophageal reflux: A novel effective technology for restoring the natural barrier to reflux. *Therapeutic Advances in Gastroenterology, 6*(4), 261-268.

Bonavina, L., Saino, G. I., Bona, D., Lipham, J., Ganz, R. A., Dunn, D., & DeMeester, T. (2008). Magnetic augmentation of the lower esophageal sphincter: Results of a feasibility clinical trial. *Journal of Gastrointestinal Surgery, 12*(12), 2133-2140. doi: 10.1007/s11605-008-0698-1

Campbell Collaboration. (2015). Campbell Collaboration systematic reviews: Policies and guidelines. *Campbell Systematic Reviews, Supplement 1*. doi: 10.4073/csrs.2015.1

Cantillon-Murphy, P., Cundy, T. P., Patel, N. K., Yang, G. Z., Darzi, A., & Teare, J. P. (2015). Magnets for therapy in the GI tract: A systematic review. *Gastrointestinal Endoscopy, 82*(2), 237-245.

Chen, M. Y., Huang, D. Y., Wu, A., Zhu, Y. B., Zhu, H. P., Lin, L. M., & Cai, X. J. (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.

Cigna. (2017). *Endoscopic anti-reflux procedures*. Retrieved from https://cignaforhcp.cigna.com/public/content/pdf/coveragePolicies/medical/mm_0019_coveragepositioncriteria_endoscopic_treatment_for_gerd.pdf

ClinicalTrials.gov. (2017). *The CALIBER study randomized controlled trial of LINX versus double-dose proton pump inhibitor therapy for reflux disease (CALIBER)*. Retrieved from https://clinicaltrials.gov/ct2/show/NCT02505945?term=LINX&cond=Gastro+Esophageal+Reflux&rank=3

Empire Blue Cross Blue Shield. (2016). *Lower esophageal sphincter augmentation devices for the treatment of gastroesophageal reflux disease (GERD)*. Retrieved from https://www.empireblue.com/medicalpolicies/policies/mp_pw_c151320.htm

Erdos, J., & Stanek, M. (2016). *Magnetic sphincter augmentation device (MSAD) in patients with gastoesophageal reflux disease (GERD): Systematic review (Decision Support Document No. 101)*. Vienna, Austria: Ludwig Boltzmann Institute for Health Technology Assessment. Retrieved from http://eprints.hta.lbg.ac.at/1098/1/DSD_101.pdf.

Excellus Blue Cross Blue Shield. (2016). *Magnetic esophageal ring for the treatment of gastroesophageal reflux disease (GERD)*. Retrieved from https://www.excellusbcbs.com/wps/wcm/connect/0eb6134f-391f-4d2a-816b-

60f9e356e9fc/mp+mag_esoph_ring+tac+.pdf?MOD=AJPERES&CACHEID=0eb6134f-391f-4d2a-816b-60f9e356e9fc

FDA. (2012). *Re: P100049, LINX Reflux Management System, Filed: December 30, 2010, Amended: October 11, 2011, November 18, 2011, Procode: LEI*. Silver Spring, MD: Department of Health & Human Services.

First Coast Service Options Inc. (2017). *Local coverage determination (LCD): Noncovered services (L33777)*. Retrieved from https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=33777&ver=40&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=43284&bc=gAAAACAAAAAAAA%3d%3d&

Ganz, R. A., Edmundowicz, S. A., Taiganides, P. A., Lipham, J. C., Smith, C. D., DeVault, K. R., . . . Dunn, D. (2016). Long-term outcomes of patients receiving a magnetic sphincter augmentation device for gastroesophageal reflux. *Clinical Gastroenterology & Hepatology, 14*(5), 671-677.

