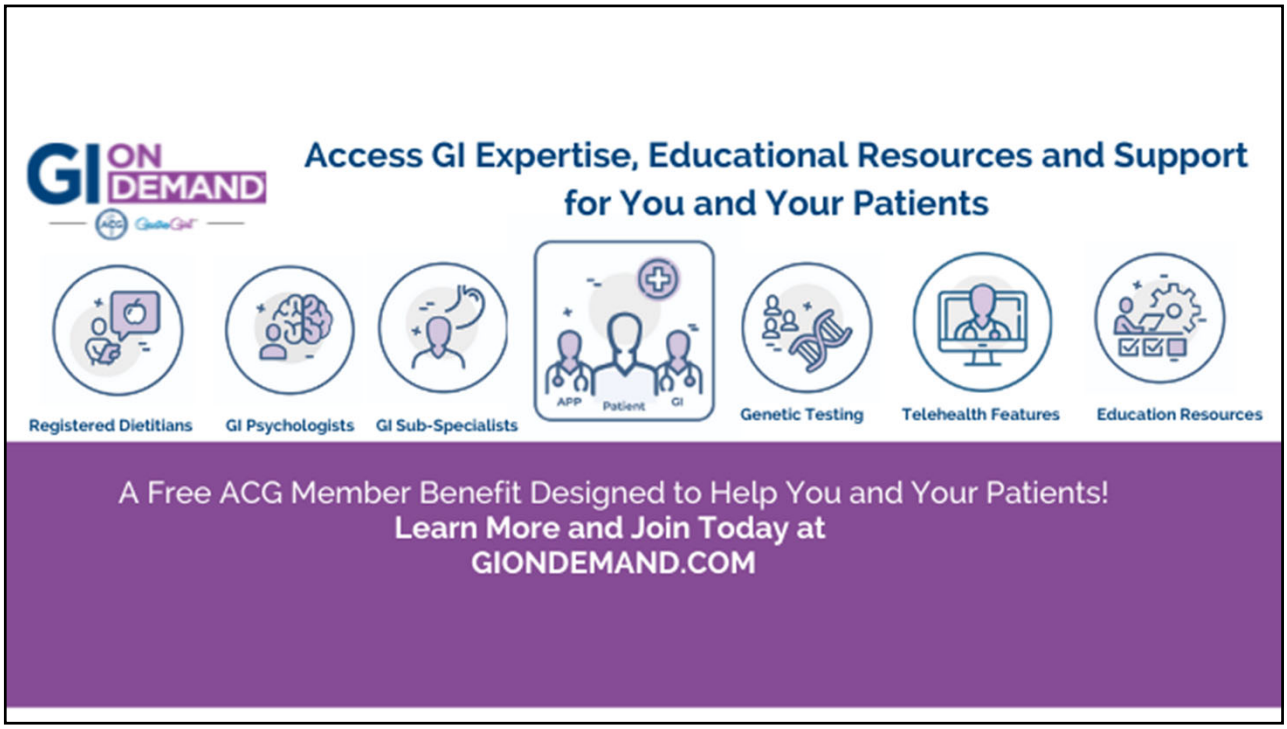
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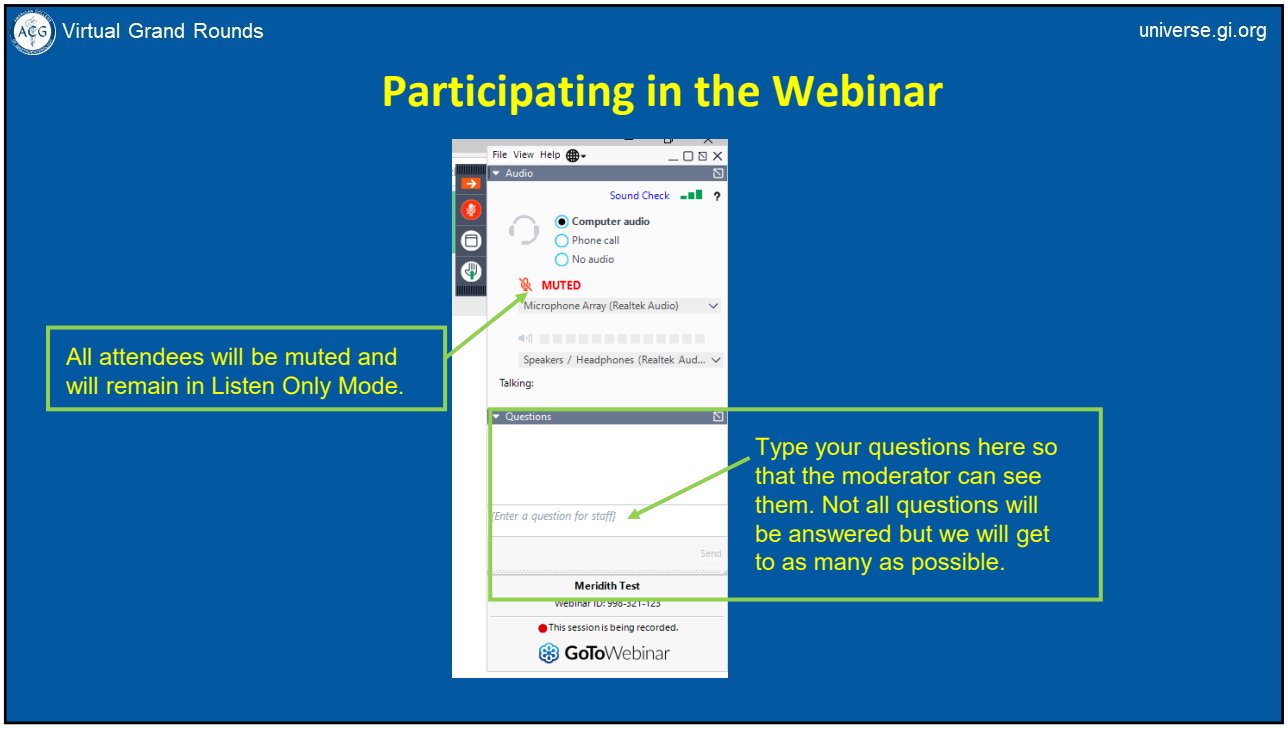
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How to Receive CME and MOC Points

