Gastrointestinal Motility Disorders, Diagnosis and Treatment

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Instructions for Use

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Application

UnitedHealthcare Commercial

This Medical Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Policy applies to Individual Exchange benefit plans.

Coverage Rationale

Gastric electrical stimulation (GES) therapy is proven and medically necessary for treating refractory Gastroparesis that has failed other therapies, or chronic intractable (drug-refractory) nausea and vomiting secondary to Gastroparesis of diabetic or idiopathic etiology.

Refer to the U.S. Food and Drug Administration (FDA) section for information regarding FDA labeling and Humanitarian Device Exemption (HDE) for GES.

The following procedures are unproven and not medically necessary due to insufficient evidence of efficacy:

- Magnetic Resonance Imaging (MRI) Defecography for evaluating Constipation and Anorectal or pelvic floor disorders
- Cutaneous, mucous, or serosal Electrogastrography, electroenterography, or body surface gastric mapping (e.g., Gastric Alimetry System, G-Tech Gut Tracker wireless patch system) for diagnosing intestinal or gastric disorders including Gastroparesis
- Esophageal Mucosal Integrity Testing by electrical impedance (e.g., MiVu™ Mucosal Integrity Testing System) for the diagnosis of gastroesophageal reflux disease (GERD), eosinophilic esophagitis (EoE) and nonacid reflux disease (non-GERD), or for the monitoring of treatment response in GERD and EoE

Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. Medical records documentation may be required to assess whether the

member meets the clinical criteria for coverage but does not guarantee coverage of the service requested; refer to the protocol titled Medical Records Documentation Used for Reviews.

Definitions

Anorectal Disorders: Structural or functional abnormalities of the anorectum or pelvic floor (Patcharatrakul and Rao, 2018).

Constipation: Infrequent or hard-to-pass bowel movements, hard stools, or incomplete bowel movement sensation; infrequent means less than three bowel movements a week (Bharucha et al., 2013a).

Electrogastrography (EGG): A non-invasive method for the measurement of gastric myoelectrical activity using cutaneous electrodes placed on the abdominal skin over the stomach (Yin and Chen, 2013).

Esophageal Mucosal Integrity Testing: An adjunct procedure to routine endoscopy to speed the diagnostic differentiation of GERD from non-GERD and EoE that is intended to be an alternative to 24- to 48- hour-long pH monitoring and biopsies (Hayes, 2022, updated 2024).

Fecal Incontinence (FI): The inability to control bowel movements causing stool (feces) to leak unexpectedly from the rectum; also called bowel or anal incontinence (Bharucha et al., 2013a).

Gastroparesis: A digestive disorder in which the motility of the stomach is either abnormal or absent; it is also known as delayed gastric emptying (Camilleri, 2013, updated 2022).

Magnetic Resonance Defecography: A noninvasive test that uses magnetic resonance imaging to obtain images at various stages of defecation to evaluate how well the pelvic muscles are working and provide insight into rectal function (RadiologyInfo.org); it can evaluate pelvic floor anatomy, dynamic motion, and rectal evacuation simultaneously (Rao and Patcharatrakul, 2016).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
0779T	Gastrointestinal myoelectrical activity study, stomach through colon, with interpretation and report
0868T	High-resolution gastric electrophysiology mapping with simultaneous patient-symptom profiling, with interpretation and report
43499	Unlisted procedure, esophagus
43647	Laparoscopy, surgical; implantation or replacement of gastric neurostimulator electrodes, antrum
43648	Laparoscopy, surgical; revision or removal of gastric neurostimulator electrodes, antrum
43881	Implantation or replacement of gastric neurostimulator electrodes, antrum, open
43882	Revision or removal of gastric neurostimulator electrodes, antrum, open
64590	Insertion or replacement of peripheral, sacral, or gastric neurostimulator pulse generator or receiver, requiring pocket creation and connection between electrode array and pulse generator or receiver
64595	Revision or removal of peripheral, sacral, or gastric neurostimulator pulse generator or receiver, with detachable connection to electrode array
72195	Magnetic resonance (e.g., proton) imaging, pelvis; without contrast material(s)
72196	Magnetic resonance (e.g., proton) imaging, pelvis; with contrast material(s)
72197	Magnetic resonance (e.g., proton) imaging, pelvis; without contrast material(s), followed by contrast material(s) and further sequences
76498	Unlisted magnetic resonance procedure (e.g., diagnostic, interventional)

CPT Code	Description
91132	Electrogastrography, diagnostic, transcutaneous
91133	Electrogastrography, diagnostic, transcutaneous; with provocative testing

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Description of Services

Several gastrointestinal motility disorders, such as Constipation, Fecal Incontinence, and Gastroparesis may require a testing before a diagnosis can be made.

Symptoms of Constipation, one of the most common digestive problems, are extremely common. The prevalence of Constipation is approximately 16% in adults overall and 33% in adults over 60. If symptoms do not improve, investigations to diagnose rectal evacuation disorders and slow-transit Constipation are sometimes performed, such as digital rectal examination, anorectal structure and function testing (including the balloon expulsion test, anorectal manometry or defecography) or colonic transit tests (such as the radiopaque marker test, wireless motility capsule test, scintigraphy) (Camilleri et al., 2017). While in most cases, Constipation is benign and due to dietary and lifestyle factors, Constipation is sometimes due to disordered colonic and/or pelvic floor/anorectal function.

Fecal Incontinence (FI) is the inability to control bowel movements causing stool to leak unexpectedly from the rectum. Continence requires the rectum, anus, and nervous system to be working normally. FI is commonly caused by altered stools (generally diarrhea, but also Constipation) or conditions that affect the ability of the rectum and anus to hold stool.

Individuals with Gastroparesis may experience symptoms of frequent nausea and vomiting, early satiety, bloating, postprandial fullness, and epigastric pain and burning. Although Gastroparesis can occur with no obvious cause, patients with diabetes frequently develop this condition. If Gastroparesis causes nausea and persistent vomiting, it can lead to frequent hospitalization for hypoglycemia, hyperglycemia, acidosis, dehydration, pseudo-obstruction, electrolyte dyscrasias, or other complications. The diagnosis of Gastroparesis requires objective evidence of clearly delayed gastric emptying in symptomatic patients. Scintigraphy is the reference standard for measurement of gastric emptying. Protocols for standardized meals prior to scintigraphy have been recommended, however for interpretation of test results, it has to be considered that clinical utility depends on complete consumption of adequate test meals and adequate duration of imaging. For all gastrointestinal function tests, adherence to adequately validated, standardized study protocols is crucial (Keller et al., 2018).

Electrogastrography (EGG) is a non-invasive technique for recording gastric myoelectrical activity using cutaneous electrodes placed on the abdominal skin over the stomach. The surface recording obtained using electrography is called the electrogastrogram. Gastric myoelectrical activity may be altered or become abnormal in diseased states or upon provocative stimulations or even spontaneously. Abnormal gastric myoelectrical activity includes gastric dysrhythmia, abnormal slow wave propagation and electro-mechanical uncoupling. In the stomach, there is lack of one-to-one correlation between spikes and contractions, and thus this abnormality cannot be accurately detected from the in vivo myoelectrical recording. In individuals with gastrointestinal motility disorders or individuals with functional gastrointestinal diseases, EGG is used to identify the pathophysiology of the diseases associated with gastric slow waves or dysrhythmia (Yin and Chen, 2013). Electroenterography is a similar procedure that records myoelectrical activity from the intestines and body surface gastric mapping (BGSM) uses high resolution electrode arrays, along with bioelectronics, automated artifact rejection and analytics, to measure and map gastric myoelectric activity.