Ganz, R. A., Peters, J. H., Horgan, S., Bemelman, W. A., Dunst, C. M., Edmundowicz, S. A., . . . Taiganides, P. A. (2013). Esophageal sphincter device for gastroesophageal reflux disease. *New England Journal of Medicine, 368*(8), 719-727. doi: 10.1056/NEJMoa1205544

GRADE Working Group. (2004). Grading quality of evidence and strength of recommendations. *British Medical Journal, 328*, 1-8.

Guyatt, G. H., Oxman, A. D., Vist, G. E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., & Schünemann, H. J. (2008). GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ, 336*(7650), 924-926. doi: 10.1136/bmj.39489.470347.AD

Higgins, J. P. T., & Green, S. (Eds.). (2011). *Cochrane handbook for systematic reviews of interventions*. http://handbook.cochrane.org/.

Katz, P. O., Gerson, L. B., & Vela, M. F. (2013). Guidelines for the diagnosis and management of gastroesophageal reflux disease. *American Journal of Gastroenterology, 108*(3), 308-328; quiz 329. doi: 10.1038/ajg.2012.444

Lipham, J. C., DeMeester, T. R., Ganz, R. A., Bonavina, L., Saino, G., Dunn, D. H., . . . Bemelman, W. (2012). The LINX reflux management system: Confirmed safety and efficacy now at 4 years. *Surgical Endoscopy, 26*(10), 2944-2949. doi: 10.1007/s00464-012-2289-1

Lipham, J. C., Taiganides, P. A., Louie, B. E., Ganz, R. A., & DeMeester, T. R. (2015). Safety analysis of first 1000 patients treated with magnetic sphincter augmentation for gastroesophageal reflux disease. *Diseases of the Esophagus, 28*(4), 305-311.

Louie, B. E., Farivar, A. S., Shultz, D., Brennan, C., Vallieres, E., & Aye, R. W. (2014). Short-term outcomes using magnetic sphincter augmentation versus Nissen fundoplication for medically resistant gastroesophageal reflux disease. *Annals of Thoracic Surgery, 98*(2), 498-504; discussion 504-495.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine, 6*(7), e1000097. doi: 10.1371/journal.pmed.1000097

National Institute for Health and Care Excellence. (2014). *Developing NICE guidelines: The manual*. Retrieved from https://www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf

National Institute for Health and Clinical Excellence. (2012). *Interventional procedure overview of laparoscopic insertion of a magnetic bead band for gastro-oesophageal reflux disease*. London: National Institute for Health and Clinical Excellence. Retrieved from https://www.nice.org.uk/guidance/ipg431.

National Institute of Diabetes and Digestive and Kidney Diseases. (2014). *Acid reflux (GER & GERD) in adults*. Retrieved from https://www.niddk.nih.gov/health-information/digestive-diseases/acid-reflux-ger-gerd-adults

Noridian Healthcare Solutions, L. (2017a). *Local coverage determination (LCD): Non-covered services (L35008)*. Retrieved from https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35008&ver=63&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=43284&bc=gAAAACAAAAAAAA%3d%3d&

Noridian Healthcare Solutions, L. (2017b). *Local coverage determination (LCD): Non covered services (L36219)*. Retrieved from https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36219&ver=50&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=43284&bc=gAAAACAAAAAAAA%3d%3d&

Novitas Solutions Inc. (2017). *Local coverage determination (LCD): Services that are not reasonable and necessary (L35094)*. Retrieved from https://www.cms.gov/medicare-coverage-database/details/lcd-

details.aspx?LCDId=35094&ver=124&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=43284&bc=gAAAACAAAAAAAA%3d%3d&

Palmetto GBA. (2017). *Local coverage determination (LCD): Upper gastrointestinal endoscopy and visualization (L34434)*. Retrieved from https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=34434&ver=29&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=43284&bc=gAAAACAAAAAAAA%3d%3d&

Reynolds, J. L., Zehetner, J., Bildzukewicz, N., Katkhouda, N., Dandekar, G., & Lipham, J. C. (2014). Magnetic sphincter augmentation with the LINX device for gastroesophageal reflux disease after U.S. Food and Drug Administration approval. *American Surgeon, 80*(10), 1034-1038.

