

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.



GASTROINTESTINAL MOTILITY DISORDERS, DIAGNOSIS AND TREATMENT

Policy Number: CS046.KJ

Effective Date: June 1, 2019 TBD

[Instructions for Use](#) ⓘ

Table of Contents	Page
COVERAGE RATIONALE	1
APPLICABLE CODES	2
DESCRIPTION OF SERVICES	3
CLINICAL EVIDENCE	6
U.S. FOOD AND DRUG ADMINISTRATION	23
CENTERS FOR MEDICARE AND MEDICAID SERVICES ..	24
REFERENCES	24
POLICY HISTORY/REVISION INFORMATION	28
INSTRUCTIONS FOR USE	28

Related Community Plan Policy

- [Bariatric Surgery](#)

Commercial Policy

- [Gastrointestinal Motility Disorders, Diagnosis and Treatment](#)

Medicare Advantage Coverage Summary

- [Gastroesophageal and Gastrointestinal \(GI\) Services and Procedures](#)

COVERAGE RATIONALE

The following procedures are proven and medically necessary:

- Gastric electrical stimulation (GES) therapy for treating refractory **diabetic** gastroparesis that has failed other therapies, or chronic intractable (drug-refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology
- Rectal manometry and rectal sensation, tone and compliance test **and anorectal manometry**
- ~~Anorectal manometry~~
- Conventional defecography for evaluating intractable constipation or constipation in members who have one or more of the following conditions that are suspected to be the cause of impaired defecation:
 - Pelvic floor dyssynergia (inappropriate contraction of the puborectalis muscle); or
 - Enterocele (e.g., after hysterectomy); or
 - Anterior rectocele

See 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:

- Colonic manometry for evaluating colon motility
- Conventional defecography for evaluating all other conditions not included above
- Magnetic resonance imaging (MRI) defecography for evaluating constipation and anorectal or pelvic floor disorders
- Cutaneous, mucous, or serosal electrogastrography or electroenterography for diagnosing intestinal or gastric disorders including gastroparesis

DEFINITIONS

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

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Anorectal Manometry: a test performed to measure the pressures of the anal sphincter muscles, the sensation in the rectum, and the neural reflexes that are needed for normal bowel movements (Motility Society).

Colonic Manometry: a functional test for severe constipation where a probe is inserted via antegrade or retrograde in the colon to measure pressure and colonic motor activities (Dinning et al., 2010).

Constipation: infrequent or hard-to-pass bowel movements, hard stools or incomplete bowel movement sensation; infrequent means less than three bowel movements a week (American Gastroenterological Association (AGA)).

Defecography: fluoroscopic examination with functional, real-time assessment of defecation mechanics; performed for longstanding constipation, unexplained anal or rectal pain, residual sensation after defecation or suspected prolapse (Kim and Rhee, 2011).

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).

Fecal Incontinence (FI): the inability to control bowel movements causing stool (feces) to leak unexpectedly from the rectum; also called bowel or anal incontinence (American College of Gastroenterology (ACG)).

Gastroparesis: a digestive disorder in which the motility of the stomach is either abnormal or absent; it is also known as delayed gastric emptying (ACG, AGA).

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 federal, state or contractual requirements 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 Coverage Determination Guidelines may apply.

CPT Code	Description
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 or gastric neurostimulator pulse generator or receiver, direct or inductive coupling
64595	Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver
76496	Unlisted fluoroscopic procedure (e.g., diagnostic, interventional)
76498	Unlisted magnetic resonance procedure (e.g., diagnostic, interventional)

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

CPT Code	Description
91117	Colon motility (manometric) study, minimum 6 hours continuous recording (including provocation tests, e.g., meal, intracolonic balloon distension, pharmacologic agents, if performed), with interpretation and report
91120	Rectal sensation, tone, and compliance test (i.e., response to graded balloon distention)
91122	Anorectal manometry
91132	Electrogastrography, diagnostic, transcutaneous
91133	Electrogastrography, diagnostic, transcutaneous; with provocative testing

CPT® is a registered trademark of the American Medical Association

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 or colonic manometry) (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, diabetics 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 taken into account 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 electrogram. 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

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

gastric slow waves or dysrhythmia (Yin and Chen, 2013). Electroenterography is a similar procedure that records myoelectrical activity from the intestines.

Gastroparesis, also referred to as gastric stasis, is a common gastrointestinal motility disorder. It is defined by delayed gastric emptying without evidence of mechanical obstruction. Individuals 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, diabetics 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 taken into account 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).

Anorectal disorders present with a variety of symptoms and result from either structural or functional dysfunction. 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).

Symptoms of constipation may be secondary to diseases of the colon (stricture, cancer, anal fissure, proctitis), metabolic disturbances (hypercalcemia, hypothyroidism, diabetes mellitus), and neurologic disorders (Parkinsonism, spinal cord lesions). Some of these will be amenable to specific therapies, but when they are not, the challenge remains one of symptomatic treatment of constipation. More frequently, constipation is due to disordered colonic and/or pelvic floor/anorectal function.

Symptoms of constipation are extremely common; the prevalence is approximately 16% in adults overall and 33% in adults over 60. Many people seek medical care for constipation, and most do not have a life-threatening or disabling disorder so the primary need is for symptom control. If therapeutic trials of laxatives fail, specialized testing should be considered (Bharucha, et al., 2013).

Diagnosis of primary chronic constipation involves a multistep process initiated by the exclusion of 'alarm' features (for example, unintentional weight loss or rectal bleeding) that might indicate organic diseases (such as polyps or tumors) and a therapeutic trial with first-line treatments such as dietary changes, lifestyle modifications and over-the-counter laxatives. If symptoms do not improve, investigations to diagnose rectal evacuation disorders and slow-transit constipation are 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 or colonic manometry) (Camilleri et al., 2017).

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.

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Assessments of colonic transit and anorectal function allow individuals to be categorized into 3 subgroups (i.e., defecatory disorders, normal transit constipation [NTC], and slow transit constipation [STC]), which facilitates management in refractory individuals:

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.

In addition to normal anorectal function, individuals with NTC and STC have normal or slow colonic transit, respectively. Some individuals with STC have colonic motor disturbances (i.e., reduced colonic propulsive activity or increased uncoordinated motor activity in the distal colon) that may impede colonic transit. However, others do not.

Fecal incontinence 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. Two groups of muscles in the wall of the anus and rectum are responsible for holding the stool in the rectum, the outer muscle group (external anal sphincter) and the inner muscle group (internal anal sphincter). Normal continence also requires the ability to sense the presence of stool in the rectum (called rectal sensation), and the ability to relax and store stool (called rectal compliance) when having a bowel movement is not convenient. Fecal incontinence is commonly caused by altered bowel habits (generally diarrhea, but also constipation) and conditions that affect the ability of the rectum and anus to hold stool.

A standard measurement of colonic transit time in individuals with constipation is the radiopaque marker test (Kim and Rhee 2012) which distinguishes constipation subgroups such as normal or slow transit constipation, and assesses segmental transit times in individuals with delayed total colon transit. This test is accomplished by observing the passage of orally administered radiopaque markers (plastic beads in capsule form) on abdominal x-ray. Interpretation is based on the identification of markers in 3 regions of the colon. In the single capsule technique with a single abdominal x-ray on day 5 (120 hours later), delayed transit is defined as > 20% retention of markers. Radiopaque markers provide only a qualitative assessment (normal or abnormal) of colon transit, require at least 2 separate visits, and are associated with radiation exposure.

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.

Anorectal manometry is a test that measures the pressures of the anal sphincter muscles, the sensation in the rectum, and the neural reflexes needed for normal bowel movements. This test is has been used to evaluate individuals with constipation or fecal incontinence. The rectal sensation, tone, and compliance test measures the sensory, motor and biomechanical function of the rectum.

Colon motility testing or colonic manometry is the recording of intraluminal pressures from within the large bowel by means of a manometric catheter. The catheter is positioned endoscopically and clipped to the colonic mucosa. Pressure activity is continuously recorded for a minimum of six hours. This test has been proposed to evaluate motility abnormalities and defecation disorders such as constipation.

Conventioanl defecography (also known as evacuation proctography) involves the x-ray imaging of the defecation process. With the aid of barium, x-rays can follow the movement of fecal matter through the rectum and anus during

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

a bowel movement. It provides useful information about structural changes such as rectoceles, rectal prolapse, and intussusception, and dyssynergic defecation and descending perineum syndrome. Defecography has been proposed as a diagnostic tool to evaluate lower bowel disorders that are not evident by direct visualization.

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).

CLINICAL EVIDENCE

Gastric Electrical Stimulation (GES) Therapy

Ducrotte et al. (2019) performed a multicenter, randomized, double-blind trial with crossover to study the efficacy of GES in patients with refractory vomiting, with or without gastroparesis. Symptoms in 172 patients with chronic refractory vomiting and with or without diabetes were assessed. A GES device (Medtronic Enterra therapy system) was implanted and left inactive for one month until patients were randomly assigned, in a double-blind manner, to groups that received 4 months of stimulation parameters (14 Hz, 5 mA, pulses of 330 μ s) or no stimulation (control). Participants were then switched over to the other condition for the following 4 months and were examined at five and nine months after device implantation. At each visit, the follow-up included the assessment of symptoms, nutritional status, QOL, and anxiety and depression levels, as well as a gastric emptying study. Primary endpoints were vomiting episodes assessed on a five point scale and the quality of life, assessed by the Gastrointestinal Quality of Life Index scoring system. The authors found that high-frequency GES, performed with standard stimulation parameters, was effective to reduce the frequency of vomiting (on average 0.4 points on a 5-point scale) in diabetic and nondiabetic patients with refractory vomiting with or without delayed gastric emptying. Quality of life, the other primary outcome, was not significantly improved.

In a multi-institutional case series review, Shada et al. (2018) collected prospective data from patients with medically refractory gastroparesis who underwent GES with the Enterra® system. A total of 119 patients (64 diabetic and 55 idiopathic) participated. All devices were placed laparoscopically. Mean follow-up was 34.1 \pm 27.2 months in diabetic and 44.7 \pm 26.2 months in idiopathic patients. A total of 18 patients died during the study interval (15.1%). No mortalities were device-related. Diabetics had the greatest rate of mortality (25%; mean interval of 17 \pm 3 months post implantation). Gastroparesis Cardinal Symptom Index (GCSI) scores improved, and prokinetic and narcotic medication use decreased significantly at \geq 1 year. Satisfaction scores were high. **Limitations of the study included lack of comparison group, a number of patients lost to follow-up and that this was a retrospective review which had its own limitations such as different referral patterns, selection criteria, and perioperative protocols. Despite these shortfalls,** the authors concluded that GES therapy led to the improvement of symptoms of gastroparesis and a better quality of life.