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ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2022 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2023 for this activity.

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MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement.
THESE ANSWERS WILL BE REVIEWED.

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ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!


Week 49 –Thursday, December 8, 2022
ADR, PDR, or IRR: What Are My Quality Metrics for Colonoscopy?
Faculty: Aasma Shaukat, MD, MPH, FACG
Moderator: Asmeen Bhatt, MD
At Noon Eastern and NEW! **8pm Eastern!**


Week 48 – Thursday, December 15, 2022
Optimal Positioning of Small Molecule Treatment Options in IBD
Faculty: David T. Rubin, MD, FACG
Moderator: Samir A. Shah, MD, FACG
At Noon Eastern and NEW! **8pm Eastern!**

There is not Virtual Grand Rounds Dec 22 or Dec 29- Have a Happy New Year!

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Disclosures

Michael Camilleri, MD, DSc, MRCP, FACP, MACG

Single-center research studies: Allergan, Takeda, and Vanda
Consulting with compensation to his employer: Takeda and Alpha Sigma Wasserman

Linda Anh Nguyen, MD

Alnylam: Consultant (Terminated, August 1, 2021); Ardelyx: Consultant; Eli Lilly Pharmaceuticals: Consultant (Terminated, November 1, 2021); Evoke Pharma: Consultant; Gemelli Biotech: Consultant; Neurogastryx: Consultant; Pendulum: Consultant; Phathom Pharmaceuticals: Consultant; RosVivo: Consultant; Salix Pharmaceuticals: Consultant; Takeda: Consultant

**All of the relevant financial relationships listed for these individuals have been mitigated*

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New Updates to the ACG's Gastroparesis Guideline

Michael Camilleri, MD, DSc, MRCP, FACP, MACG
Mayo Clinic, Rochester

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Gastroparesis records in EMBASE, PubMed, Ovid MEDLINE, Web of Science, and Cochrane (N = 4,031)

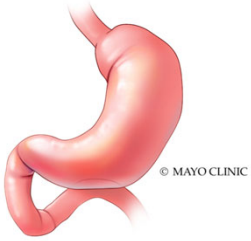
↓

Full-text articles reviewed (N = 123)