Reynolds, J. L., Zehetner, J., Nieh, A., Bildzukewicz, N., Sandhu, K., Katkhouda, N., & Lipham, J. C. (2016). Charges, outcomes, and complications: A comparison of magnetic sphincter augmentation versus laparoscopic Nissen fundoplication for the treatment of GERD. *Surgical Endoscopy, 30*(8), 3225-3230.

Reynolds, J. L., Zehetner, J., Wu, P., Shah, S., Bildzukewicz, N., & Lipham, J. C. (2015). Laparoscopic magnetic sphincter augmentation vs laparoscopic Nissen fundoplication: A matched-pair analysis of 100 patients. *Journal of the American College of Surgeons, 221*(1), 123-128.

Riegler, M., Schoppman, S. F., Bonavina, L., Ashton, D., Horbach, T., & Kemen, M. (2015). Magnetic sphincter augmentation and fundoplication for GERD in clinical practice: One-year results of a multicenter, prospective observational study. *Surgical Endoscopy, 29*(5), 1123-1129.

Saino, G., Bonavina, L., Lipham, J. C., Dunn, D., & Ganz, R. A. (2015). Magnetic sphincter augmentation for gastroesophageal reflux at 5 years: Final results of a pilot study show long-term acid reduction and symptom improvement. *Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A, 25*(10), 787-792. doi: 10.1089/lap.2015.0394

Schwameis, K., Schwameis, M., Zorner, B., Lenglinger, J., Asari, R., Riegler, F. M., & Schoppmann, S. F. (2014). Modern GERD treatment: Feasibility of minimally invasive esophageal sphincter augmentation. *Anticancer Research, 34*(5), 2341-2348.

Scottish Intercollegiate Guidelines Network. (2009). *Critical appraisal: Notes and checklists*. Retrieved from http://www.sign.ac.uk/methodology/checklists.html

Sheu, E. G., Nau, P., Nath, B., Kuo, B., & Rattner, D. W. (2015). A comparative trial of laparoscopic magnetic sphincter augmentation and Nissen fundoplication. *Surgical Endoscopy, 29*(3), 505-509.

Skubleny, D., Switzer, N. J., Dang, J., Gill, R. S., Shi, X., de Gara, C., . . . Karmali, S. (2016). LINX(R) magnetic esophageal sphincter augmentation versus Nissen fundoplication for gastroesophageal reflux disease: A systematic review and meta-analysis. *Surgical Endoscopy, 31*(8), 3078-3084. doi: 10.1007/s00464-016-5370-3

Smith, C. D., DeVault, K. R., & Buchanan, M. (2014). Introduction of mechanical sphincter augmentation for gastroesophageal reflux disease into practice: Early clinical outcomes and keys to successful adoption. *Journal of the American College of Surgeons, 218*(4), 776-781. doi: 10.1016/j.jamcollsurg.2013.12.034

Smith, C. D., Ganz, R. A., Lipham, J. C., Bell, R. C., & Rattner, D. W. (2017). Lower esophageal sphincter augmentation for gastroesophageal reflux disease: The safety of a modern implant. *Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A, 27*(6), 586-591.

Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). (2013). *SAGES TAVAC (Technology and Value Assessment Committee) Safety and Effectiveness Analysis. LINX Reflux Management System.* Los Angeles, California: Retrieved from https://www.sages.org/publications/tavac/tavac-safety-and-effectiveness-analysis-linx-reflux-management-system/.