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. (Author Chu et al. (2012) which was previously cited in this policy, is included in the Levinthal and Bielefeldt (2017) meta-analysis.)

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

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. Gastroparesis patients (n= 151; (120 females) with refractory gastroparesis (72 diabetic, 73 idiopathic, 6 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 diabetics was better than in nondiabetic patients. 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.**

~~In a retrospective multi-center cohort study, Laine et al. (2017) evaluated the efficacy and safety of GES in patients (n=14) in whom gastroparesis could not be controlled by conservative means. No surgical or late complications were reported. Symptoms were relieved markedly in 8 patients, and partially in 3 patients (79%). Nutritional status improved in 79% of patients. The follow-up period was not provided.~~

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 3 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), Gastroparesis Cardinal Symptom Index (GCSI), Monthly and Weekly Vomiting Frequency, Monthly and Weekly Nausea Frequency, and Gastrointestinal Symptoms Rating Scale (GSR). All studies investigating gastric emptying used a 2-hour and 4-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, with the exception of 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. (Author McCallum et al. (2010) which was previously cited in this policy, is included in the Lal et al. (2015) systematic review.)

Jayanthi et al. (2013) conducted a clinical audit of 71 gastroparesis patients, 35 who were selected for GES, from May 2008 to January 2012. The etiology of gastroparesis was idiopathic (61%), diabetes (21%), or post-surgical (18%). Outcome data for 31 patients (idiopathic, 21 patients; diabetes, 3; post-surgical, 7) with a median follow-up period of 10 months (1-28) showed 22 patients (71%) with intractable gastroparesis had good response to permanent GES at follow-up of up to 2 years.

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 1-11 years were retrospectively assessed; 188 had follow-up visits and data were collected for at least 1 year. Total symptom scores (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

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

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.

McCallum et al. (2010) performed a controlled, multicenter, prospective study to evaluate the safety and efficacy of Enterra therapy in 55 patients with chronic intractable nausea and vomiting from diabetic gastroparesis (DGP). After surgery, all patients had the stimulator turned on for 6 weeks and then they randomly were assigned to groups that had consecutive 3-month, cross-over periods with the device on or off. After this period, the device was turned on in all patients and they were followed up, unblinded, for 4.5 months. The median reduction in weekly vomiting frequency (WVF) at 6 weeks, compared with baseline, was 57%. There was no difference in WVF between patients who had the device turned on or off during the cross-over period (median reduction, 0%). At 1 year, the WVF of all patients was significantly lower than baseline values (median reduction, 67.8%). The investigators concluded that in patients with intractable DGP, 6 weeks of GES therapy with Enterra significantly reduced vomiting and gastroparetic symptoms. Patients had improvements in subjective and objective parameters with chronic stimulation after 12 months of GES, compared with baseline.

McCallum et al. (2011) assessed the long-term clinical outcomes of GES therapy with Enterra® in a large cohort of patients with severe gastroparesis. Gastroparesis patients (n=221; 142 diabetic, 48 idiopathic, and 31 postsurgical) treated with Enterra (Medtronic) for 1-11 years were retrospectively assessed; 188 had follow-up visits and data were collected for at least 1 year. Total symptom scores (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.

In a retrospective analysis of 214 patients, there was no significant difference in survival rates between patients who underwent GES and 54 historical controls. However, for patients with diabetes, there was a significant survival benefit for those who received permanent GES versus patients who received standard medical treatment. The 36-month survival rate was 60.7% for gastric stimulation compared with 33.3% in the medical therapy group. At the last follow-up (median, 4 years), significant improvements were reported in vomiting (62%), nausea (59%), and total symptom (84%) (Anand et al. 2007).

Musunuru et al. (2010) evaluated the use of GES therapy in 15 patients. Four patients with idiopathic gastroparesis failed to improve more than 20% on multiple assessments after a year of therapy. All diabetic patients experienced a durable symptomatic improvement with GES. The investigators concluded that diabetic gastroparesis patients respond best to GES. Responders tend to have more severe vomiting preoperatively. According to the investigators, patients with idiopathic gastroparesis who do not experience severe vomiting should be cautioned about a potentially higher rate of poor response to GES and may be better served with alternative treatments.

Jayanthi et al. (2014) conducted a clinical audit of 71 gastroparesis patients, 35 who were selected for GES, from May 2008 to January 2012. The etiology of gastroparesis was idiopathic (61%), diabetes (21%), or post-surgical (18%). Outcome data for 31 patients (idiopathic, 21 patients; diabetes, 3; post-surgical, 7) with a median follow-up period of 10 months (1-28) showed 22 patients (71%) with intractable gastroparesis had good response to permanent GES at follow-up of up to 2 years.

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

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

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.

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. 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.

Chu et al. (2012) conducted a meta-analysis to assess the effects of GES on symptoms and gastric emptying in patients with gastroparesis, and the effects of GES on the three subgroups of gastroparesis. Data on the total symptom severity score (TSS), nausea severity score, vomiting severity score, and gastric emptying were extracted and analyzed. The statistic effect index was weighted mean differences. Ten studies ($n = 601$) were included in the meta-analysis. In the comparison to baseline, there was significant improvement of symptoms and gastric emptying. It was noted that GES significantly improved both TSS and gastric retention at 2 hours and 4 hours in patients with diabetic gastroparesis (DG), while gastric retention at 2 hours in idiopathic gastroparesis (IG) patients, and gastric retention at 4 hours in postsurgical gastroparesis (PSG) patients, did not reach significance. Based on this meta-analysis, the authors concluded that the substantial and significant improvement of symptoms and gastric emptying, and the good safety indicate that high frequency GES is an effective and safe method for treating refractory gastroparesis. DG patients seem the most responsive to GES, both subjectively and objectively, while the IG and PSG subgroups are less responsive and need further research.

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.

Professional Societies

American College of Gastroenterology (ACG)

The ACG published a clinical guideline for the management of gastroparesis that states that GES may be considered for compassionate treatment in patients with refractory symptoms, particularly nausea and vomiting. According to the guideline, symptom severity and gastric emptying have been shown to improve in patients with diabetic gastroparesis (DG), but not in patients with idiopathic gastroparesis (IG) or post-surgical gastroparesis (PSG). (moderate level of evidence) (Camilleri 2013).

American Gastroenterological Association (AGA)

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

Anorectal Manometry

In a retrospective review, Chedid et al. (2019) audited records of 449 consecutive patients with chronic constipation (CC). Anal sphincter tone and contraction, puborectalis tenderness, and perineal descent on digital rectal exam (DRE); maximum resting and squeeze pressures, and rectoanal pressure gradient on HRM; weight or time to balloon expulsion; colonic transit, and area of rectal area on radiograph (RASf) were evaluated. The investigators based the diagnosis of rectal evacuation disorders (RED) on ≥ 2 abnormalities on both DRE and anorectal manometry (HRM), excluding results of balloon expulsion test (BET), as the performance of BET is being investigated. Results of RED vs

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

non-RED and results obtained using **time-based BET (tbBET)** vs **weight-based BET (wbBET)** groups were compared. The final analysis included 276 patients (74 RED and 202 non-RED). Predominant exclusions were for no HRM (n=79) or use of low resolution anorectal manometry (n=77). Logistic regression models for abnormal tbBET showed time >60 seconds, RASF and age-predicted RED. For tbBET, the current cutoff of 60 seconds had sensitivity of 39.0% and specificity 93.0% to diagnose RED; on the other hand, applying the cutoff at 22 seconds, the sensitivity was 77.8% and specificity 69.8%. **Limitations of study included more patients enrolled with wbBET versus tbBET and no established gold standard for diagnosis of CC.** The authors concluded that the clinical diagnosis of RED in patients with CC is achieved with combination of DRE, HRM and an optimized, time-based BET. They recommend prospective studies to confirm the proposed 22 second cutoff for tbBET.

In a systematic review and meta-analysis, Yeap et al. (2017) assessed the diagnostic accuracy of anorectal manometry (ARM) for fecal incontinence. Seven studies were included out of an initial search of 1499 studies. The summary sensitivity and specificity for ARM as an overall test were 0.80 (95% confidence interval (CI): 0.69-0.88) and 0.80 (95% CI: 0.65-0.90), respectively. The diagnostic odds ratio (DOR) for ARM was found to be 16.61 (95% CI: 5.52-50.03). The positive likelihood ratio (PLR) and negative likelihood ratio (NLR) for ARM were found to be 4.09 (95% CI: 2.11-7.94) and 0.25 (95% CI: 0.14-0.42), respectively. Subgroup analysis based on four studies reporting on maximum resting pressure (MRP) demonstrated a sensitivity, specificity, DOR, PLR and NLR of 0.60 (95% CI: 0.38-0.79), 0.93 (95% CI: 0.80-0.97), 20.0 (95% CI: 4.00-91.00), 8.60 (95% CI: 3.00-24.30) and 0.43 (95% CI: 0.24-0.76), respectively. The authors concluded that ARM has been shown to be an accurate test for diagnosing FI, but suggest that further studies are required to establish the diagnostic accuracy of individual ARM measures.

In a retrospective analysis, Prichard et al. (2017) compared anorectal high-resolution manometry (HRM), magnetic resonance imaging (MRI), or balloon expulsion test (BET) for assessing rectal evacuation and structural abnormalities in women. Their analysis included 188 patients with constipation (n = 51), fecal incontinence (n = 48), or rectal prolapse (n = 19), and 30 asymptomatic women serving as a control group. The authors used principal components analysis of HRM variables to identify rectoanal pressure patterns associated with rectal prolapse and phenotypes of patients with prolapse. They concluded that HRM alone and together with anorectal descent during evacuation, may identify rectal prolapse and large rectoceles, respectively, and also identify unique phenotypes of rectal prolapse.