↓

Studies included in synthesis (N = 13)

→ Excluded (N = 110)



	Definite	Probable	Possible
Jung (2009)	**Prevalence**/100,000 persons (95% CI)		
	24.2 (15.7-32.6)	33.4 (23.3-43.3)	50.5 (38.1-62.8)
	Incidence/100,000 person-years (95% CI)		
	6.3 (4.9-7.7)	9.8 (8.1-11.6)	17.2 (14.9-19.5)
Ye (2022)	**Prevalence**/100,000 persons (95% CI)		
	21.5 (20.6-22.4)	126.8 (124.8-128.8)	92.7 (92.0-95.4)
	Incidence/100,000 person-years (95% CI)		
	NA	NA	NA

Dilmaghani, Zheng, Camilleri CGH 2022

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2013 ACG Clinical Guideline: Management of Gastroparesis

Gastroparesis is *identified* in clinical practice through the recognition of the clinical symptoms and documentation of delayed gastric emptying in the absence of gastric outlet obstruction.

***Symptoms* from gastroparesis include nausea, vomiting, early satiety, postprandial fullness, bloating, and upper abdominal pain.**

***Management* of gastroparesis should include assessment and correction of nutritional state, relief of symptoms, improvement of gastric emptying and, in diabetics, glycemic control.**

Camilleri M, Parkman H, Shafi M, Abell T, Gerson L Am J Gastroenterol.2013;108:18-37

Cited by 263 articles

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Clinical Guideline on Gastroparesis

Michael Camilleri, MD, MRCP (UK), MACG, AGAF, Mayo Clinic, MN
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American Journal of Gastroenterology August 2022

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Objective of this new guideline

- To document, summarize, and update the evidence and develop recommendations for the **clinical management of gastroparesis**, updating the 2013 ACG guideline on gastroparesis.
- To address the topics of clinical relevance in the Patient Intervention Comparison and Outcomes (PICO) format.
- To acknowledge the **limitations of guideline recommendations on therapies**

- the absence of FDA-approved therapies for gastroparesis in the United States and
- the limitation in duration of prescription to 3 months for the only currently-approved medication, metoclopramide.

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Methods

- Key questions developed by the authors and vetted through American College of Gastroenterology leadership
- To address the topics of clinical relevance in the Patient Intervention Comparison and Outcomes (PICO) format.
- Emphasis on having practical recommendations that would be helpful for practicing providers in the U.S.
- A broad literature search was conducted to document, by tables, information pertaining to PICO questions,
- Focused evaluation of the most relevant literature to develop recommendations.
- Literature Search + Screening by no fewer than 2 reviewers, with a third reviewer resolving any conflicts.
- *Inclusion criteria* were original research studies on the incidence, diagnosis, and treatment of gastroparesis in adult populations, predominantly based on observational studies and randomized, controlled trials.
- *Exclusion criteria*
  - inclusion in the previous 2013 ACG guideline (where relevant, included in tables for completeness of literature),
  - theoretical studies using computational models,
  - animal trials,
  - pediatric populations
  - publications without original data analysis

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Select Open-Label Trial of Gastric Electrical Stimulation			
Multicenter, open-label GES experience in France	142 patients (60 diabetic, 82 non-diabetic) and medico-economic data were available for 96 patients (36 diabetic, 60 non-diabetic)	24 months after implantation. GIQLI score increased, with a more significant improvement in non-diabetic than in diabetic patients. Proportion of patients vomiting less than once per month increased by 25.5%. GES decreased mean overall healthcare costs (saving of average $3348 /patient/year), with. savings greater for diabetic patients (4096 US$ /patient/year).	Gourcerol 2020

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Methods

- After screening, a total of 121 references were identified for inclusion
- Progressed for evidence appraisal in July 2021 using GRADE process by two formally trained GRADE methodologists (RHY & KG) to evaluate the quality of the evidence and strength of the recommendations.