Anorectal Disorders present with a variety of symptoms and result from either structural or functional disorders. Clinical correlation is essential before labeling an abnormal finding as clinically significant. Together with a detailed history, a thorough physical and digital rectal examination and appropriate testing, in most patients the underlying cause and type of anorectal disorder can be correctly identified, and treatment can be tailored (Patcharatrakul and Rao, 2018).

Defecatory disorders are primarily characterized by impaired rectal evacuation from inadequate rectal propulsive forces and/or increased resistance to evacuation; the latter may result from high anal resting pressure (“anismus”) and/or incomplete relaxation or paradoxical contraction of the pelvic floor and external anal sphincters (“dyssynergia”) during defecation. Structural disturbances (e.g., rectocele, intussusception) and reduced rectal sensation may coexist.

Magnetic Resonance Imaging (MRI) Defecography is being studied as an imaging tool that may provide an enhanced view of the bowel movement process including the underlying anatomic and pathophysiologic background of pelvic floor disorders. It can evaluate pelvic floor anatomy, dynamic motion, and rectal evacuation simultaneously (Rao and Patcharatrakul, 2016).

Gastric Electrical Stimulation (GES) Therapy

Cassidy et al. (2024) conducted a retrospective, single-center case series of patients who were treated for medically refractory gastroparesis (MRG) with GES to evaluate the safety and efficacy of GES. The study included 157 patients (median age 45.3 years, 61.8% female) who underwent placement of GES and who completed Gastroparesis Cardinal Symptom Index (GCSI) surveys preoperatively and at subsequent follow-up visits with data extracted from a prospective, internal review board (IRB) approved database. The patients included 57 (36.3%) with diabetic gastroparesis, 93 (59.2%) with idiopathic gastroparesis, and 7 (4.5%) with postsurgical gastroparesis. At one year follow-up, 141 patients (89.8%) completed the GCSI survey, while 110 patients (70.1%) completed the GCSI survey at five-year follow-up. The authors reported that symptom severity in all nine gastroparesis symptoms evaluated by the GCSI, as well as the total GCSI score, was reduced significantly at one-year post-implantation, and that the improvements were sustained through the five-year follow-up. Patient satisfaction with improvement in their gastroparesis symptoms was reported by the authors to be high with 87.1% “satisfied” or “very satisfied” at one year and 79.7% at five years. When the authors evaluated the efficacy of GES in patients based on the cause of gastroparesis, they reported that they observed no difference between patients with idiopathic gastroparesis and those with diabetic gastroparesis. The authors also reported that the use of prokinetic and antiemetic medications was reduced during the follow-up period with reduction in prokinetic medications from 1.9 agents preoperatively to 0.3 at one year and 0.4 at five years, and with reduction in antiemetics from 2.1 agents preoperatively to 0.6 at one year and 0.7 at five years. Hospitalizations due to gastroparesis symptoms were also reported to be reduced with 91 hospitalizations reported preoperatively to 18 in the first year and 16 in the fifth year. GES devices were reported to be explanted in five patients (one for infection and four for lack of sufficient improvement), while 12 patients required generator exchanges, and seven patients required reoperation for mechanical issues (four for lead erosion and fracture, and three for displaced device leads) over the five-year study period. The authors concluded that GES was associated with sustained symptomatic relief, reduced reliance on medications on medications, and reduced gastroparesis related hospitalizations. Limitations of the study include the retrospective design, the lack of a comparison group, the inability to capture potential hospitalizations at other facilities, and the single-center design.

In an observational study of two cohorts, Gourcerol et al. (2023) compared the efficacy of GES and gastric-peroral endoscopic myotomy (G-POEM) on nausea and vomiting scores in patients with gastroparesis. The study included 64 patients with MRG with predominant nausea and vomiting who had undergone either GES (n = 34) or G-POEM (n = 30) and were followed for 24 months post procedure. The sex ratio, mean age, mean body mass index, and frequency of conditions associated with gastroparesis were not significantly different between groups; however, the median duration of disease at baseline was significantly shorter for GES at 34 months than for the G-POEM cohort at 57 months. Clinical response was defined by the authors as a decrease of one or more points in nausea and vomiting subscale without premature exclusion due to a switch from one to the other technique before the end of the 24-month follow-up period. The authors reported that the mean score of nausea and vomiting subscale was higher in the GES group (3.0) compared to G-POEM (2.6) while other parameters were comparable. At the 24-month follow-up, clinical response was achieved in 21 of the 34 patients with GES (61.7%) and 21 of the 30 patients who had undergone G-POEM (70%) while the mean scores of nausea and vomiting subscale decreased in both GES (from 3.0 to 1.6) and G-POEM (from 2.6 to 1.2) even though there was no difference between groups. The authors also reported that symptomatic and quality of life scores improved at the end of the follow-up period without difference between the two groups. Limitations of the study include the different patient severity at baseline as the nausea and vomiting sub scores were higher while quality of life was worse at baseline in the group treated with GES compared to the group treated with G-POEM, the lack of randomization and blinding, the small population size, and the use of different symptomatic scales used by the two cohorts. The authors concluded that they did not observe significant difference in efficacy of GES and G-POEM in MRG with predominant nausea and vomiting.

Samaan et al. (2022) conducted a single-center, retrospective study of 181 consecutive patients who underwent GES or primary gastrectomy (PG) for MRG between January 2003 to December 2017 to compare the therapeutic efficacy of GES versus PG for MRG. The authors collected data through chart review and a follow-up telephone survey. There were 130 patients (68.5% female, median age 42 years) who underwent GES and 51 (74.5% female, median age 44 years) who underwent PG as their primary intervention. Of the 130 patients that underwent GES placement, 44 (33.8%) underwent GES removal and subsequent secondary gastrectomy (SG) for clinically significant persistence of gastroparesis symptoms. The authors reported that patients who underwent GES were more likely to have diabetic and idiopathic gastroparesis (GES 95% versus PG 39%) while the patients who underwent PG were more likely to have post-surgical gastroparesis (GES 5% versus PG 43%) and that postoperatively, primary PG patients had a higher rate of major inpatient morbidity events (GES 5% versus PG 18%) and longer lengths of stay (GES three days versus PG nine days). Although previous foregut surgery was more common in patients with PG (66.7% versus GES 43.1%) The authors noted that, over an average of 37.3 month (range 0.3-176.8) follow-up period, there were no differences between the GES patient population and the PG patient population in the rates of major morbidity, readmissions or mortality and that

multivariable regression analysis showed that patients who underwent GES as their primary intervention were less likely to report improvement in symptoms on follow-up when compared to patients with PG. The authors also reported that patients who converted to PG from GES were more likely to have post-surgical gastroparesis as the primary etiology. Limitations of the study include the retrospective, observational, single-center design, the potential for recall bias related to the use of the postoperative telephone survey, the heterogeneity of the types of gastropareses and with the various gastrectomy types that were performed, and the potential for selection bias as the cohort consisted of patients who were willing to comply with the survey and follow-up requirement of the study. The authors concluded that patients who underwent GES as a first-line surgical treatment of MRG had worse outcomes than those who underwent PG. They also concluded that post-surgical etiology was associated with an increased likelihood of GES failure and that for patients who experienced GES failure, upfront gastrectomy may be a superior alternative to GES. The authors recommended further studies to determine patient selection criteria for operative treatment of MRG.