Pucciani and Ringressi (2012) evaluated the clinical usefulness of ARM in patients affected by obstructed defecation (OD). A total of 370 patients (287 women and 92 men) affected by OD were evaluated. After a preliminary clinical evaluation, defecography and ARM were performed. The results were compared with those from 20 healthy control subjects. Overall anal resting pressure was not significantly different between patients and controls. Maximal voluntary contraction (MVC) data were significantly lower when compared with those of controls. The straining test was considered positive in 143 patients. No significant difference was noted between patients and controls in maximal tolerated volume data. Patients had a significantly higher conscious rectal sensitivity threshold than controls. According to the authors, a positive straining test, low MVC and impaired rectal sensation are the main abnormalities detected in ARM in patients with OD.

Noviello et al. (2009) evaluated the role of anorectal manometry (ARM) in 85 children with severe constipation. The mean age was 5 years (range, 1-13). Based on the results of the study, the investigators concluded that ARM is a noninvasive diagnostic tool to study the mechanism of defecation in children with constipation in order to prescribe the appropriate treatment. According to the authors, this procedure can be used in every child, aged more than 1 year, with severe constipation and concluded that assessment of the recto-anal inhibitory reflex (RAIR) can select the cases for rectal suction biopsies (RSB).

~~Pucciani and Ringressi (2012) evaluated the clinical usefulness of ARM in patients affected by obstructed defecation (OD). A total of 379 patients (287 women and 92 men) affected by OD were evaluated. After a preliminary clinical evaluation, defecography and AM were performed. The results were compared with those from 20 healthy control subjects. Overall anal resting pressure was not significantly different between patients and controls. Maximal~~

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

voluntary contraction (MVC) data were significantly lower when compared with those of controls. The straining test was considered positive in 143 patients. No significant difference was noted between patients and controls in maximal tolerated volume data. Patients had a significantly higher conscious rectal sensitivity threshold than controls. According to the authors, a positive straining test, low MVC and impaired rectal sensation are the main abnormalities detected by AM in patients with OD.

In a retrospective analysis, Prichard et al. (2017) compared anorectal high-resolution manometry (HRM), magnetic resonance imaging (MRI), or balloon expulsion test (BET) for assessing rectal evacuation and structural abnormalities in women. Their analysis included 188 patients with constipation (n=51), fecal incontinence (n=48), or rectal prolapse (n=19), and 30 asymptomatic women serving as a control group. The authors used principal components analysis of HRM variables to identify rectoanal pressure patterns associated with rectal prolapse and phenotypes of patients with prolapse. They concluded that HRM alone and together with anorectal descent during evacuation, may identify rectal prolapse and large rectoceles, respectively, and also identify unique phenotypes of rectal prolapse.

Muñoz-Yagüe et al. (2003) evaluated the role of the clinical, ARM and surface electromyography in the assessment of patients with fecal incontinence. Ninety-three patients with fecal incontinence were reviewed and data was obtained from the clinical history, physical examination of the anal region, digital rectal examination, anorectal manometry and surface electromyography. Treatment was administered in accordance with the alterations encountered and the results evaluated at 3 and 12 months. The anorectal manometry (ARM) demonstrated some alterations in 90.3% of the patients, whereas a hypotonic sphincter was the most common finding (85.7%). Rectal sensitivity or distensibility alterations were present in the rest of the patients. In 79.2% of the cases, hypotonic sphincter was associated with rectal sensitivity or distensibility alterations. In 65.2% of patients with hypotonic external anal sphincter, damage of the pudendal nerve was found. According to the investigators, the clinical study of the patients, together with the anorectal manometry and surface electromyography enables the identification of the cause of FI and its treatment.

Heinrich et al. (2015) assessed conventional high resolution (HR) ARM findings with magnetic resonance (MR) defecography in the clinical assessment of 188 consecutive patients with symptoms of obstructive defecation defined by Rome III criteria. Sphincter function and pressure were measured during simulated defecation. Abnormal manometric findings were classified according to the Rao system and compared with MR defecography as the reference standard. The authors concluded that diagnostic agreement between anorectal HR ARM and MR defecography is high; pressure measurements accurately identify recto-anal dyssynergia and intra-anal outlet obstruction by structural pathology as causes of obstructive defecation.

In a systematic review and meta-analysis, Yeap et al. (2017) assessed the diagnostic accuracy of ARM for fecal incontinence. Seven studies were included out of an initial search of 1499 studies. The summary sensitivity and specificity for ARM as an overall test were 0.80 (95% confidence interval (CI): 0.69-0.88) and 0.80 (95% CI: 0.65-0.90), respectively. The diagnostic odds ratio (DOR) for ARM was found to be 16.61 (95% CI: 5.52-50.03). The positive likelihood ratio (PLR) and negative likelihood ratio (NLR) for ARM were found to be 4.09 (95% CI: 2.11-7.94) and 0.25 (95% CI: 0.14-0.42), respectively. Subgroup analysis based on four studies reporting on maximum resting pressure (MRP) demonstrated a sensitivity, specificity, DOR, PLR and NLR of 0.60 (95% CI: 0.38-0.79), 0.93 (95% CI: 0.80-0.97), 20.0 (95% CI: 4.00-91.00), 8.60 (95% CI: 3.00-24.30) and 0.43 (95% CI: 0.24-0.76), respectively. The authors concluded that ARM has been shown to be an accurate test for diagnosing FI, but suggest that further studies are required to establish the diagnostic accuracy of individual ARM measures.

Professional Societies

American Society of Colon and Rectal Surgeons (ASCRS)

In a practice guideline for the treatment of fecal incontinence, the ASCRS indicates that anorectal physiology studies (anal manometry) may be helpful in guiding management of fecal incontinence (Grade of Recommendation: Strong recommendation based on low- or very low-quality evidence) (Paquette et al., 2015).

In their updated clinical practice guideline for the evaluation and management of constipation, the ASCRS indicates that anorectal physiology and colon transit investigations may help identify the underlying etiology and are useful in patients with refractory constipation. This includes measurement of resting and squeeze pressures with anal

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

manometry, measurement of rectal volume sensation, testing of rectoanal inhibitory reflex, and balloon expulsion (strong recommendation based on low-quality evidence) (Paquette et al., 2016).

American Gastroenterological Association (AGA)

An AGA medical position statement on constipation states that anorectal manometry and a rectal balloon expulsion should be performed in patients who fail to respond to laxatives (strong recommendation, moderate-quality evidence) (Bharucha et al., 2013a).

American College of Gastroenterology (ACG)

In a clinical guideline on management of benign anorectal disorders, the ACG states that confidence in the diagnosis of a defecation disorder is increased if there is a combination of a clinical history of chronic constipation and two abnormal tests, e.g., impaired ability to evacuate a 50-ml water-filled balloon or abnormal defecography and evidence from pelvic floor EMG or ARM that the patient is unable to relax pelvic floor muscles or increase rectal pressure during simulated defecation (strong recommendation, moderate quality of evidence) (Wald et al., 2014).

Conventional Defecography

Grossi et al. (2018) conducted a systematic review and meta-analysis to evaluate rates of structural and functional abnormalities diagnosed by barium defecography and/or magnetic resonance imaging defecography (MRID) in patients with symptoms of chronic constipation and in healthy volunteers. From a total of 1760 records identified, 175 full-text articles were assessed for eligibility. Sixty-three studies were included, providing data on outcomes of 7519 barium defecographies and 668 MRIDs in patients with CC, and 225 barium defecographies and 50 MRIDs in healthy volunteers. Pathological high-grade (Oxford III and IV) intussuscepta and large (>4 cm) rectoceles were diagnosed in 23.7% (95% CI: 16.8-31.4) and 15.9% (10.4-22.2) of patients, respectively. Enterocoele and perineal descent were observed in 16.8% (12.7-21.4) and 44.4% (36.2-52.7) of patients, respectively. Barium defecography detected more intussuscepta than MRID (OR: 1.52 [1.12-2.14]; P = 0.009). Normative data for both barium defecography and MRID structural and functional parameters were limited, particularly for MRID (only one eligible study). The authors concluded that since structural abnormalities cannot be evaluated using non-imaging test modalities (balloon expulsion and anorectal manometry), defecography should be considered the first-line diagnostic test.

Rafiei et al. (2017) evaluated the findings of defecography in 100 patients with severe idiopathic chronic constipation. An analysis of radiographs was performed for the diagnosis of descending perineum syndrome, rectocoele, enterocoele, rectal ulcer, rectal prolapse, fecal residue of post defecation, or other diagnosis and compared between the two sexes. Normal defecography was only observed in two participants. Descending perineum syndrome was the most common abnormality (73.3%). The results showed that rectocoele (80.8%) and descending perineum syndrome (69.2%) were most frequent in women. In males, descending perineum syndrome and rectal prolapse were more prevalent (87% and 43.5%, respectively). Compared with men, rectocoele and rectal ulcer were more frequently observed in women (p<0.001, and p=0.04, respectively), while men were more affected by descending perineum syndrome (p=0.04). In total, women had a greater incidence of abnormal defecographic findings compared with men (p=0.02). The authors concluded that defecography can be performed to detect anatomic abnormalities in patients with severe idiopathic chronic constipation, and abnormal balloon expulsion test. This technique can assist physicians in making the most suitable decision for a surgical procedure.

Fabrizio et al. (2017) observed that as obstructed defecation is a complex disorder it requires a multimodal evaluation process. Testing done to elicit a diagnosis can incorporate defecography, proctoscopy, colonic transit time studies, anorectal manometry, a rectal balloon expulsion test, electromyography, and ultrasound. They advise that results from these studies be taken in the context of each patient's clinical situation.

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Professional Societies

American Gastroenterological Association (AGA)

An AGA guideline on constipation states that defecography should not be performed before anorectal manometry and a rectal balloon expulsion test (strong recommendation, low-quality evidence). Defecography should be considered when results of anorectal manometry and rectal balloon expulsion are inconclusive for defecatory disorders (strong recommendation, low-quality evidence) (Bharucha et al., 2013a).

According to the AGA's Technical Review on Constipation, defecography is particularly useful when the results of anorectal testing are inconsistent with the clinical impression and/or to identify anatomic abnormalities. The most relevant findings in defecatory disorders include inadequate (spastic disorder) or excessive (flaccid perineum, descending perineum syndrome) widening of the anorectal angle and/or perineal descent during defecation. Excessive straining, internal intussusception, solitary rectal ulcers, rectoceles, and rectal prolapse may also be observed. If the vagina and small intestine are opacified, enteroceles as well as bladder and uterovaginal prolapse can also be visualized (Bharucha et al., 2013b).