United Healthcare. (2017). *Minimally invasive procedures for gastroesophageal reflux disease (GERD)*. Retrieved from https://www.unitedhealthcareonline.com/ccmcontent/ProviderII/UHC/en-US/Assets/ProviderStaticFiles/ProviderStaticFilesPdf/Tools%20and%20Resources/Policies%20and%20Protocols/Medical%20Policies/Medical%20Policies/Minimally_Invasive_Procedures_for_GERD.pdf

Velanovich, V. (2007). The development of the GERD-HRQL symptom severity instrument. *Diseases of the Esophagus, 20*(2), 130-134. doi: 10.1111/j.1442-2050.2007.00658.x

Warren, H. F., Reynolds, J. L., Lipham, J. C., Zehetner, J., Bildzukewicz, N. A., Taiganides, P. A., . . . Louie, B. E. (2016). Multi-institutional outcomes using magnetic sphincter augmentation versus Nissen fundoplication for chronic gastroesophageal reflux disease. *Surgical Endoscopy, 30*(8), 3289-3296.

Washington Health Care Authority. (2017). *Medicaid outpatient fee schedule effective April 2, 2017*. Retrieved from https://www.hca.wa.gov/billers-providers/claims-and-billing/professional-rates-and-billing-guides

Zhang, H., Dong, D., Liu, Z., He, S., Hu, L., & Lv, Y. (2016). Revaluation of the efficacy of magnetic sphincter augmentation for treating gastroesophageal reflux disease. *Surgical Endoscopy, 30*(9), 3684-3690.

Appendix A. Methods

General Search Strategy

Evidence

A full search of Center's core clinical evidence primary sources was conducted to identify systematic reviews, meta-analyses, and technology assessments using the search terms *magnet*, sphincter**, and *LINX*. Searches of core sources were limited to citations published after 2006. Center researchers also searched the Ovid MEDLINE database for relevant systematic reviews and meta-analyses or technology assessments, and for individual studies published after the search dates of the identified systematic reviews, and cost-effectiveness studies published after 2006.

The core sources searched included the following:

Agency for Healthcare Research and Quality (AHRQ)

BMJ – Clinical Evidence

Cochrane Library (Wiley Interscience)

National Institute for Health and Care Excellence (NICE)

PubMed Health

Tufts Cost-Effectiveness Analysis Registry

Veterans Administration Evidence-based Synthesis Program (ESP)

Washington State Health Technology Assessment Program

Clinical Practice Guidelines

Center researchers conducted a full search of Center clinical practice guidelines primary sources to identify clinical practice guidelines using the terms *magnet*, sphincter**, and *LINX*. Searches were limited to citations published within the last five years.

The guideline sources included the following:

American College of Gastroenterology

Australian Government National Health and Medical Research Council (NHMRC)

Institute for Clinical Systems Improvement (ICSI)

National Guidelines Clearinghouse

National Institute for Health and Care Excellence (NICE)

Scottish Intercollegiate Guidelines Network (SIGN)

Society of American Gastrointestinal and Endoscopic Surgeons

United States Preventive Services Task Force (USPSTF)

Veterans Administration/Department of Defense (VA/DOD)

World Health Organization (WHO)

Coverage Policies

Center researchers searched for policies on the coverage of MSADs for the treatment of GERD from Aetna, Anthem, Blue Shield of Northeastern New York, Capital District Physicians' Health Plan, Centers for Medicare and Medicaid Services, Cigna, Emblem Health, Empire BCBS, Excellus BCBS, Tufts Health Plan, UnitedHealthcare, and nine state Medicaid programs (CA, FL, MA, NJ, NY, OR, PA, TX, WA).

General Exclusion Criteria

Staff members excluded studies that were not systematic reviews, meta-analyses, or technology assessments, or individual studies (as applicable by topic) that were published before 2007, or were published in a language other than English.

Quality Assessment

Center researchers assessed the methodological quality of the included studies using standard instruments developed and adapted by the Center that are modifications of the systems in use by the Campbell Collaboration, Cochrane, the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA), the National Institute for Health and Care Excellence (NICE), and the Scottish Intercollegiate Guidelines Network (SIGN) (Campbell Collaboration, 2015; Guyatt et al., 2008; Higgins & Green, 2011; Moher, Liberati, Tetzlaff, & Altman, 2009; NICE, 2014; SIGN, 2009). Two Center researchers independently rated all studies. In cases where there was not agreement about the quality of a study, consensus was reached through discussion.