In a systematic review of the therapeutic role of gastric pacemakers in adults with gastroparesis, Rajamanuri et al. (2021) reviewed 12 studies that included data on adults with MRG that required GES therapy and found that the studies showed varying effects of GES on gastroparesis symptoms like nausea, vomiting, and abdominal bloating. They also concluded that there was significant weight gain noted based on the evidence in the studies they reviewed and that, while most of the studies suggested a significant improvement in the quality of life and the Gastroparesis Cardinal Symptom Index (GCSI) scores, the evidence supporting no difference in the quality of life seemed stronger, as shown by the meta-analysis and randomized controlled trials vs. open-label trials that showed positive results for quality of life with gastric pacing. The authors also found other beneficial effects of GES including reductions in inflammatory indicators, improved metabolic hormone levels and improved mucosal electrogram frequencies over baseline that were sustained for over six months. The authors noted that their review was limited due to the inclusion of open-labeled studies. They recommended additional RCTs to analyze the impact of gastric pacemakers in the improvement of symptoms in patients with gastroparesis, studies that evaluate the efficacy for the different causes of gastroparesis, such as diabetes, idiopathic and post-surgical, and future studies that include the pediatric population. (Ducrotte et al. 2020, Chu et al. 2012 and Shada et al. 2018, which were previously cited in this policy, are included in this systematic review.)

Hayes (2018, updated 2022) published a Health Technology Assessment (HTA) on the safety and efficacy of GES for gastroparesis following their review of 12 studies, including three RCTs, six pretreatment/ posttreatment studies, one non-randomized comparative study, one comparative cohort study and one compilation of case series. The Hayes HTA stated that the effectiveness of GES for treating chronic gastroparesis remains uncertain, as findings have not provided consistent evidence. They noted that the available randomized studies provide little confirmation of the apparent benefit that was seen in unblinded studies. The report noted that GES appears safe in most patients but that serious complications can occur, including the movement of the stimulator and/or the electrical leads following implantation. They noted that the device removal rates in the studies they reviewed were between 7% to 12%. The overall quality of the evidence for GES for the treatment of gastroparesis was low due to the individual study limitations and inconsistency in the findings. The HTA concluded that additional randomized and placebo-controlled studies are needed to determine whether GES is a reliable therapy for gastroparesis and whether the benefits of GES treatment outweigh the potential risks.

Levinthal and Bielefeldt (2017) conducted a systematic review and meta-analysis to determine if GES is effective in reducing symptoms in patients with gastroparesis. Five studies randomly allocated patients to periods with or without GES. Total symptom severity (TSS) scores did not differ between these periods (0.17 [95% confidence interval: -0.06 to 0.4]; $p = 0.15$). However, sixteen open label studies of GES showed a significant TSS decrease (2.68 [2.04-3.32]; $q = 39.0$; $p < 0.001$). Other treatment modalities similarly improved TSS by 1.97 [1.5-2.44] for medical therapy (MED), by 1.52 [0.9-2.15] for placebo arms (PLA), and by 2.32 [1.56-3.06] for botulinum toxin (BTx). There were significant differences in baseline TSS ratings among these studies (GES: 6.28 [6.28-7.42]; MED: 4.76 [4.09-5.42]; PLA: 4.59 [3.77-5.42]; BTx: 6.02 [5.3-6.74]; $q = 35.1$; $p < 0.001$). Meta-regression analysis showed these baseline differences to significantly impact TSS ratings during treatment ($q = 71.8$; $p < 0.001$). Independent of the treatment modality, baseline symptom severity impacts treatment results in gastroparesis. Considering the skewed population with refractory symptoms, regression to the mean likely contributes to the substantial discrepancies between the reported results of controlled and open label GES studies. (Chu et al. 2012, which was previously cited in this policy is included in this systematic review.)

Heckert et al. (2016) assessed the effectiveness of GES with Enterra® for treatment for refractory symptoms of gastroparesis, the improvement in specific symptoms of gastroparesis, and clinical factors impacting on outcome in a cohort of 151 patients with refractory gastroparesis at a single center. Patients with gastroparesis (n = 151; (120 females) with refractory gastroparesis (72 diabetic, 73 idiopathic, six other) underwent GES with Enterra® (Medtronic). Patients filled out a symptom severity questionnaire (PAGI-SYM) prior to insertion. At each follow-up visit, the patient filled out PAGI-SYM and assessed their therapeutic response using the Clinical Patient Grading Assessment Scale (CPGAS). The investigators concluded that GES improved symptoms in 75% of patients with 43% being at least moderately improved.

Response in patients with diabetes was better than in patients without diabetes. Nausea, loss of appetite, and early satiety responded the best. The unknown length of study follow-up did not allow for assessment of intermediate and long-term outcomes. Furthermore, lack of comparison group limits the conclusions that can be derived from this case series.

Lal et al. (2015) performed a systematic review of GES using the Enterra System. The final review consisted of 21 out of 53 potentially relevant studies published since 2003; eighteen were prospective cohort studies and three were crossover studies. The overall risk of bias was considered medium to high in the majority of studies. The main reason was the frequency of non-randomized trials which tend to have a higher risk of bias. There was a variation in the methods used to assess the improvement in symptoms in the patients with GES implants. The most commonly used measures were: Total Symptom Score (TSS), GCSI, Monthly and Weekly Vomiting Frequency, Monthly and Weekly Nausea Frequency, and Gastrointestinal Symptoms Rating Scale (GSRS). All studies investigating gastric emptying used a two hour and four-hour Gastric Emptying Test (GET) after a low-fat meal. The studies in this systematic review included a variety of outcome measures and variety of preoperative assessments, making it difficult to combine data and offer firm conclusions. The evidence base for the use of GES in gastroparesis is limited with a total of just five months of blinded, randomized study including only 83 patients. However, accepting the limitations of the evidence base, the majority of studies reported an improvement in symptomology and quality of life with GES. An improvement in gastric emptying was seen in most studies, with only two failing to demonstrate an improvement. However, except for one study, improved gastric emptying did not correlate with the improved symptomology. The authors concluded that while current evidence has shown a degree of efficacy in these patients, high-quality, large clinical trials are needed to establish the efficacy of this therapy and to identify the patients for whom this therapy is inappropriate. A consensus view on essential preoperative assessment and postoperative measurement is needed. McCallum et al. 2010, which was previously cited in this policy, is included in this systematic review.)