Study Design	Quality of Evidence	Reduced Factors	Increased Factors
Randomized trials	High	Risk of bias	Large effect
		-1 serious	+1 large
		-2 very serious	+2 very large
	Moderate	Inconsistency	Dose response
		-1 serious	+1 if gradient
		-2 very serious	
		Indirectness	Confounding
		-1 serious	+1
		-2 very serious	
Observational studies	Low	Imprecision	
		-1 serious	
		-2 very serious	
	Very low	Publication bias	
		-1 likely	
		-2 very likely	

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Recommendation	GRADE Level of Evidence	Strength of Recommendation
Risk Factors		
In patients with diabetic gastroparesis, optimal glucose control is suggested to reduce the future risk of aggravation of gastroparesis.	Low	Conditional
Diagnostic Testing		
Scintigraphic gastric emptying assessment is the standard test for the evaluation of gastroparesis in patients with upper GI symptoms. The suggested method of testing includes appraising the emptying of a solid meal over a duration of 3 hours or greater.	Moderate	Strong
Radiopaque markers testing is not suggested for the diagnostic evaluation of gastroparesis in patients with upper GI symptoms.	Very Low	Conditional
Wireless motility capsule testing may be alternative to the scintigraphic gastric emptying assessment for the evaluation of gastroparesis in patients with upper GI symptoms.	Low	Conditional
Stable isotope (^{13}C-spirulina) breath testing is a reliable test for the evaluation of gastroparesis in patients with upper GI symptoms.	Low	Conditional

Diagnostic Considerations discussed: Additional value of gastric function tests that do not measure emptying, including
EGG
WMC for assessment of pan-GI dysmotility
Intra-gastric food identified at endoscopy
Gastric Full-Thickness Biopsies

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Recommendation	GRADE Level of Evidence	Strength of Recommendation
Management		
Dietary management of gastroparesis should include a small particle diet to increase likelihood of symptom relief and enhanced gastric emptying.	Low	Conditional
In patients with idiopathic and diabetic gastroparesis, pharmacologic treatment should be considered to improve gastric emptying and gastroparesis symptoms, taking into account benefits and risks of treatment.	Low	Conditional
In patients with gastroparesis, we suggest treatment with metoclopramide over no treatment for management of refractory symptoms	Low	Conditional
In patients with gastroparesis where domperidone is approved, we suggest use of domperidone for symptom management	Low	Conditional
In patients with gastroparesis, we suggest use of 5HT4 agonists over no treatment to improve gastric emptying	Low	Conditional

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Summary of efficacy of other prokinetic agents (5-HT$_4$ receptor agonists) on symptoms or gastric emptying

Medication/trial design	N, Etiology	Dose (p.o.)	Duration	Efficacy	Reference
				5-HT4 agonists	
Clebopride PC, DB, RCT	76 with dyspeptic syndromes and x-ray proven delayed GE	0.5 mg tid	3 months	Clebopride was more effective than placebo in reducing or relieving symptoms	Bavestrello 1985, ref. 87
Prucalopride PC, DB, XO, RCT	13 DM, 2 connective tissue disease	4mg/day	Two 4-wk treatments with 2 wks washout	GE faster on prucalopride; GCSI scores were lower than baseline but not different between treatment arms. Meal-related symptom scores over time or cumulative score were not significantly different between groups. GE was more rapid in the prucalopride treatment period,	Andrews 2021, ref. 88
Prucalopride PC, DB, XO, RCT	28 IG, 6 DG	2mg/day	Two 4-wk treatments with 2 wks washout	Prucalopride significantly improved the total GCSI, subscales of fullness/satiety, nausea/vomiting, and bloating/distention, overall PAC-QOL score and gastric emptying $T_{1/2}$; also all efficacies were shown only in the idiopathic group	Carbone 2019, ref. 89
Revexepride: PG, DB, PC, stratified, repeated dose RCT	62 non-DM; 30 DM (55 female, 37 male); gastroparesis symptoms, and slower baseline GEBT $T_{1/2}$ in placebo group	0.02, 0.1, or 0.5 mg tid	4 weeks	Large inter-individual differences in GEBT with no significant treatment effect; GCSI and PAGI-SYM scores decreased at Week 2 and decreased further at Week 4 in all groups including placebo. Quality of life improved in all treatment groups after 4 weeks of treatment.	Tack et al 2016, ref. 90
Velusetrag: DB, PC, RCT; 3-period XO	18 DG, 16 IG	5, 15 or 30 mg po daily	7 days each period	GE $T_{1/2}$ numerically reduced with all 3 doses of velusetrag vs placebo. Efficacy was similar between subjects with diabetic and idiopathic gastroparesis.	Kuo 2021, ref. 91
Felcisetrag: DB, PC, RCT	36: 22 IG, 14 DG	0.1, 0.3 or 1.0mg i.v., daily	3 days	Felcisetrag significantly accelerated GE, small bowel transit, ascending colon emptying ($T_{1/2}$) and colonic transit at 48 hours	Chedid 2021, ref. 92