Each rater assigned the study a rating of good, fair, or poor, based on its adherence to recommended methods and potential for biases. In brief, good-quality systematic reviews include a clearly focused question, a literature search sufficiently rigorous to identify all relevant studies, criteria used to select studies for inclusion (e.g., RCTs) and assess study quality, and assessments of heterogeneity to determine if a meta-analysis would be appropriate. Good-quality RCTs include a clear description of the population, setting, intervention, and comparison groups; a random and concealed allocation of patients to study groups; low dropout rates; and intention-to-treat analyses. Good-quality systematic reviews and RCTs also have low potential for bias from conflicts of interest and funding source(s). Fair-quality systematic reviews and RCTs have incomplete information about methods that might mask important limitations. Poor-quality systematic reviews and RCTs have clear flaws that could introduce significant bias.

Specific Search Details

The search terms *CPT 43284* (Google and Google Scholar only), and *magnet*, magnet, sphincter*, sphincter, LINX, GERD*, and *esophageal*, were used in the remaining core source searches. Archived government reports were not included.

Inclusion Criteria

Population: Individuals with GERD (as defined by abnormal pH testing) who continue to have chronic GERD symptoms despite maximum medical therapy for the treatment of reflux

Intervention: Laparoscopic surgical esophageal sphincter augmentation procedure; placement of sphincter augmentation device (i.e., magnetic band), including cruroplasty when performed (CPT 43284 replaces 0392T)

Comparators: Open or laparoscopic Nissen fundoplication; other minimally invasive procedures; maximal medical and lifestyle therapies

Outcomes: Function; quality of life; pain; prevention and/or healing of Barrett's metaplasia, adenocarcinoma, and other types of esophageal damage such as esophagitis and strictures; procedure or device-related adverse events; utilization of other subsequent procedures (e.g., endoscopy procedures); cost and cost-effectiveness

Exclusion Criteria

Study exclusion criteria included the following:

- Retrospective or single arm, non-comparative studies for efficacy outcomes
- Retrospective studies for harms (unless part of large comprehensive registry for safety outcomes)
- Studies involving MSADs that are not currently approved for use in the U.S.
- Duplicate information from a research study published in more than one source (only the highest quality, most recent publication with outcome of interest was included)
- Systematic reviews that included only studies that were summarized by more comprehensive systematic reviews or systematic reviews of higher quality and/or that were more recently published
- Studies identified that were included in a summarized systematic review or technology assessment

Ovid MEDLINE Search

The Ovid MEDLINE search strategy was developed for broad inclusion of relevant systematic reviews and individual studies. Individual studies published after the search dates of the included systematic review (Erdos & Stanek, 2016) or studies that were eligible and not included in the systematic review were included to update the existing systematic review.

MEDLINE search dates: 1996 through June 22, 2017

MEDLINE search strategy:

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions(R) Search Strategy:

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1 GERD.mp. or exp Gastroesophageal Reflux/
2 GORD.mp
3 LINX.mp
4 magnetic sphincter augmentation.mp
5 Gastroesophageal Reflux/
6 Esophageal Sphincter, Lower/
7 Magnets/
8 1 or 2 or 5 or 6
9 3 or 4 or 7
10 8 and 9
11 limit 10 to english language