McCallum et al. (2011) assessed the long-term clinical outcomes of GES therapy with Enterra® in a large case series of patients with severe gastroparesis. Patients with gastroparesis (n = 221; 142 diabetic, 48 idiopathic, and 31 postsurgical) treated with Enterra (Medtronic) for one to 11 years were retrospectively assessed; 188 had follow-up visits and data were collected for at least one year. TSS, hospitalization days, and use of medications were significantly reduced among all patients. More patients with diabetic (58%) and postsurgical gastroparesis (53%) had a greater than 50% reduction in TSS than those with idiopathic disease (48%). Weight significantly increased among all groups, and 89% of J-tubes could be removed. At end of the follow-up period, all etiological groups had similar, abnormal delays in mean gastric retention. Thirteen patients (7%) had their devices removed because of infection at the pulse generator site. The investigators concluded that GES therapy significantly improved subjective and objective parameters in patients with severe gastroparesis; efficacy was sustained for up to 10 years and was accompanied by good safety and tolerance profiles. Patients with diabetic or postsurgical gastroparesis benefited more than those with idiopathic disease. Lack of comparison group however limits the conclusions that can be derived from this case series.

Clinical Practice Guidelines

American College of Gastroenterology (ACG)

The ACG published a clinical guideline for the management of gastroparesis that states that GES may be considered for control of gastroparesis symptoms as a humanitarian use device (HUD), as defined by the Food and Drug Administration (FDA) for medically refractory diabetic gastroparesis or idiopathic gastroparesis. This conditional recommendation was based on a low-quality body of evidence (Camilleri, 2013, updated 2022).

American Gastroenterological Association (AGA)

The AGA published a clinical practice update on the management of MRG based on a review of existing literature combined with expert opinion to provide practical advice. Based on this review, the AGA stated that clinicians can consider gastric electrical stimulation for patients with gastroparesis and refractory/intractable nausea and vomiting who have failed standard therapy and are not on opioids. This guidance was based on their review of six published studies that they stated showed that GES improved refractory nausea and vomiting in some patients with gastroparesis and may improve glycemic control, nutritional status, and quality of life, while reducing hospitalizations and medication use. They noted that this document was not based on a systematic review, so no formal rating of the quality of evidence or strength of recommendation was made (Lacy, 2022).

In a white paper on current approaches for the treatment of gastroparesis, the AGA (Pasricha et al., 2017n) includes GES therapy (recommendation: conditional; level of evidence: moderate).

National Institute for Health and Care Excellence (NICE)

The National Institute for Health and Care Excellence (NICE) (2014) interventional procedure guidance on GES for gastroparesis notes that GES is an option for treating chronic, intractable nausea and vomiting secondary to

gastroparesis, observing that further publications providing data about the effects of the procedure on symptoms in the long term and on device durability would be useful.

MRI Defecography

There is insufficient evidence regarding the effectiveness and efficacy of MRI defecography. Existing data suggest that this approach is not superior and, in some cases, inferior to conventional defecography.

In a retrospective single-center test development study with 46 adults with chronic constipation, Thanaracthanon et al. (2023) evaluated the diagnostic performance of MR defecographic findings in diagnosis of dyssynergic defecation (DD). Study participants were divided into two groups based on the presence of DD in two of three diagnostic tests (ARM, BET, and anal surface electromyography), with 24 in the DD group (37.5% female) and 22 in the non-DD group (81.8% female). All patients underwent MR defecography according to the institutional standard protocol with both static and dynamic MR defecography images obtained. The study included analysis by two radiologists of nine parameters: anorectal angle (ARA) and M line at rest, defecation, and change between two phases; anal canal width; prominent puborectalis muscle; abnormal evacuation. The authors reported that seven of the nine parameters showed statistically significant difference between the DD and the non-DD group with M line at defecation having the highest odds ratio, followed by ARA change, ARA defecation, M line change, prominent puborectalis muscle, abnormal evacuation, and anal canal width, respectively. The authors also reported that the ARA change and prominent puborectalis muscle had the highest specificity and that multivariate logistic regression revealed two significant findings in differentiating between DD and non-DD, including M line at defecation and ARA at defecation. Limitations include the single-center, retrospective study design, the small sample size, the lack of a comparison test, the heterogeneity of other diseases in the non-DD group that were not seen in the DD group, and the use of a consensus panel which may incorporate bias. The authors concluded that MR defecography had high diagnostic performance in diagnosis of DD with ARA change of less than 1.5 degrees and prominent puborectalis muscle having good specificity in DD diagnosis. The authors recommend additional prospective studies with normal healthy patients as a control group. The findings need to be validated in an independent group of patients and the clinical utility of the test needs to be defined.

Pääkkö et al. (2022) completed a single-center, retrospective review of both magnetic resonance defecography (MRD) and video defecography (VD) studies that were done on 64 women with defecation disorders who underwent both VD and MRD within a year to compare the findings of the two methods and to analyze the success rates. In 58 patients, the indication for the first study were symptoms of obstructive defecation with incontinence as the primary diagnosis for the remaining six patients. The indication for the second study was insufficient information from the first study in 48 patients and for preoperative planning to get more anatomical information in the remaining 16 cases, the second imaging was performed before operative treatment to get more anatomical information or to confirm the findings of the first study Both studies were analyzed in consensus by two radiologists who were blinded to clinical patient data and radiology reports. The authors reported that 96.9% of the VD studies were technically fully diagnostic compared with 45.3% for MRD and that 1.6% of the VD studies were partially diagnostic versus 32.8% for MRD. They reported that 30 enteroceles were observed by VD compared with seven in MRD with moderate agreement, 53 intussusceptions were observed by VD compared with 27 by MRD with poor agreement, 47 cases of rectocele were diagnosed by VD versus 29 by MRD with moderate agreement, and dyssynergic defecation was observed in three patients by VD and in 11 patients by MRD with slight agreement. Limitations of the study included the variability of which study was done first, the retrospective nature of the study, the small sample size, and the variability of the amount and consistency of the gel used in the studies. The authors concluded that technical success and diagnostic capabilities of VD were better than those of MRD and that VD remains the method of choice in the imaging of defecation disorders.

A Cochrane Database systematic review and meta-analysis by van Gruting, et al. (2021) evaluated imaging modalities for the detection of posterior pelvic floor disorders in women with obstructed defecation syndrome (ODS). The review included 39 studies (including the Foti (2013), Poncelet (2017), van Iersel (2017), Vitton (2011), and Zafar (2017) studies previously included in this section) with 2483 women that evaluated the diagnostic accuracy of evacuation proctography (EP), dynamic magnetic resonance imaging (MRI) and pelvic floor ultrasound for detecting posterior pelvic floor disorders. The meta-analysis was done using Bayesian hierarchical latent class analysis and the overall quality of evidence (QoE) was assessed using the GRADE approach for diagnostic test accuracy. The authors reported that the sensitivity of EP for diagnosis of rectocele was 98%, enterocele 91% and pelvic floor descent 98% while the specificity of enterocele was 96%, intussusception 92% and anismus 97%, all with high QoE. The sensitivity for anismus of 80% and the specificity for rectocele of 78% and pelvic floor descent 83% had a moderate to low QoE. The specificity of MRI defecography for diagnosis of rectocele was 90%, enterocele 99% and intussusception 97% with high QoE. The heterogeneity analysis completed in the study showed that sensitivity of MRI performed with evacuation phase was higher than without for rectocele (94% with and 65% without), and for enterocele (87% with and 62% without), while the sensitivity of MRI without evacuation phase was significantly lower than EP. The study also showed that the specificity of transperineal ultrasound (TPUS) for diagnosis of rectocele was 89%, enterocele was 98% and intussusception 96% while the sensitivity for

anismus was 92%. The authors concluded that neither MRI defecography or TPUS met meet the criteria to replace EP as the reference standard for diagnosis of posterior pelvic floor disorders although both met the criteria of a triage test as a positive test confirms the diagnosis of rectocele, enterocele and intussusception, and a negative test rules out diagnosis of anismus. The results of the other ultrasound techniques including endovaginal ultrasound, dynamic anal endosonography, and echodefecography were of too low a quality of evidence to draw conclusions. The authors recommended more well-designed studies to define the role of MRI defecography in the diagnostic pathway of ODS.