American Society of Colon and Rectal Surgeons (ASCRS)

In an updated clinical practice guideline on the evaluation and management of constipation, the ASCRS (Paquette et al., 2016) states that if anorectal physiology testing is not diagnostic for defecation dysfunction, other imaging studies, such as defecography, can be useful to identify anatomic abnormalities, such as rectocele, enterocele, internal intussusception, or prolapse that may be associated with constipation. Imaging with cinedefecography, MRI defecography, or transperineal ultrasound echo defecography may be useful in identifying anatomical abnormalities associated with obstructive defecation (Grade of Recommendation: strong recommendation based on low-quality evidence, 1C).

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 balloon expulsion testing 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).

Colonic Motility Testing or Colonic Manometry

Currently there is insufficient evidence regarding the effectiveness of colon manometry or colonic motility. Patient selection criteria and the role of colonic manometry in the management of refractory constipation must be better defined in statistically robust, well-designed clinical trials.

In a consensus document on anorectal and colonic manometry in children (based on a systematic review of the evidence), the American Neurogastroenterology and Motility Society (ANMS) and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) state that colon manometry is deemed useful to differentiate children with functional constipation from those with a colonic motor disorder, such as colonic inertia; surgical intervention planning, and to assess the improvement of colonic motility after long term use of ACE. The authors add that colonic manometry in combination with ARM has emerged as an important tool in understanding the pathophysiology and guiding the management of persistent postoperative symptoms of patients with Hirschsprung's disease and anorectal malformations, such as imperforate anus (Rodriguez et al., 2016).

Singh et al. (2013) investigated whether colonic manometric evaluation is useful for characterizing colonic sensorimotor dysfunction and for guiding therapy in slow transit constipation (STC). Twenty-four hour ambulatory colonic manometry was performed in 80 patients with STC by placing a six sensor solid-state probe, along with assessment of colonic sensation with barostat. Anorectal manometry was also performed. Manometrically, patients were categorized as having colonic neuropathy or myopathy based on gastrocolonic response, waking response and high amplitude propagated contractions (HAPC); and based on colonic sensation, as colonic hyposensitivity or hypersensitivity. Clinical response to pharmacological, biofeedback, and surgical treatment was assessed at 1 year and correlated with manometric findings. Forty seven (59%) patients who had abnormal colonic manometry, with

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

features suggestive of neuropathy (26%), and myopathy (33%); 41% had normal colonic manometry. Seventy-four percent of the patients had abnormal colonic sensation and 61% had overlapping dyssynergic defecation. Patients with neuropathy were more likely to have colonic hyposensitivity. Sixty-four percent of patients with colonic myopathy or normal manometry improved with medical/biofeedback therapy when compared to 15% with colonic neuropathy. Selected patients with colonic neuropathy had excellent response to surgery, but many developed bacterial overgrowth. The authors concluded that colonic manometry demonstrates significant colonic sensorimotor dysfunction in STC patients and reveals considerable pathophysiological heterogeneity. According to the authors, colonic manometry can be useful for characterizing the underlying pathophysiology and for guiding clinical management in STC, especially surgery. The study is limited due to a lack of a controlled comparator group or reference standard diagnostic test.

Giorgio et al. (2013) correlated neuromuscular histological phenotypes in pediatric STC with colonic manometric phenotypes using high-resolution manometry (HRM) and tested the hypothesis that failure of motor quiescence (FQ) between bisacodyl-induced high amplitude propagating sequences (HAPSs) might predict neuromuscular pathology. Eighteen children (10 males, median age: 7.5 years) with refractory STC underwent stationary colonic HRM before segmental colonic resection. Six age-matched constipated children with normal colonic transit served as controls. Conventional manometric parameters and area under the curve (AUC) during a 1-minute period following bisacodyl-induced HAPSs [PBAUC(1)], as measure of FQ, were calculated. In segments with HAPS, PBAUC(1) was predictive of colonic neuropathy (Sensitivity 100%, specificity 86%, PPV92%, NPV100%). Based on the results of the study, the authors concluded that PBAUC(1) is increased in multiple colonic segments in neuropathic pediatric STC and constitutes a sensitive and specific biomarker of neuropathy. The small study population limits the validity of the conclusion of this study.

Sood et al. (2012) evaluated the variability in interpretation of colon manometry in children. Fifty-seven colon motility studies were independently reviewed by five observers. Each observer was required to report on the colonic motility during fasting, after administration of a meal and after bisacodyl stimulation. They were also asked to comment whether colon manometry study was normal or abnormal and if in their opinion the postprandial recording provided clinically useful information. The median (range) agreement regarding the presence of high amplitude propagating contractions (HAPC) was 83% (80% to 92%). The interpretation of gastrocolonic response produced the most inconsistent results with median (range) agreement of 64% (53% to 95%). The post-prandial period was reported to be useful in only 3% to 24% of the studies. The median (range) agreement regarding the overall interpretation of the study being either normal or abnormal was 87% (83% to 90%). According to the authors, the most easily recognizable contraction pattern during colon manometry is the HAPC. Visual interpretation of the gastrocolonic response produces the most inconsistent results and maximum variability. The authors concluded that abbreviated colon manometry studies without the post-prandial period or routine calculation of the motility index to evaluate gastrocolonic response can help make colon manometries more objective and reliable. Further studies to evaluate colon manometry are needed to determine the validity of this test.

Tipnis et al. (2012) compared oro-anal transit time (OTT) measured by radio-opaque markers with colon motility (CM) findings in children with chronic constipation and assessed clinical outcomes in 24 children with chronic constipation evaluated by OTT and CM studies. Patients were studied for a median of 23 months and outcomes reviewed. According to the authors, OTT studies may be helpful to predict which children should be referred for CM studies. Normal OTT studies may predict normal colon manometry; however, abnormal OTT studies may not predict abnormalities in colonic manometry in children with chronic constipation. The authors concluded that patients with slow transit marker studies should be assessed by colon manometry to evaluate colon neuromuscular integrity. This study did not evaluate the impact of colon manometry for patient management or disease outcomes.

Rao et al. (2004b) evaluated whether colonic manometry is reproducible in a study that included 7 healthy volunteers (three men, four women, mean age = 34 years). Study participants underwent two studies of 24-hour ambulatory colonic manometry, each 2 weeks apart. Paired t-test was used to examine the reproducibility and variability. The number of pressure waves and propagating pressure waves and high-amplitude propagating contractions (HAPC), and

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

area-under-curve (AUC) were similar between the two studies. Diurnal variation, waking, and meal-induced gastrocolonic responses were also reproducible. There was some variability in the incidence of individual colonic motor patterns. The investigators concluded that colonic manometry findings were generally reproducible, particularly for the assessment of key physiologic changes such as meal-induced gastrocolonic, HAPC, and waking responses. Further research is needed to determine the clinical relevance of these findings.

Rao et al. (2004) studied prolonged colonic motility with colon manometry and assessed its clinical significance in 21 patients with slow-transit constipation and 20 healthy controls by placing a 6-sensor solid-state probe up to the hepatic flexure. The study results indicated that patients with slow-transit constipation exhibited either normal or decreased pressure activity with manometric features suggestive of colonic neuropathy or myopathy. According to the investigators, in refractory patients, colonic manometry may be useful in characterizing the underlying pathophysiology and in guiding therapy. **Due to the limitations of this study, these findings and the clinical utility of the test** require confirmation ~~in a larger study.~~

Pensabene et al. (2003) evaluated the impact of colonic manometry in clarifying pathophysiology of childhood defecatory disorders and evaluated its impact on management in a retrospective review of 145 children. After colonic manometry, treatment changes were recommended in 93% of patients. Changes in medical treatment were suggested for 121 patients (81%). Surgical treatment (cecostomy, subtotal or total colectomy, myectomy) was suggested for 102 (68%), mostly in addition to the changes in medical treatment or recommended in case the medical treatment had failed. Surgery was the only recommendation for 18 children. Follow up was done in 65% of the families. When recommendations were followed (96% of the contacted patients), the symptoms improved in 78%, were unchanged in 18%, and were worse in 4% of patients. Among the parents, 88% believed that the suggestions given after colonic manometry had been helpful in improving their children's health. According to the authors, the study limitations include the shortcomings of a retrospective study. In addition, the duration of follow-up was variable, there was no control group, and only two thirds of the families were contacted for follow up.

~~Sood et al. (2012) evaluated the variability in interpretation of colon manometry in children. Fifty seven colon motility studies were independently reviewed by five observers. Each observer was required to report on the colonic motility during fasting, after administration of a meal and after bisacodyl stimulation. They were also asked to comment whether colon manometry study was normal or abnormal and if in their opinion the postprandial recording provided clinically useful information. The median (range) agreement regarding the presence of high amplitude propagating contractions (HAPC) was 83% (80% to 92%). The interpretation of gastrocolonic response produced the most inconsistent results with median (range) agreement of 64% (53% to 95%). The post prandial period was reported to be useful in only 3% to 24% of the studies. The median (range) agreement regarding the overall interpretation of the study being either normal or abnormal was 87% (83% to 90%). According to the authors, the most easily recognizable contraction pattern during colon manometry is the HAPC. Visual interpretation of the gastrocolonic response produces the most inconsistent results and maximum variability. The authors concluded that abbreviated colon manometry studies without the post prandial period or routine calculation of the motility index to evaluate gastrocolonic response can help make colon manometries more objective and reliable. Further studies to evaluate colon manometry are needed to determine the validity of this test.~~

~~Tipnis et al. (2012) compared oro-anal transit time (OTT) measured by radio-opaque markers with colon motility (CM) findings in children with chronic constipation and assessed clinical outcomes in 24 children with chronic constipation evaluated by OTT and CM studies. Patients were studied for a median of 23 months and outcomes reviewed. According to the authors, OTT studies may be helpful to predict which children should be referred for CM studies. Normal OTT studies may predict normal colon manometry; however, abnormal OTT studies may not predict abnormalities in colonic manometry in children with chronic constipation. The authors concluded that patients with slow transit marker studies should be assessed by colon manometry to evaluate colon neuromuscular integrity. This study did not evaluate the impact of colon manometry for patient management or disease outcomes.~~

~~Wiklendt et al. (2013) evaluated an automated analysis technique of colonic manometry data that was developed to differentiate the motor patterns of 17 patients with STC from those recorded in 14 healthy controls. According to the authors, manual analysis of data acquired from manometric studies of colonic motility is laborious, subject to laboratory bias and not specific enough to differentiate all patients from control subjects. The authors found that~~

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

~~automated analysis of colonic manometry data using cross-correlation separated all patients from controls. This study is limited by a small sample size.~~

~~According to Sharma and Rao (2017), the advent of high resolution colonic manometry allows for the improved identification of colonic motor patterns and may provide further insight into pathophysiological mechanisms. In a minority of cases of STC, identification of colonic neuropathy suggests a medically refractory condition, warranting consideration of colectomy. The pathophysiology of IBS with constipation (IBS-C) is poorly understood with multiple etiological factors implicated.~~

Professional Societies

American Gastroenterological Association (AGA)

An AGA guideline on constipation states that colonic intraluminal testing (manometry, barostat) should be considered to document colonic motor dysfunction before colectomy (weak recommendation, moderate-quality evidence). A weak recommendation implies that benefits, risks, and the burden of intervention are more closely balanced, or appreciable uncertainty exists in regards to patient's values and preferences (Bharucha et al., 2013a).