Appendix B. Articles Selected for Full-Text Review Inclusion/Exclusion Rationale

Citation	Inclusion/Exclusion Rationale
Asti, Bonitta, Lovece, Lazzari, and Bonavina (2016)	Exclude: retrospective design
Asti et al. (2017)	Exclude: retrospective, non-comparative design
Bonavina et al. (2008)	Exclude: non-comparative, feasibility study
Bonavina et al. (2010)	Exclude: non-comparative, superseded by other publications with longer follow up on this cohort
Bonavina et al. (2013a)	Exclude: included in Erdos and Stanek (2016) SR
Bonavina, Saino, Lipham, and Demeester (2013b)	Exclude: general description of technology
Cantillon-Murphy et al. (2015)	Exclude: SR without data on MSAD
Chen et al. (2017)	Exclude: SR, did not include prospective comparative studies
Erdos and Stanek (2016)	Included: SR/HTA for efficacy and harms
Ganz et al. (2013)	Include: prospective, single-arm follow-up study for harms only
Ganz et al. (2016)	Exclude: included in Erdos and Stanek (2016) SR
Katz et al. (2013)	Include: guideline
Lipham et al. (2012)	Exclude: non-comparative design
Lipham et al. (2015)	Include: comprehensive, multisource safety study for harms only
Louie et al. (2014)	Exclude: retrospective design
National Institute for Health and Clinical Excellence (2012)	Exclude: SR, superseded by more recent SR Erdos and Stanek (2016)
(NIDDK, 2014)	Exclude: general condition description, patient education
Reynolds et al. (2014)	Exclude: included in Erdos and Stanek (2016) SR
Reynolds et al. (2015)	Exclude: retrospective design
Reynolds et al. (2016)	Include: although retrospective, it is the only study that presents economic outcomes and is included as a comparative cohort study for economic outcomes only
Riegler et al. (2015)	Exclude: included in Erdos and Stanek (2016) SR
Saino et al. (2015)	Include: prospective, single-arm follow-up study for harms only
Schwameis et al. (2014)	Exclude: included in Erdos and Stanek (2016) SR

Citation	Inclusion/Exclusion Rationale
Sheu, Nau, Nath, Kuo, and Rattner (2015)	Exclude: retrospective design
Skubleny et al. (2016)	Exclude: SR, Erdos and Stanek (2016) more comprehensive
Smith, Ganz, Lipham, Bell, and Rattner (2017)	Exclude: included in Erdos and Stanek (2016) SR
Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) (2013)	Include: guideline
Warren et al. (2016)	Exclude: retrospective design
Zhang et al. (2016)	Exclude: not an SR

Abbreviations. HTA: health technology assessment; MSAD: magnetic sphincter augmentation device; SR: systematic review.

Appendix C. List of Ongoing Trials

Trial	Status	Intervention
LINX Reflux Management System Clinical Study Protocol	Completed	Device: Magnetic Sphincter Augmentation
A Study of Reflux Management With the LINX® System for Gastroesophageal Reflux Disease After Laparoscopic Sleeve Gastrectomy (RELIEF)	Recruiting	Device: LINX device
The CALIBER Study Randomized Controlled Trial of LINX Versus Double-Dose Proton Pump Inhibitor Therapy for Reflux Disease (CALIBER)	Active, not recruiting	Drug: Omeprazole Device: LINX Reflux Management System
A Post-Approval Study of the LINX® Reflux Management System	Active, not recruiting	Device: LINX device
RELIEF Europe Study	Terminated	Device: The LINX Reflux Management System
Registry of Outcomes From AntiReflux Surgery (ROARS)	Recruiting	Procedure: Laparoscopic Fundoplication Device: LINX Antireflux
A Prospective Evaluation of the Torax Medical Inc. Magnetic Esophageal Sphincter	Completed	Device: Magnetic Esophageal Sphincter
A Prospective Evaluation of the Torax Medical Inc. Magnetic Esophageal Sphincter	Completed	Device: Torax Medical, Inc. LINX Reflux Management System
An Observational Clinical Feasibility Study of the Magnetic Esophageal Sphincter	Completed	Device: Torax Medical, Inc. LINX Reflux Management System
Observational Study of Anti-Reflux Surgery: Clinical Experience With the LINX Reflux Management System and Fundoplication	Completed	Procedure: Fundoplication Device: LINX Reflux Management System

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