Ramage et al. (2018) assessed whether MRI features indicative of pelvic floor dysfunction correlated with patient-reported symptom severity. Univariate and multivariate analyses were performed using pre-treatment questionnaire responses to the Birmingham Bowel, Bladder and Urinary Symptom Questionnaire (BBUSQ), Wexner Incontinence Score (WIS), and modified Obstructed Defecation Symptom (ODS) Score. 302 MRI proctograms were performed (n = 170). Patients with a rectocele larger than two centimeters (p = 0.003; OR 5.756) or MRD features suggestive of puborectalis syndrome (p = 0.025; OR 8.602) were more likely to report a higher ODS score on multivariate analysis. Lack of rectal evacuation was negatively associated with an abnormal WIS (p = 0.007; OR 0.228). Age > 50 (p = 0.027, OR 2.204) and a history of pelvic floor surgery (p = 0.042, OR 0.359) were correlated with an abnormal BBUSQ incontinence score. Lack of rectal evacuation (p = 0.027, OR 3.602) was associated with an abnormal BBUSQ constipation score. Age > 50 (p = 0.07, OR 0.156) and the presence of rectoanal intussusception (p = 0.010, OR 0.138) were associated with an abnormal BBUSQ evacuation score. The authors concluded that while MRD is a useful tool in aiding multidisciplinary decision making, overall, it is poorly correlated with patient-reported symptom severity, and treatment decisions should not rest solely on results. Limitations of this study included lack of a reference standard test and a questionnaire with questions directed at only females.

In a systematic review and meta-analysis of MRD versus clinical examination and fluoroscopy, Ramage et al. (2017) compared detection and miss rates of pelvic floor abnormalities with MRD versus clinical examination and traditional fluoroscopic techniques. Twenty-eight studies were included: 14 studies compared clinical examination to MRD, and 16 compared fluoroscopic techniques to MRD. Detection and miss rates with MRD were not significantly different from clinical examination findings for any outcome except enterocele, where MRD faired significantly better than clinical examination. However, when comparing MRD versus fluoroscopy, MRD have no better detection rate or lower miss rate of a structural abnormality than fluoroscopy. In some studies, fluoroscopy was considered the gold standard, and therefore, a distinct possibility exists that there was a degree of reporting bias with regards to the miss rates of fluoroscopy in particular. Limitations included the large variation in techniques employed during MRD along with numerous fluoroscopic techniques that were utilized across the different studies. Based on their analysis, the authors concluded that MRD has a role in the assessment of pelvic floor dysfunction. However, they advise that clinicians need to be mindful of the risk of under-diagnosis and consideration of the use of additional imaging.

Cappabianca et al. (2011) compared the diagnostic efficacy of dynamic MR defecography (MR-D) with entero-colpo-cysto-defecography (ECCD) in the assessment of midline pelvic floor hernias (MPH) in female pelvic floor disorders. 1,142 participants underwent MR-D with analysis. The results of the study indicated that MR-D shows lower sensitivity than ECCD in the detection of MPH development.

Clinical Practice Guidelines

American Gastroenterological Association (AGA)

The AGA guideline on constipation states that although ARM and a rectal BET generally suffice to diagnose or exclude a defecatory disorder, defecography, which is generally performed with barium, or at some centers with magnetic resonance imaging, is useful if results are inconclusive (Bharucha et al. 2013a).

American College of Gastroenterology (ACG)

The ACG clinical guideline for management of benign anorectal disorders notes that barium or MRD can identify structural causes of outlet obstruction if one is expected. They may also confirm or exclude the diagnosis of defecatory disorders (DD) when the clinical features suggest DD, but the results of ARM and BET are equivocal (moderate recommendation, moderate quality of evidence) (Wald et al., 2014, updated 2021).

The same ACG 2014 guideline also cites the advantages of MRI over defecography as being better resolution of soft tissue surrounding the rectum and anal canal, including the bladder, uterus, and small intestine during dynamic imaging; improved ability to visualize anal sphincter and levator ani muscles with endoanal MRI, and lack of radiation (Wald et al., 2014, updated 2021).

American Society of Colon and Rectal Surgeons (ASCRS)

The ASCRS clinical practice guideline for the evaluation and management of chronic constipation states individuals who exhibit no improvement with dietary changes, fiber therapy and osmotic laxatives should be evaluated for outlet obstruction. Anorectal testing or dynamic imaging by fluoroscopic defecography, MRI defecography may assist in identifying functional or structural causes related to an evacuation disorder. Although MRI, performed in the supine position, permits excellent assessment of all pelvic floor compartments and the surrounding musculature, fluoroscopic defecography performed in the seated position is considered the evacuation examination with the most construct validity (Alavi et al., 2024). (Grade of Recommendation: conditional recommendation based on low-quality evidence).

In an updated clinical practice guideline on the treatment of rectal prolapse, the ASCRS (Bordeianou et al., 2017) states that if prolapse is suggested but cannot be seen during physical examination, fluoroscopic defecography, MRI defecography, or BET may reveal the problem. Defecography may also reveal associated anterior pelvic floor support defects, such as cystocele, vaginal vault prolapse, and enterocele (Grade of Recommendation: strong recommendation based on moderate-quality evidence, 1B).

Electrogastrography (EGG)/Electroenterography/Body Surface Gastric Mapping (BSGM)

Despite a possible use in clinical research, the studies of electrogastrography and body surface gastric mapping fail to provide convincing evidence that this technique is accurate for diagnosis of gastric disorders such as gastric stasis in clinical practice or that it has a positive impact on patient management or disease outcome. Additional studies are needed to determine if EGG is a useful adjunctive test or alternative to radioscintigraphy for the diagnosis of gastric stasis. These studies should involve a standardized procedure for diagnosis of gastroparesis with electrogastrography including recording, analysis, and interpretation. No studies were found to indicate electroenterography has a positive impact on patient management or disease outcome.

ECRI (2024) published a Clinical Evidence Assessment on the Gastric Alimetry System and concluded that the published evidence available for review was very low quality. The report assessed one diagnostic cohort study that reported measures of diagnostic accuracy and one retrospective case series that reported test impact on clinical decision making. ECRI did not find any direct clinical utility studies that reported improvements in patient-relevant outcomes following Alimetry-guided clinical decision making. The report concluded that additional clinical validity studies using appropriate reference standards and larger sample sizes are needed to assess Alimetry's diagnostic accuracy and that clinical utility studies are also needed to determine whether the use of this device to guide treatment and clinical decision making will result in improvements in patient-relevant outcomes.