According to the AGA's *Technical Review on Constipation*, colonic manometry or barostat-manometric testing should be considered in patients with medically refractory STC. However, these tests are only available in highly specialized centers with a research interest and their role in management is not well established. Colonic manometry may identify a subset of patients with STC colonic motor dysfunctions that may be explained by a marked reduction in colonic intrinsic nerves and interstitial cells of Cajal. This should prompt consideration of colonic resection in medically refractory patients who do not have pelvic floor dysfunction (Bharucha et al., 2013b).

American Neurogastroenterology and Motility Society (ANMS) and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)

In a consensus document on anorectal and colonic manometry in children (based on a systematic review of the evidence), the American Neurogastroenterology and Motility Society (ANMS) and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) state that colon manometry is deemed useful to differentiate children with functional constipation from those with a colonic motor disorder, such as colonic inertia, surgical intervention planning, and to assess the improvement of colonic motility after long-term use of ACE. The authors add that colonic manometry in combination with ARM has emerged as an important tool in understanding the pathophysiology and guiding the management of persistent postoperative symptoms of patients with Hirschsprung's disease and anorectal malformations, such as imperforate anus (Rodriguez et al., 2017).

Conventional Defecography

Grossi et al. (2018) conducted a systematic review and meta-analysis to evaluate rates of structural and functional abnormalities diagnosed by barium defecography and/or magnetic resonance imaging defecography (MRID) in patients with symptoms of chronic constipation and in healthy volunteers. From a total of 1760 records identified, 175 full-text articles were assessed for eligibility. Sixty-three studies were included, providing data on outcomes of 7519 barium defecographies and 668 MRIDs in patients with CC, and 225 barium defecographies and 50 MRIDs in healthy volunteers. Pathological high-grade (Oxford III and IV) intussuscepta and large (>4 cm) rectoceles were diagnosed in 23.7% (95% CI: 16.8-31.4) and 15.9% (10.4-22.2) of patients, respectively. Enterocele and perineal descent were observed in 16.8% (12.7-21.4) and 44.4% (36.2-52.7) of patients, respectively. Barium defecography detected more intussuscepta than MRID (OR: 1.52 [1.12-2.14]; P = 0.009). Normative data for both barium defecography and MRID structural and functional parameters were limited, particularly for MRID (only one eligible study). The authors concluded that since structural abnormalities cannot be evaluated using non-imaging test modalities (balloon expulsion and anorectal manometry), defecography should be considered the first-line diagnostic test.

Rafiei et al. (2017) evaluated the findings of defecography in 100 patients with severe idiopathic chronic constipation. An analysis of radiographs was performed for the diagnosis of descending perineum syndrome, rectocele, enterocele, rectal ulcer, rectal prolapse, fecal residue of post-defecation, or other diagnosis and compared between the two sexes. Normal defecography was only observed in two participants. Descending perineum syndrome was the most common abnormality (73.3%). The results showed that rectocele (80.8%) and descending perineum syndrome (69.2%) were most frequent in women. In males, descending perineum syndrome and rectal prolapse were more prevalent (87%

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

and 43.5%, respectively). Compared with men, rectocele and rectal ulcer were more frequently observed in women ($p < 0.001$, and $p = 0.04$, respectively), while men were more affected by descending perineum syndrome ($p = 0.04$). In total, women had a greater incidence of abnormal defecographic findings compared with men ($p = 0.02$). The authors concluded that defecography can be performed to detect anatomic abnormalities in patients with severe idiopathic chronic constipation, and abnormal balloon expulsion test. This technique can assist physicians in making the most suitable decision for a surgical procedure.

Fabrizio et al. (2017) observed that as obstructed defecation is a complex disorder it requires a multimodal evaluation process. Testing done to elicit a diagnosis can incorporate defecography, proctoscopy, colonic transit time studies, anorectal manometry, a rectal balloon expulsion test, electromyography, and ultrasound. They advise that results from these studies be taken in the context of each patient's clinical situation.

Professional Societies

American Gastroenterological Association (AGA)

An AGA guideline on constipation states that defecography should not be performed before anorectal manometry and a rectal balloon expulsion test (strong recommendation, low quality evidence). Defecography should be considered when results of anorectal manometry and rectal balloon expulsion are inconclusive for defecatory disorders (strong recommendation, low quality evidence) (Bharucha et al., 2013a).

According to the AGA's *Technical Review on Constipation*, defecography is particularly useful when the results of anorectal testing are inconsistent with the clinical impression and/or to identify anatomic abnormalities. The most relevant findings in defecatory disorders include inadequate (spastic disorder) or excessive (flaccid perineum, descending perineum syndrome) widening of the anorectal angle and/or perineal descent during defecation. Excessive straining, internal intussusception, solitary rectal ulcers, rectoceles, and rectal prolapse may also be observed. If the vagina and small intestine are opacified, enteroceles as well as bladder and uterovaginal prolapse can also be visualized (Bharucha et al., 2013b).

American College of Gastroenterology (ACG)

The ACG practice guideline on fecal incontinence states that conventional defecography is useful in patients with suspected rectal prolapse or in those with poor rectal evacuation, but it is otherwise of limited value (Rao, 2004a).

American Society of Colon and Rectal Surgeons (ASCRS)

In an updated clinical practice guideline on the evaluation and management of constipation, the ASCRS (Paquette et al., 2016) states that if anorectal physiology testing is not diagnostic for defecation dysfunction, other imaging studies, such as defecography, can be useful to identify anatomic abnormalities, such as rectocele, enterocele, internal intussusception, or prolapse that may be associated with constipation. Imaging with cinedefecography, MRI defecography, or transperineal ultrasound echo defecography may be useful in identifying anatomical abnormalities associated with obstructive defecation (Grade of Recommendation: strong recommendation based on low quality evidence, 1C).

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 balloon expulsion testing 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).

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.

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

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Score (WIS), and modified Obstructed Defecation Symptom (ODS) Score. 302 MRI proctograms were performed. (n=170). Patients with a rectocele > 2 cm (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 retrospective study, Poncelet et al. (2017) compared X-ray (conventional) defecography with magnetic resonance (MR) defecography in 503 women (average age 65.5 years) with a clinical suspicion of posterior compartment dysfunction. The results of the combination of X-ray defecography and MR defecography were used as the standard of reference. Differences in sensitivities between X-ray defecography and MR defecography were compared using the McNemar test. The sensitivities of X-ray defecography were 90.9% for the diagnosis of peritoneocele, 71.4% for rectocele, 81.1% for rectal prolapse and 63.6% for anismus. The sensitivities of MR defecography for the same diagnoses were 86.4%, 78.6%, 62.2% and 63.6%, respectively. For all these pathologies, no significant differences between X-ray defecography and MR defecography were found. In this clinical scenario, the authors concluded that dynamic MR defecography is equivalent to X-ray defecography for the diagnosis of abnormalities of the posterior compartment of the pelvic floor. Randomized controlled trials with larger patient populations are needed to further evaluate MR defecography in this clinical scenario.

Zafar et al. (2017) conducted a prospective comparative study of magnetic resonance defecography (MRD) and evacuation proctography (EP) in the evaluation of obstructed defecation. Fifty-five patients underwent both MRD and EP. The results showed that although MRD provides a global assessment of pelvic floor function and anatomical abnormality, it is not as sensitive as EP in detecting trapping rectoceles and intussusceptions. **Well-designed RCTs with larger patient populations are needed to further evaluate MRD in comparison to other diagnostic modalities.**

~~Martin-Martin et al. (2017) conducted a prospective cohort test to evaluate the diagnostic accuracy of MRD in comparison to videodefecography in the evaluation of 40 patients with obstructed defecation syndrome. The degree of agreement between the two tests was almost perfect for anismus ($\kappa = 0.88$) and rectal prolapse ($\kappa = 0.83$), substantial for enterocele ($\kappa = 0.80$) and rectocele grade III ($\kappa = 0.65$), moderate for intussusception ($\kappa = 0.50$) and rectocele grade II ($\kappa = 0.49$), and slight for rectocele grade I ($\kappa = 0.30$) and excessive perineal descent ($\kappa = 0.22$). Eighteen cystoceles and 11 colpoceles were diagnosed only by MRD. Findings of this study need to be validated by well-designed studies with larger sample sizes.~~

van Iersel et al. (2017) compared dynamic MRD with conventional defecography (CD) in 45 patients with symptoms of prolapse of the posterior compartment of the pelvic floor. Patients underwent both procedures. Outcome measures were the presence or absence of rectocele, enterocele, intussusception, rectal prolapse and the descent of the anorectal junction on straining, measured in millimeters. Cohen's Kappa, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and the positive and negative likelihood ratio of D-MRI were compared with CD. Cohen's Kappa and Pearson's correlation coefficient were calculated and regression analysis was performed to determine inter-observer agreement. The results showed that accuracy of dynamic MRD for diagnosing rectocele and enterocele is less than that of CD. However, dynamic MRD appears superior to CD in identifying intussusception. The authors concluded that dynamic MRD and CD are complementary imaging techniques in the evaluation of patients with symptoms of prolapse of the posterior compartment. **Additional well-designed studies with larger patient populations are needed to further evaluate MRD.**

~~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~~

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

~~clinical examination findings for any outcome except enterocele, where MRD had a higher detection rate. Based on their review, 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.~~

In a systematic review and meta-analysis of magnetic resonance defecography (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 fared 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.

~~In a review of diagnosis and treatment of dyssynergic defecation, Rao and Patcharatrakul (2016) concluded that although MR defecography can provide an excellent resolution of anal sphincters, levator ani muscles and soft tissue surrounding the rectum without radiation exposure, limitations include its high cost, lack of availability, and possible low sensitivity to detect rectal intussusception because it is more difficult to evacuate the contrast compared to barium defecography.~~

Foti et al. (2013) prospectively compared the diagnostic capabilities of magnetic resonance imaging (MRI) with conventional defecography (CD) in outlet obstruction syndrome in 19 patients. Comparison between CD and MRI with evacuation phase (MRWEP) showed no significant differences in sphincter hypotonia, dyssynergia, rectocele or rectal prolapse and significant differences in descending perineum. Comparison between CD and MRI without evacuation phase (MRWOEP) showed no significant differences in sphincter hypotonia, dyssynergia or enterocele but significant differences in rectocele, rectal prolapse and descending perineum. Comparison between MRWEP and MRWOEP showed no significant differences in sphincter hypotonia, dyssynergia, enterocele or descending perineum but significant differences in rectocele, rectal prolapse, peritoneocele, cervical cystoptosis and hysteroptosis. The authors concluded that MRI provides morphological and functional study of pelvic floor structures and may offer an imaging tool complementary to CD in multicompartiment evaluation of the pelvis. The findings of this study need to be validated by well-designed studies with larger sample sizes.

Vitton et al. (2011) compared the accuracy of dynamic anorectal endosonography and dynamic MRI defecography with conventional defecography as the criterion standard in the diagnosis of pelvic floor disorders. The study was a prospective crossover design in which 56 patients with dyschezia underwent each procedure in random order by 3 blinded operators within the same month. No significant differences were observed between dynamic anorectal endosonography and dynamic MRI in the number of patients with rectocele, perineal descent, or enterocele. Diagnostic concordance with conventional defecography as the standard did not differ significantly between dynamic MRI and dynamic anorectal endosonography: concordance rates for dynamic MRI were 82% for rectocele, 57% for perineal descent, 93% for enterocele, and 55% for rectal intussusception. Significantly more internal anal sphincter defects were found with dynamic anorectal endosonography than with dynamic MRI defecography. Patient tolerance was significantly better for dynamic anorectal endosonography than for dynamic MRI or conventional defecography.

Cappabianca et al. (2011) compared the diagnostic efficacy of dynamic MR defecography (MR-D) with entero-colpocysto-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.

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Reiner et al. (2011) evaluated the diagnostic value of MR defecography in 48 patients referred with suspicion of dyssynergic defecation. Patients were divided into patients with dyssynergic defecation (n=18) and constipated patients without dyssynergic defecation (control group, n=30). The most frequent finding was impaired evacuation, which was seen in 100% of patients with dyssynergic defecation and in 83% of the control group, yielding a sensitivity for MR defecography for the diagnosis of dyssynergic defecation of 100% but a specificity of only 23%.

Otto et al. (2011) assessed the correlation of conventional defecography and MR-defecography after rectopexy in 21 patients. According to the authors, both methods revealed consistent results with respect to anorectal angle and perineal motility. The authors also stated that the concomitant depiction of structures in MR-defecography is helpful in the assessment of descent of pelvic organs and permits visualization of enteroceles. However, in 30% of patients, MR-defecography wrongly showed incomplete evacuation.

Professional Societies

American Gastroenterological Association (AGA)

The AGA guideline on constipation states that although anorectal manometry and a rectal balloon expulsion test 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 practice guidelines on fecal incontinence (Rao, 2004a) noted that MR defecography may more precisely define the anorectal anatomy, but comparative studies are needed to determine clinical utility and how this test would influence treatment decisions.~~

The ACG clinical guideline for management of benign anorectal disorders notes that barium or magnetic resonance defecography 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 anorectal manometry and balloon expulsion test are equivocal (moderate recommendation, moderate quality of evidence) (Wald et al., 2014).

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.

American Society of Colon and Rectal Surgeons (ASCRS)

In an updated clinical practice guideline on the evaluation and management of constipation, the ASCRS (Paquette et al., 2016) states that if anorectal physiology testing is not diagnostic for defecation dysfunction, other imaging studies, such as defecography, can be useful to identify anatomic abnormalities, such as rectocele, enterocele, internal intussusception, or prolapse that may be associated with constipation. Imaging with cinedefecography, MRI defecography, or transperineal ultrasound echo defecography may be useful in identifying anatomical abnormalities associated with obstructive defecation (Grade of Recommendation: strong recommendation based on low-quality evidence, 1C).

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 balloon expulsion testing 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) or Electroenterography

~~**Despite a possible use in clinical research, the studies of electrogastrography 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**~~

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

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 found to indicate electroenterography has a positive impact on patient management or disease outcome.

Gharibans et al. (2019) performed a case-control study of cutaneous high resolution electrogastrography (HR-EGG) in 32 subjects to evaluate associations between gastric myoelectric abnormalities, symptoms (based on a validated questionnaire), and gastric emptying. The study consisted of 7 healthy individuals (control), 7 subjects with functional dyspepsia and normal gastric emptying, and 18 subjects with gastroparesis. All subjects were assessed by CT imaging of the abdomen and HR-EGG and completed the PGI-SYM questionnaire on foregut symptoms, which includes the gastroparesis cardinal symptom index. The authors found abnormal spatial parameters, detected by cutaneous HR-EGG, correlated with severity of upper gastrointestinal symptoms, regardless of gastric emptying. Despite mixed results (slow-wave abnormalities were detected in only 44% of subjects with foregut symptoms), they concluded this noninvasive, repeatable approach might be useful to identify patients for whom gastric myoelectric dysfunction contributes to functional dyspepsia and gastroparesis. Limitations of the study included small sample size, CT imaging not performed at time of electrode placement and the gastric emptying test not performed at time of HR-EGG.

Kayar et al. (2016⁷) utilized transcutaneous EGG to compare patients with functional dyspepsia (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, reliable, 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.

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 2 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 doesn't support the use of EGG in clinical practice or beyond its use for research.**

O'Grady et al. (2012) applied high-resolution electrical mapping to quantify and classify gastroparesis slow-wave abnormalities in spatiotemporal detail. Serosal high-resolution mapping was performed using flexible arrays at stimulator implantation in 12 patients with diabetic or idiopathic gastroparesis. The authors found that intraoperative 256 electrode serosal recordings in gastroparetics revealed abnormal slow wave initiation, reduced velocities, conduction blocks, and increased amplitudes undetectable on cutaneous recordings. According to the authors, this reflects relative insensitivity of clinical EGG methodologies.

Lin et al. (2010) investigated the association between the status of interstitial cells of Cajal (ICC) and electrogastrogram (EGG) parameters, gastric emptying, and symptoms in a cohort of patients with gastroparesis. Forty-one patients with refractory gastroparesis who were referred for gastric electrical stimulation (GES) underwent full thickness gastric (antrum) biopsy during the surgery to place the GES device. The biopsy samples were stained with c-kit and scored for the presence of ICC based on criteria obtained from 10 controls. All patients underwent EGG recordings, a 4-hour standardized scintigraphic gastric emptying study and symptom assessment prior to the surgery. According to the investigators, the study suggested that the EGG may have a role for predicting ICC status during clinical evaluation of gastroparetic patients. However, this study failed to show how EGG would impact patient management or disease outcomes.

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Sha et al. (2009) evaluated 31 patients with functional dyspepsia who were assessed for severity of upper gastrointestinal symptoms with EGG and antroduodenal manometry. The EGG was abnormal in 71.0% of patients. Antral motility was abnormal in 80.6% of patients and duodenal motility was abnormal in 74.2% of patients. No one-to-one correlation was noted between the symptom scores and any of the EGG or motility parameters. The investigators concluded that more than two-thirds of patients with functional dyspepsia have abnormalities in the EGG and antral/duodenal motility. The sensitivity of these 2 different methods is essentially the same. EGG and antroduodenal manometry can complement each other in demonstrating gastric motor dysfunction in patients with functional dyspepsia. These findings require confirmation in a larger study.

Frasko et al. (2008) conducted a prospective study to characterize the disturbance of gastric electrical control activity in different types of ileus and to correlate surface electrogastrography (EGG) findings with a set of inflammatory markers. Fifty-four adult patients with mechanic, vascular and paralytic ileus proven on clinical and radiological exams and 14 age- and sex-matched controls were examined. Irregular EGG activity without a dominant frequency or bradygastria was seen in all patients with both vascular and paralytic ileus and in 67.86% of the patients with obstructive ileus. According to the investigators, EGG examination confirmed a high sensitivity in the evaluation of gastric electrical control activity in both vascular and paralytic ileus. This study failed to show how EGG would impact patient management or disease outcomes.