A systematic review and meta-analysis by Peralta-Palmezano et al (2024) examined the prevalence and range of abnormalities in gastric slow waves in adults with gastroparesis who underwent EGG. The systematic review included 31 prospective studies with 1545 patients with gastroparesis and 340 controls (reported in 14 studies). In the 23 studies that reported the sex of the patients, 71.1% were women. The majority of the studies (67.7%) were conducted in the United States, four were conducted in Germany, and one each in Taiwan, Turkey, the Netherlands, France, Israel, and Germany. The authors reported that patients with gastroparesis had less normogastria (fasting: 50.3% versus 65.8%) (post-stimulus: 54.3% versus 66.5%), more bradygastria (fasting: 37.7% versus 13%) (post-stimulus: 31.9% versus 16.3%), and more tachygastria (fasting: 16.1% versus 4.6%) (post-stimulus: 18.3% versus 5.2%). Limitations of this systematic review include the heterogeneity of the included studies' test protocols, concomitant medications used, and total duration of recordings during the EGG procedures. Additionally, the study did not address the clinical utility of the test and whether its use improves patients' outcomes. The authors concluded that adults with gastroparesis had a significantly lower percentage of normogastria than the controls, while they also had a higher percentage of bradygastria and tachygastria. This systematic review and meta-analysis included the Al Kafee et al. (2022) and Gharibans et al. (2019) studies previously summarized in this policy.

Xu et al. (2024) conducted a test-validation cohort study to investigate gastric myoelectrical abnormalities and symptoms in patients after fundoplication using noninvasive BSGM. The study included 16 adults (median age 34.5 years; 37.5% female) who had undergone a previous fundoplication operation (median time since fundoplication was 5 years) and who had ongoing significant gastroduodenal symptoms and 16 adult matched controls (based on age, biological sex, and BMI). BSGM using the Gastric Alimetry device was performed on each study participant. The authors reported that six of the 16 participants (37.5%) who had previously undergone a fundoplication operation showed significant spectral abnormalities defined by unstable gastric myoelectrical activity (n = 2), abnormally high gastric frequencies (n = 3), or high gastric amplitudes (n = 1) and that these participants had higher Patient Assessment of Upper Gastrointestinal Disorders-Symptom Severity Index scores than the remaining 10 patients with normal BSGM spectrograms. According to the authors, two of the three patients with abnormally high gastric frequencies had presumed vagal nerve injury documented

in their procedure notes. The authors also reported that seven of 16 participants had BSGM test results suggestive of gut-brain axis contributions and without myoelectrical dysfunction. The authors concluded that a significant number of patients with persistent post-fundoplication symptoms displayed abnormal gastric functioning on BSGM testing, which correlated with symptom severity. Limitations of the study include the small cohort size, the inclusion of patients with a single procedure and with multiple revisional procedures, the lack of blinding, and the consecutive sample patient selection methodology. Also, the study does not address the clinical utility of the test and whether its use improves outcomes of patients after fundoplication.

Patient-specific phenotyping using BSGM was compared to gastric emptying testing (GET) in an exploratory comparison study by Wang, et al. (2024) that included 75 adults (77% female, median age 43 years) with chronic gastroduodenal symptoms. All patients had undergone a clinical work-up by a gastroenterologist, including upper gastrointestinal endoscopy, to exclude alternative pathologies, had withheld any medications affecting gastrointestinal motility for 48 hours, had completed an overnight fast, and were asked to avoid caffeine, nicotine, opiates, and cannabis the morning of to their testing. Each study participant underwent simultaneous GET and BSGM that consisted of a 30-minute baseline reading, consumption of a 99mTC-labelled egg meal, and 4-four-hour postprandial recording. Before motility testing was done, 56 patients met Rome IV Criteria for chronic nausea and vomiting syndromes (CNVS) (75%, with 52/56 also meeting functional dyspepsia (FD) criteria. There were 14 participants who met FD criteria alone, and five did not meet either criteria, indicating a high chronic gastroduodenal symptom burden in the study cohort The authors reported that motility abnormality detection rates were 22.7% for GET with 14 delayed and three rapid while BSGM spectral analysis was 33.3% with 14 low rhythm stability/low amplitude, five high amplitude, and six abnormal frequency. The authors also reported that, in patients with normal spectral analysis, BSGM symptom phenotypes included sensorimotor 17% (where symptoms strongly paired with gastric amplitude), continuous 30%, and other 53%. The authors reported that BSGM phenotypes showed superior correlations with the Gastroparesis Cardinal Symptom Index (GCSI), the Patient Assessment of Upper Gastrointestinal Symptom Severity Index, and anxiety scales while the Rome IV Criteria did not correlate with psychometric scores. The authors concluded that BSGM improves patient phenotyping in chronic gastroduodenal disorders in the presence and absence of motility abnormalities with increased correlation with symptoms and psychometrics compared with GET and Rome IV criteria. Whether use of BSGM improves patients' outcomes is however not addressed in this study.

Xu et al. (2023) performed a study using BSGM in people with longstanding type 1 diabetes (T1D) with and without symptoms to define phenotypes of gastric myoelectrical abnormalities. The study included 64 people, 32 of which had a medical history of T1D of more than 10 years (mean age of 50 years; 64% female), and 32 were controls. Of the 32 patients with T1D, 15 were noted to have a high symptom burden (12 with CNVS and FD, and three with FD only) based on their assessment using the Rome IV criteria for CNVS if they met at least one of the criteria. The 32 participants with T1D were then matched to a database of controls in a 1:1 ratio using the nearest neighbor based on age, sex, and body mass index. The authors reported that the patients with T1D with symptoms showed more unstable gastric myoelectrical activity and lower average special covariance compared to controls and that symptomatic patients also had a higher prevalence of peripheral neuropathy, anxiety/depression diagnoses, and higher mean hemoglobin A1C levels. They also reported that deviation in gastric frequency was positively correlated with symptoms of bloating, upper gut pain, nausea and vomiting and fullness. Limitations of the study included the lack of blood glucose monitoring for all the participants (due to device availability), different meals given to the study participants with T1D than the control group received, the ongoing development of reference values for the emerging spatial metrics and the small sample size. The authors concluded that gastric symptoms in people with longstanding T1D correlated with myoelectrical abnormalities on BSGM testing, in addition to glycemic control, psychological comorbidities and peripheral neuropathy.

Schamberg et al. (2023) conducted a multi-center, retrospective observational study to compare BGSM and EGG to quantify performance differences. The study included EGG and BSGM data from 178 subjects (43 patients with nausea and vomiting (NVS), 32 patients with type 1 diabetes (T1D) and 110 healthy volunteers). The study assessed the use of BSGM and EGG in the following three domains: group level-differences in measures of gastric activity, the relationship between gastric abnormalities and symptoms, and patient-level classifications of gastric health. The comparisons followed standard methodologies for each test including pre-processing, post-processing, and analysis. Statistical evaluations were done for group-level differences, symptom correlations and patient-level classifications. The authors reported that BSGM showed substantially tighter frequency ranges when compared to EGG in the control group and that both tests detected rhythm instability in NVS, but EGG showed opposite frequency effects in T1D. The authors also reported that BSGM showed an eight times increase in the number of significant correlations with symptoms and that BSGM accuracy for patient-level classification was 0.78 for patients when compared to controls and 0.96 when compared to a blinded consensus panel while EGG accuracy was 0.54 and 0.43. Limitations of the study include the automated EGG analysis methodology, the possibility that proprietary signal processing steps may exist but were not used, the lack of testing with other meal preparations, only using a single electrode configuration for EGG testing, the heterogeneity of EGG processing approaches, and the focus on only spectral analyses of BSGM and EGG. The authors concluded that EGG detected

group-level differences in patients but lacked symptom correlations and showed poor accuracy for patient-level classification while BSGM demonstrated substantial performance improvements across all three domains.