~~Chen et al. (2005) assessed the gastric myoelectrical functioning in 20 patients with Parkinson's disease (PD) and in 11 healthy controls by using EGG and determined the clinical utility of EGG in differentiating PD patients with or without upper gastrointestinal symptoms. The PD patients were stratified into two subgroups: 9 were assessed as PD without upper gastrointestinal symptoms (group A) and 11 as PD with upper gastrointestinal symptoms (group B). The investigators concluded that gastric myoelectrical activity is impaired in both groups of PD patients and that EGG appears to have a limited, if any, clinical utility in the differentiation of PD patients with or without upper gastrointestinal symptoms.~~

~~Bentur et al. (2006) investigated EGG abnormalities in 23 cystic fibrosis (CF) patients and examined whether EGG correlates with gastric emptying as assessed by scintigraphy. Pre- and postprandial EGG indexes were compared to 19 healthy control patients. Gastric emptying was assessed simultaneously by gastric scintigraphy in 11 of the 23 CF patients. Abnormal patterns of EGG were found in 78.3% of CF patients compared to 31.3% of controls during fasting and in 56.5% of CF patients compared to 15.7% in healthy controls postprandially. Gastric emptying results on scintigraphy were in agreement with EGG results in 9 of 11 (two normal and seven pathological). Five of the six patients treated with cisapride (83.3%) showed significant improvement in EGG indexes. According to the investigators, the similar rate of EGG and gastric scintigraphy abnormalities suggests that EGG may be a useful clinical tool in CF patients. This study is limited by a small sample size.~~

~~Sha et al. (2009) evaluated 31 patients with functional dyspepsia who were assessed for severity of upper gastrointestinal symptoms with EGG and antroduodenal manometry. The EGG was abnormal in 71.0% of patients. Antral motility was abnormal in 80.6% of patients and duodenal motility was abnormal in 74.2% of patients. No one-to-one correlation was noted between the symptom scores and any of the EGG or motility parameters. The investigators concluded that more than two-thirds of patients with functional dyspepsia have abnormalities in the EGG and antral/duodenal motility. The sensitivity of these 2 different methods is essentially the same. EGG and antroduodenal manometry can complement each other in demonstrating gastric motor dysfunction in patients with functional dyspepsia. These findings require confirmation in a larger study.~~

~~Lin et al. (2010) investigated the association between the status of interstitial cells of Cajal (ICC) and electrogastrogram (EGG) parameters, gastric emptying, and symptoms in a cohort of patients with gastroparesis. Forty-one patients with refractory gastroparesis who were referred for gastric electrical stimulation (GES) underwent full thickness gastric (antrum) biopsy during the surgery to place the GES device. The biopsy samples were stained with c-kit and scored for the presence of ICC based on criteria obtained from 10 controls. All patients underwent EGG recordings, a 4 hour standardized scintigraphic gastric emptying study and symptom assessment prior to the surgery. According to the investigators, the study suggested that the EGG may have a role for predicting ICC status during~~

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

~~clinical evaluation of gastroparetic patients. However, this study failed to show how EGG would impact patient management or disease outcomes.~~

Professional Societies

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. Gastric electric stimulation is an emerging therapy for refractory gastroparesis and further studies are needed to better evaluate the efficacy of gastric electric stimulation.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Instruments to perform cutaneous electrogastrography are regulated by the FDA as Class II devices. See the following website for more information (use product code MYE or FFX):

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>. (Accessed February 17~~2~~, 20~~20~~19)

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. See the following website for more information:

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfhde/hde.cfm?id=376493>. (Accessed February 17~~2~~, 20~~20~~19)

An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market. The labeling must state that the effectiveness of the device for the specific indication has not been demonstrated.

HDE is a special regulatory marketing approval that makes the device available on a limited basis provided that: (1) The device is to be used to treat or diagnose a disease or condition that affects fewer than 4,000 individuals in the United States; (2) the device would not be available to a person with such a disease or condition unless the exemption is granted; (3) no comparable device (other than a device that has been granted such an exemption) is available to treat or diagnose the disease or condition; and (4) the device will not expose patients to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

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 February 17~~2~~, 20~~20~~19)

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Several radiopaque markers have been approved by the FDA for colonic transit testing. See the following website for more information (use product code FFX): <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>. (Accessed February 17, 2019)

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 web page: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>. (Accessed February 17, 2019)

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for gastric electrical stimulation (GES) therapy. Local Coverage Determinations (LCDs) do not exist at this time.

Medicare does not have an NCD for defecography or for colonic manometry. LCDs do not exist at this time.

Medicare does not have an NCD for anorectal manometry. LCDs exist; see the LCDs for Anorectal Manometry, Anal Electromyography, and Biofeedback Training for Perineal Muscles and Anorectal or Urethral Sphincters, Anorectal Manometry and Electromyography (EMG) of the Urinary and Anal Sphincters and Pelvic Floor Dysfunction: Anorectal Manometry and EMG.

Medicare does not have an NCD for cutaneous, mucous, or serosal electrogastrography or electroenterography. LCDs exist; see the LCDs for Non-Covered Services and Noncovered Services other than CPT® Category III Noncovered Services.

(Accessed March 19, 2020) Medicare does not have a National Coverage Determination (NCD) for gastric electrical stimulation (GES) therapy. Local Coverage Determinations (LCDs) do not exist at this time.

~~Medicare does not have an NCD for rectal manometry and rectal sensation, tone and compliance test. LCDs do not exist at this time.~~

~~Medicare does not have an NCD for anorectal manometry. LCDs exist; see the LCDs for Anorectal Manometry, Anal Electromyography, and Biofeedback Training for Perineal Muscles and Anorectal or Urethral Sphincters and Pelvic Floor Dysfunction: Anorectal Manometry and EMG.~~

~~Medicare does not have an NCD for electrogastrography or electroenterography. LCDs exist; see the LCDs for Non-Covered Services and Noncovered Services other than CPT® Category III Noncovered Services.~~

~~Medicare does not have an NCD for defecography. LCDs do not exist at this time.~~

~~Medicare does not have an NCD for colonic manometry. LCDs do not exist at this time. (Accessed January 17, 2019)~~

REFERENCES

~~Anand C, Al Juburi A, Familoni B, et al. Gastric electrical stimulation is safe and effective: a long term study in patients with drug refractory gastroparesis in three regional centers. Digestion. 2007;75(2-3):83-89.~~

~~Bentur L, Hino B, Shamir R, et al. Impaired gastric myoelectrical activity in patients with cystic fibrosis. J Cyst Fibros. 2006 Aug;5(3):187-91.~~

~~Bharucha AE, Dorn SD, Lembo A, et al. American Gastroenterological Association medical position statement on constipation. Gastroenterology. 2013a Jan;144(1):211-17.~~

~~Bharucha AE, Pemberton JH, Locke GR 3rd. American Gastroenterological Association technical review on constipation. Gastroenterology. 2013b Jan;144(1):218-38.~~

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Bordeianou L, Paquette I, Johnson E, et al. American Society of Colon and Rectal Surgeons. Clinical practice guidelines for the treatment of rectal prolapse. *Dis Colon Rectum*. 2017 Nov;60(11):1121-1131.

Camilleri M, Ford AC, Mawe GM, et al. Chronic constipation. *Nat Rev Dis Primers*. 2017 Dec 14;3:17095.

Camilleri M, Parkman HP, Shafi MA, et al. American College of Gastroenterology. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013 Jan;108(1):18-37. Available at: <https://gi.org/guideline/management-of-gastroparesis/>. Accessed February 12, 2019.

Cappabianca S, Reginelli A, Iacobellis F, et al. Dynamic MRI defecography vs. entero-colpo-cysto-defecography in the evaluation of midline pelvic floor hernias in female pelvic floor disorders. *Int J Colorectal Dis*. 2011 Sep;26(9):1191-6.

~~Chen CL, Lin HH, Chen SY, et al. Utility of electrogastrography in differentiating Parkinson's disease with or without gastrointestinal symptoms: a prospective controlled study. *Digestion*. 2005;71(3):187-91.~~

Chu H, Lin Z, Zhong L, et al. Treatment of high-frequency gastric electrical stimulation for gastroparesis. *J Gastroenterol Hepatol*. 2012 Jun;27(6):1017-26.

Fabrizio AC, Alimi Y, Kumar AS. Methods of evaluation of anorectal causes of obstructed defecation. *Clin Colon Rectal Surg*. 2017 Feb;30(1):46-56.

Foti PV, Farina R, Riva G, et al. Pelvic floor imaging: comparison between magnetic resonance imaging and conventional defecography in studying outlet obstruction syndrome. *Radiol Med*. 2013 Feb;118(1):23-39.

Frasko R, Maruna P, Gurlich R, et al. Transcutaneous electrogastrography in patients with ileus. Relations to interleukin-1beta, interleukin-6, procalcitonin and C-reactive protein. *Eur Surg Res*. 2008;41(2):197-202.

Gharibans AA, Coleman TP, Mousa H, et al. Spatial Patterns From High-Resolution Electrogastrography Correlate With Severity of Symptoms in Patients With Functional Dyspepsia and Gastroparesis. *Clin Gastroenterol Hepatol*. 2019 Dec;17(13):2668-2677.

Giorgio V, Borrelli O, Smith VV, et al. High-resolution colonic manometry accurately predicts colonic neuromuscular pathological phenotype in pediatric slow transit constipation. *Neurogastroenterol Motil*. 2013 Jan;25(1):70-8.e8-9.

Grossi U, Di Tanna GL, Heinrich H, et al. Systematic review with meta-analysis: defecography should be a first-line diagnostic modality in patients with refractory constipation. *Aliment Pharmacol Ther*. 2018 Dec;48(11-12):1186-1201.

Hayes, Inc. Medical Technology Directory. Gastric electrical stimulation for gastroparesis. Lansdale, PA: Hayes, Inc.; October 2018. **Updated January 2020.**

Heckert J, Sankineni A, Hughes WB, et al. Gastric Electric Stimulation for Refractory Gastroparesis: A Prospective Analysis of 151 Patients at a Single Center. *Dig Dis Sci*. 2016 Jan; 61(1):168-75.

~~Heinrich H, Sauter M, Fox M, et al. Assessment of Obstructive Defecation by High-Resolution Anorectal Manometry Compared With Magnetic Resonance Defecography. *Clin Gastroenterol Hepatol*. 2015 Jul;13(7):1310-1317.~~

Jayanthi N, Dexter S, Sarela A, et al. Gastric electrical stimulation for treatment of clinical severe gastroparesis. *J Minim Access Surg*. 2013 Oct;9(4).

Kayar Y, Danalıoğlu A, Kafee AA, et al. Gastric myoelectrical activity abnormalities of electrogastrography in patients with functional dyspepsia. *Turk J Gastroenterol*. 2016 Sep;27(5):415-420.

Keller J, Bassotti G, Clarke J, et al. Expert consensus document: Advances in the diagnosis and classification of gastric and intestinal motility disorders. *Nat Rev Gastroenterol Hepatol*. 2018 May;15(5):291-308.

Kim F, Rhee PL. How to interpret a functional or motility test – colon transit study. *J Neurogastroenterol Motil*. 2012 Jan; 18(1): 94-99.

~~Laine M, Sirén J, Koskenpato J, et al. Outcomes of high-frequency gastric electric stimulation for the treatment of severe, medically refractory gastroparesis in Finland. *Scand J Surg*. 2017 Dec 1:1457496917748222~~

Lal N, Livermore, S, Declan D, et al. Gastric electric stimulation with the Enterra System: a systemic review. *Gastroenterol Res Pract*. 2015; 2015:762972.

Levinthal DJ, Bielefeldt K. Systematic review and meta-analysis: Gastric electrical stimulation for gastroparesis. *Auton Neurosci*. 2017 Jan;202:45-55.