In a study to evaluate CNVS pathologies, Gharibans et al. (2022) performed BSGM in 43 patients with NVS and 43 matched controls. The study participants were adults, primarily female (76.7%) with a median age of 33 years (range 26 to 44). Each participant underwent BSGM that entailed a fasting baseline, ingestion of a 482-kilocalorie meal and a four-hour postprandial recording, then spectral and spatial biomarker analyses. The authors reported that meal responses were impaired in NVS with multiple BSGM abnormalities compared to the study controls, impaired fed-fasting power ratios, and disorganized slow waves. The authors also reported that most patients (62%) had normal BSGM results with increased psychological comorbidities and anxiety scores while a smaller subgroup (31%) had markedly abnormal BSGM with biomarkers that correlated with symptoms and that patients with NVS shared overlapping symptoms but comprised distinct underlying phenotypes that correlated with symptoms. Limitations of the study include the small sample size that may have affected the subanalyses performed, and the use of a consensus panel classification which may introduce subjectivity and limit reproducibility. Other limitations of the study included the lack of a control group, the under-representation of patients with diabetes as only 7% of the participants had diabetes, and the inclusion of patients with BMI > 35 as a high BMI may result in overestimating the low rhythm stability phenotype due to declining signal-to-noise ratio. The authors concluded that the study showed that BSGM expanded the phenotyping of patients with chronic gastroduodenal disorders when compared to GET and that the results of BSGM could improve clinical management of these patients by separating those with gastric dysfunction from those with gut-brain dysregulation or other etiologies.

A systematic review and meta-analysis was completed by Bhat et al. (2021) involving electrogastography (EGG) use in adults with gastroesophageal reflex disease (GERD). After the published literature was reviewed, thirteen studies were included in the analysis with a total of 591 participants (427 with GERD; 164 healthy controls) who had completed an EGG procedure. The study found that patients with GERD spent significantly less time with normal gastric slow-wave activity compared to healthy controls. The authors noted that correlations between GERD symptoms and EGG recordings were inconsistently studied; EGG apparatus and techniques also varied across the studies. They also recognized the limitations of the studies available including the known limitations to low-resolution EGG methodologies (as high-resolution EGG is now available), and the inclusion of studies that relied on subjective symptom-based diagnostic criteria. They concluded that further investigation for the use of EGG in adults with GERD is warranted.

In an evaluation of 54 patients with FD, Russo et al. (2017) utilized the results of EGG to differentiate postprandial distress syndrome (PDS) with epigastric pain syndrome (EPS). Using a symptom questionnaire, 42 patients were classified as PDS and 12 as EPS, although an overlap between the symptom profiles of the two subgroups was recorded. The EGG parameters (the postprandial instability coefficient of dominant frequency, the dominant power, and the power ratio) were significantly different between the subgroups, whereas the gastric emptying time did not differ significantly. In addition, EPS was characterized by a different gut peptide profile compared with PDS. Finally, neurotensin polymorphism was shown to be associated with neurotensin levels. The authors concluded that this evidence deserves further studies into FD. This study however does not support the use of EGG in clinical practice or beyond its use for research.

Kayar et al. (2016) utilized transcutaneous EGG to compare patients with FD (n = 30) to control subjects (n = 30) in terms of motility abnormalities according to the EGG results. A high incidence of gastric motility and myoelectrical activity abnormalities was observed in patients with FD. The authors concluded that although still considered an experimental method, EGG is an effective, dependable, and non-invasive method in differentiating the subgroups and may be an essential and irreplaceable test to diagnose and follow-up patients with FD with motor dysfunction.

Clinical Practice Guidelines

American Gastroenterological Association (AGA)

A position statement from the AGA (Parkman, et al. 2004) on the diagnosis and treatment of refractory gastroparesis does not recommend the use of EGG. In their 2022 Clinical Practice update (Lacy, et al), the AGA guideline does not focus on the etiology, pathophysiology or diagnostic testing for refractory gastroparesis and there is no longer any mention or direction for the use of electrogastrography for the diagnosis of gastroparesis.

Esophageal Mucosal Integrity Testing

The limited number of published clinical studies on the use of esophageal mucosal integrity testing by electrical impedance fail to provide convincing evidence that this technology is safe and effective for diagnosing GERD, eosinophilic esophagitis (EoE), or nonacid reflux disease (non-GERD), or for the monitoring of treatment response in GERD and EoE. Additional studies are needed to provide evidence of the efficacy of this technology.

Hayes (2022, updated 2024) published an Evolving Evidence Review on the safety and efficacy of MiVu Mucosal Integrity Testing (Diversatek, Inc.) for the diagnosis of GERD in adults. Following their review of three "very poor-quality" studies and one systematic review that compared several emerging diagnostic tests, Hayes stated that the system may distinguish previously diagnosed EoE from GERD at least as well as esophagogastroduodenoscopy (EGD) and potentially better than pH testing but that there was a lack of data from participants that did not yet have a definitive diagnosis. Hayes also stated that insufficient data was published addressing the clinical utility of the device in terms of impact on clinical management or outcomes to draw conclusions regarding level of support for that use. In their review of medical society guidelines, Hayes assigned a weak level of support to reflect that the guidelines they identified indicated there is "promise" in this device as an adjunctive diagnostic tool but that the societies did not recommend it as preferable to standard diagnostic methods. Hayes' assessment recommended that the literature continue to be monitored, as MI testing technology is still developing. In their 2024 update, Hayes identified one relevant newly published single-center, case-controlled study since this report was published in 2022; however, Hayes stated that this study would not result in a change to their minimal level of support for this device as there was no new evidence regarding the safety of the device or regarding longer-term follow-up. The Choksi et al. (2018) and Patel et al. (2019) studies summarized below are included in this report.

ECRI (2021) published an Evidence Analysis on the efficacy of the MiVu Mucosal Integrity Testing System (Diversatek, Inc.) for help diagnosing GERD and its ability to obtain real-time measurements of esophageal epithelial impedance during an endoscopy. The device is not for use as a sole diagnostic screening tool. ECRI's review identified three studies for inclusion. Based on their review of the abstracts, ECRI concluded that the available published evidence was limited and that additional clinical validity studies with larger sample sizes are needed to assess the diagnostic accuracy of this device. ECRI also stated that clinical utility studies are needed to determine whether the use of this device to guide treatment and clinical decision making will result in improvements in patient-relevant outcomes. The ECRI review included the Patel et al. (2019) and Choksi et al. (2018) studies summarized below.

Patel et al. (2019) conducted a prospective, multi-center test-validation study to evaluate the ability of a balloon mucosal impedance (MI) catheter system to detect and evaluate esophageal disorders such as GERD and EoE. The study included 69 adult participants (91.7% Caucasian) who underwent esophagogastroduodenoscopy (EGD) then balloon MI testing during endoscopy and prior to wireless pH monitoring or esophageal biopsies for suspected GERD. The participants were classified based on endoscopic, pH monitoring and pathology findings as having GERD (n = 24; median age 48; 54% female), EoE (n = 21; median age 33; 33% female), or non-GERD (n = 24; median age 62; 71% female). The authors reported that the MI pattern along the esophageal axis differed significantly among participants with GERD, EoE and non-GERD as the MI pattern for GERD was easily distinguished from that of EoE with low MI values in the distal esophagus and normalized values along the proximal esophagus in those individuals with GERD while the measurements were low in all segments of the esophagus in participants with EoE. The authors also reported that those with non-GERD had higher baseline MI values in the distal esophagus and MI that the values remained elevated along the esophagus. One adverse event was reported by the authors in a participant with EoE who showed a small distal esophageal mucosal tear similar to that seen during endoscopic dilation. The authors concluded that the balloon MI catheter system instantly detected changes in esophageal mucosal integrity during endoscopy which could potentially obviate the need for 24-to-48-hour ambulatory wireless pH monitoring or esophageal biopsies for histopathology. The authors also concluded that the MI was safe and effective in identifying patients with GERD, EoE, or non-GERD. Limitations of the study include the small sample size, the lack of blinding, the homogeneity of the study population, and the assumption that the participants must belong to one of the three diagnosis groups with an equal baseline prevalence of GERD, non-GERD and EoE. Furthermore, the findings of this study need to be validated in an independent patient population and the clinical utility of the test in improving patients' outcome is not addressed.

Choksi et al. (2018) conducted a retrospective analysis of 91 adult individuals (80.32% Caucasian) with upper gastrointestinal symptoms (non-GERD, n = 30) who were referred for GERD (n = 38) and EoE (n = 23) diagnostic testing to quantify MI testing that measured epithelial integrity during EGD and to identify patterns that differentiated individuals with and without GERD from those with EoE. Additionally, the authors sought to determine whether MI values and patterns were sufficient in identifying individuals with EoE utilizing histologic findings as a reference. The individuals underwent initial endoscopy with MI measurements obtained. The authors utilized statistical modeling to identify MI patterns within the esophagus that were associated with GERD versus EoE. The authors reported there were no statistically significant differences within the groups regarding race. MI parameters were determined for distinguishing EoE from non-EoE conditions (GERD or normal). The authors reported that the data showed significant improvement in sensitivity (100% vs 86%) and specificity (96% vs 59%) when predicting a diagnosis of EoE using MI pattern. Findings were validated by the authors in a prospective cohort of 49 individuals, symptomatic for dysphagia with no prior diagnosis, who underwent EGD for dysphagia, to test the ability of MI patterns to identify individuals with versus without EoE. The authors reported individuals with EoE had a unique MI pattern and low values long with esophageal axis and that MI measurements differentiated the individual populations. The authors reported per the validation cohort, that the

assessment of mucosal integrity by MI values and pattern alone without endoscopic or clinical presentation was sufficient with a high level of accuracy in providing the correct diagnosis. Limitations of the study include the use of only two impedance rings, forming a single MI sensing channel and that the catheter was manually repositioned to various sites of the esophagus which may have resulted in some variability. Additional limitations include the small sample size as well as the homogeneity of the study population.

Clinical Practice Guidelines

American College of Gastroenterology (ACG)

The ACG's Clinical Guideline addressing the diagnosis and management of GERD states that ACG expects new diagnostic tools and treatments to be developed and refined. The statement goes on to state that mucosal integrity testing is available commercially but that it is not developed sufficiently to warrant discussion in this guideline (Katz, et al. 2022).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Instruments to perform cutaneous electrogastrography, electroenterography, and body surface gastric mapping are regulated by the FDA as Class II devices. Refer to the following website for more information (use product code MYE or FFX): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April 2, 2025)

The only gastric electrical stimulation (GES) device for gastroparesis treatment approved for marketing in the United States is the Enterra™ Therapy System, manufactured by Medtronic, Inc. On March 31, 2000, the FDA approved a Humanitarian Device Exemption (HDE) for the marketing of the Enterra gastric electrical stimulation system for the treatment of chronic, intractable (drug-refractory) nausea and vomiting secondary to paresis of diabetic or idiopathic etiology. Enterra is indicated for the treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology in patients aged 18 to 70 years. Based upon the FDA label, the Enterra device should not be used for patients with gastric obstruction or pseudo-obstruction, prior gastric resection, fundoplication, eating disorders, history of seizures, primary swallowing disorders, chemical dependency, or psychogenic vomiting. Refer to the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfhde/hde.cfm?id=376493. (Accessed April 2, 2025)

Humanitarian use devices may only be used in facilities that have obtained an institutional review board (IRB) approval to oversee the usage of the device in the facility, and after an IRB has approved the use of the device to treat or diagnose the specific rare disease. Additional information may be obtained directly from the U.S. Food and Drug Administration (FDA) [website] Center for Devices and Radiological Health (CDRH) at: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm. (Accessed April 2, 2025)

Several radiopaque markers have been approved by the FDA for colonic transit testing. Refer to the following website for more information (use product code FFX): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April 2, 2025)

Defecography is a procedure and, therefore, is not subject to FDA regulation. However, any medical equipment, drugs or tests used as part of this procedure may be subject to FDA regulation. A general list of cleared magnetic resonance imaging systems for MRI defecography can be found by entering the code LNH into the "product code" window in the form at the following FDA 510(k) database website: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April 2, 2025)

The MiVu™ Mucosal Integrity Testing System (MiVu) (Diversatek Healthcare, Highlands Ranch, CO) received FDA clearance as a Class II de novo device on December 23, 2019 as a new approach to assessing esophageal mucosal integrity. FDA 510(k) Premarket Notification was received on April 25, 2023 under 510(k) Number K230056. Refer to the following website and search using either the product name or the Product Code of QIS for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April 2, 2025)

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Policy History/Revision Information

Date	Summary of Changes

08/01/2025	**Coverage Rationale**
	• Added language to indicate Esophageal Mucosal Integrity Testing by electrical impedance (e.g., MiVu™ Mucosal Integrity Testing System) for the diagnosis of gastroesophageal reflux disease (GERD), eosinophilic esophagitis (EoE), and nonacid reflux disease (non-GERD), or for the monitoring of treatment response in GERD and EoEI are unproven and not medically necessary due to insufficient evidence of efficacy
	• Removed language indicating:
	  ○ Rectal manometry, rectal sensation, tone, and compliance test, conventional defecography, and anorectal manometry are proven and medically necessary for evaluation of colorectal function
	  ○ Colonic manometry for evaluating colon motility is unproven and not medically necessary due to insufficient evidence of efficacy
	  ○ Ingestible vibrating capsule devices (e.g., the Vibrant® System) for the treatment of Constipation are unproven and not medically necessary due to insufficient evidence of efficacy
	Definitions
	• Added definition of “Esophageal Mucosal Integrity Testing”
	• Removed definition of:
	  ○ Anorectal Manometry
	  ○ Colonic Manometry
	  ○ Defecography
	Applicable Codes
	• Added CPT codes 43499 and 76498
	• Removed CPT/HCPCS codes 74270, 76496, 91117, 91120, 91122, A9286, A9900, A9999, and E1399
	Supporting Information
	• Updated *Description of Services*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information
	• Archived previous policy version 2025T0415EE

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.