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Lin Z, Sarosiek I, Forster J, et al. Association of the status of interstitial cells of Cajal and electrogastrogram parameters, gastric emptying and symptoms in patients with gastroparesis. *Neurogastroenterol Motil.* 2010 Jan;22(1):56-61, e10.

~~Martín-Martín GP, García-Armengol J, Roig-Vila JV, et al. Magnetic resonance defecography versus videodefecography in the study of obstructed defecation syndrome: is videodefecography still the test of choice after 50 years? *Tech Coloproctol.* 2017 Oct;21(10):795-802.~~

McCallum RW, Lin Z, Forster J, et al. Gastric electrical stimulation improves outcomes of patients with gastroparesis for up to 10 years. *Clin Gastroenterol Hepatol.* 2011 Apr;9(4):314-319.e1.

McCallum RW, Snape W, Brody F, et al. Gastric electrical stimulation with Enterra therapy improves symptoms from diabetic gastroparesis in a prospective study. *Clin Gastroenterol Hepatol.* 2010 Nov;8(11):947-54.

~~Muñoz Yagüe T, Alvarez-Sánchez V, Ibáñez-Pinto A, et al. Clinical, anorectal manometry and surface electromyography in the study of patients with fecal incontinence. *Rev Esp Enferm Dig.* 2003 Sep;95(9):635-9, 629-34.~~

~~Musunuru S, Beverstein G, Gould J. Preoperative predictors of significant symptomatic response after 1 year of gastric electrical stimulation for gastroparesis. *World J Surg.* 2010 Aug;34(8):1853-8.~~

National Institute for Health and Care Excellence (NICE). NICE interventional procedure guidance IPG489. Gastroelectrical stimulation for gastroparesis. London (UK): 2014 May.

Noviello C, Cobellis G, Papparella A, et al. Role of anorectal manometry in children with severe constipation. *Colorectal Dis.* 2009 Jun;11(5):480-4.

O'Grady G, Angeli TR, Du P, et al. Abnormal initiation and conduction of slow-wave activity in gastroparesis, defined by high-resolution electrical mapping. *Gastroenterology.* 2012 Sep;143(3):589-98.e1-3.

Otto SD, Oesterheld A, Ritz JP, et al. Rectal anatomy after rectopexy: cine-defecography versus MR-defecography. *J Surg Res.* 2011 Jan;165(1):52-8.

Paquette IM, Varma M, Ternent C, et al. Clinical practice guidelines. The American Society of Colon and Rectal Surgeons' clinical practice guideline for the evaluation and management of constipation. *Dis Colon Rectum.* 2016 Jun;59(6):479-92. Available at: <https://www.fascrs.org/physicians/clinical-practice-guidelines>. Accessed February 17, 2019.

Paquette I, Varma M, Kaiser A, et al. The American Society of Colon and Rectal Surgeons' clinical practice guideline for the treatment of fecal incontinence. *Dis Colon Rectum* 2015; 58: 623-636. Available at: <https://www.fascrs.org/physicians/clinical-practice-guidelines>. Accessed February 17, 2019.

Pasricha PJ, Camilleri M, Hasler WL, et al. White paper AGA: gastroparesis: clinical and regulatory insights for clinical trials. *Clin Gastroenterol Hepatol.* 2017 Aug;15(8):1184-1190.

Patcharatrakul T, Rao SSC. Update on the pathophysiology and management of anorectal disorders. *Gut Liver.* 2018 Jul 15;12(4):375-384.

Pensabene L, Youssef NN, Griffiths JM, et al. Colonic manometry in children with defecatory disorders. Role in diagnosis and management. *Am J Gastroenterol.* 2003 May;98(5):1052-7.

Poncelet E, Rock A, Quinton J, et al. Dynamic MR defecography of the posterior compartment: Comparison with conventional X-ray defecography. *Diagn Interv Imaging.* 2017 Apr;98(4):327-332.

Prichard DO, Lee T, Parthasarathy G, et al. High-resolution anorectal manometry for identifying defecatory disorders and rectal structural abnormalities in women. *Clin Gastroenterol Hepatol.* 2017 Mar;15(3):412-420

Pucciani F, Ringressi MN. Obstructed defecation: the role of anorectal manometry. *Tech Coloproctol.* 2012 Feb;16(1):67-72.

Rafiei R, Bayat A, Taheri M, et al. Defecographic findings in patients with severe idiopathic chronic constipation. *Korean J Gastroenterol.* 2017 Jul 25;70(1):39-43.

Ramage L, Georgiou P, Qiu S, et al. Can we correlate pelvic floor dysfunction severity on MR defecography with patient-reported symptom severity? *Updates Surg.* 2018 Dec;70(4):467-476.

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Ramage L, Simillis C, Yen C, et al. Magnetic resonance defecography versus clinical examination and fluoroscopy: a systematic review and meta-analysis. *Tech Coloproctol.* 2017 Dec;21(12):915-927.

Rao SS, Patcharatrakul T. Diagnosis and treatment of dyssynergic defecation. *J Neurogastroenterol Motil.* 2016 Jul 30;22(3):423-35.

~~Rao SS; American College of Gastroenterology Practice Parameters Committee. Diagnosis and management of fecal incontinence. *Am J Gastroenterol.* 2004a Aug;99(8):1585-604.~~

Rao SS, Sadeghi P, Beaty J, Kavlock R. Ambulatory 24-hour colonic manometry in slow-transit constipation. *Am J Gastroenterol.* 2004b Dec;99(12):2405-16.

Rao SS, Singh S, Mudipalli R. Day-to-day reproducibility of prolonged ambulatory colonic manometry in healthy subjects. *Neurogastroenterol Motil.* 2010a Jun;22(6):640-e178.

Reiner CS, Tutuian R, Solopova AE, et al. MR defecography in patients with dyssynergic defecation: spectrum of imaging findings and diagnostic value. *Br J Radiol.* 2011 Feb;84(998):136-44.

Rodriguez L, Sood M, Di Lorenzo C, et al. An ANMS-NASPGHAN consensus document on anorectal and colonic manometry in children. *Neurogastroenterol Motil.* 2017 Jan;29(1).

Russo F, Chimienti G, Clemente C, et al. Gastric activity and gut peptides in patients with functional dyspepsia: postprandial distress syndrome versus epigastric pain syndrome. *J Clin Gastroenterol.* 2017 Feb;51(2):136-144.

Sha W, Pasricha PJ, Chen JD. Correlations among electrogastrogram, gastric dysmotility, and duodenal dysmotility in patients with functional dyspepsia. *J Clin Gastroenterol.* 2009 Sep;43(8):716-22.

Shada A, Nielsen A, Marowski S, et al. Wisconsin's Enterra Therapy Experience: A multi-institutional review of gastric electrical stimulation for medically refractory gastroparesis. *Surgery.* 2018 Oct;164(4):760-765.

~~Sharma A, Rao S. Constipation: pathophysiology and current therapeutic approaches. *Handb Exp Pharmacol.* 2017;239:59-74.~~

Singh S, Heady S, Coss-Adame E, et al. Clinical utility of colonic manometry in slow transit constipation. *Neurogastroenterol Motil.* 2013 Feb 6.

Sood MR, Mousa H, Tipnis N, et al. Interobserver variability in the interpretation of colon manometry studies in children. *J Pediatr Gastroenterol Nutr.* 2012 Nov;55(5):548-51.

~~Tabbers M, DiLorenzo M, Berger C, et al. Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations. *J Pediatr Gastroenterol Nutr.* 2014 Feb;58(2): 258-274.~~

Tipnis NA, El-Chammas KI, Rudolph CD, et al. Do oro-anal transit markers predict which children would benefit from colonic manometry studies? *J Pediatr Gastroenterol Nutr.* 2012 Feb;54(2):258-62.

van Iersel JJ, Formijne Jonkers HA, Verheijen PM, et al. Comparison of dynamic magnetic resonance defaecography with rectal contrast and conventional defaecography for posterior pelvic floor compartment prolapse. *Colorectal Dis.* 2017 Jan;19(1):O46-O53.

~~Varma M, Rafferty J, Buie WD; Standards Practice Task Force of American Society of Colon and Rectal Surgeons. Practice parameters for the management of rectal prolapse. *Dis Colon Rectum.* 2011 Nov;54(11):1339-46.~~

Vitton V, Vignally P, Barthet M, et al. Dynamic anal endosonography and MRI defecography in diagnosis of pelvic floor disorders: comparison with conventional defecography. *Dis Colon Rectum.* 2011 Nov;54(11):1398-404.

Wald A, Bharucha A, Cosman B, et al. ACG clinical guideline: management of benign anorectal disorders. *Am J Gastroenterol.* 2014 Aug;109(8):1141-57.

~~Wiklendt L, Mohammed SD, Scott SM, et al. Classification of normal and abnormal colonic motility based on cross-correlations of pancolonic manometry data. *Neurogastroenterol Motil.* 2013 Mar;25(3):e215-23.~~

Yeap ZH, Simillis C, Qiu S, et al. Diagnostic accuracy of anorectal manometry for fecal incontinence: a meta-analysis. *Acta Chir Belg.* 2017 Dec;117(6):347-355.

Yin J, Chen JDZ. Electrogastrography: methodology, validation and applications. *J Neurogastroenterol Motil.* 2013 Jan;19(1):5-17.

UnitedHealthcare, Inc. ("UHC") Proprietary and Confidential Information: The information contained in this document is confidential, proprietary and the sole property of UHC. The recipient of this information agrees not to disclose or use it for any purpose other than to facilitate UHC's compliance with applicable State Medicaid contractual requirements. Any other use or disclosure is strictly prohibited and requires the express written consent of UHC.

Zafar A, Seretis C, Feretis M, et al. Comparative study of magnetic resonance defaecography and evacuation proctography in the evaluation of obstructed defaecation. Colorectal Dis. 2017 Jun;19(6):O204-O209.

POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
<u>TBD</u>	<u>Coverage Rationale</u> <ul style="list-style-type: none"><u>Removed word "diabetic" as listed twice in statement</u><u>Added Definitions section</u> <u>Supporting Information</u> <ul style="list-style-type: none"><u>Updated Clinical Evidence, FDA, CMS, and References sections to reflect the most current information</u><u>Archived previous policy version CS046.J</u>

INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. 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.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The 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.