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Summary of efficacy of other prokinetic agents (ghrelin and motilin receptor agonists) on symptoms or gastric emptying

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Medication/trial design	N, Etiology	Dose (p.o.)	Duration	Efficacy	Reference
Ghrelin Agonist					
Relamorelin RCT, PC, XO	10 T1DM with previous delayed GE	100 µg SQ	Single dose	Decreased gastric retention of solids at 1h and 2h and decreased GCSI-DD scores and nausea/vomiting/ fullness/pain scores	Shin 2013, ref. 93
Relamorelin RCT, PC, PG	204 DG + moderate to severe symptoms and delayed GE	10 µg SQ daily or 10 µg SQ bid	12 weeks	Relamorelin (10 µg bid) significantly accelerated GE and significantly reduced vomiting vs. placebo. Among patients with baseline vomiting, relamorelin accelerated GE, reduced vomiting and improved other symptoms	Lembo 2016, ref. 94
Relamorelin RCT, PC, PG	393 DM with moderate to severe gastroparesis symptoms	10 µg, or 30 µg or 100 µg or placebo SQ bid	12 weeks	75% reduction in vomiting frequency vs baseline (NS compared with placebo). All 4 symptoms of DG (composite or individual symptoms) significantly reduced over 12-wk in all 3 relamorelin doses and accelerated GE vs. placebo. Adverse effect: impaired glycemic control with relamorelin	Camilleri 2017, ref. 95
Relamorelin and TZP-101 or TZP 102: 6 RCTs in SRMA	DG (N=557)	Diverse doses		Significantly improved overall gastroparesis symptoms (standardized mean difference, -0.34; 95% CI, -0.56 to -0.13) and significantly improved symptoms, including nausea, vomiting, early satiety, and abdominal pain	Hong 2020, ref. 96
Motilin Agonists					
Erythromycin RCT, PC, XO	10 T1DM	200mg iv; 250mg p.o. tid	4 weeks	Solid meal retention at 2h: 63±9% with placebo; 4±1% with erythromycin; no effects on the symptoms	Janssens 1990, ref. 97
Erythromycin open trials of i.v. and p.o.	10 IG and 4 DG; 4 patients dropped out	6 mg/kg i.v. 500 mg tid-ac and qhs	Single dose; 4 wk and open 8.4 mo	Solid meal retention at 2h: 85±11% (SD) at baseline; 20±29% on iv erythromycin (p <0.001); 48±21% after 4 wk of oral therapy (p <0.01). Reduction in total symptom scores and a significant reduction in global assessment scores	Richards 1993, ref. 98
Erythromycin vs metoclopramide RCT, XO	13 DG	p.o. 250 mg tid erythromycin; p.o.10 mg tid metoclopramide	3 weeks each period	Compared with baseline, improved GE parameters after both erythromycin and metoclopramide, with improved total GI symptom scores, more pronounced with erythromycin	Erbas 1993, ref. 64
Erythromycin RCT, PC, XO	20 IG (functional dyspepsia + delayed GE)	200mg i.v.	Single dose	Erythromycin accelerated (breath test) solid GE T½=146 (27) vs 72 (7) min, and liquid GE T½=87 (6) vs 63 (5) min; no overall symptom improvement except for bloating	Arts 2005, ref. 99
Erythromyin vs azithromycin retrospective case-control analysis	120 patients (27 DM) underwent SGE with provocative testing	250mg i.v. of each drug	Single dose	Both treatments accelerated gastric emptying with no difference between the 2 treatments: erythromyin GE T½=166±68min baseline to 11.9±8.4min; azithromycin GE T½=178±77min baseline to 10.4±7.2min	Larson 2010, ref. 100

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Recommendation	GRADE Level of Evidence	Strength of Recommendation
Management		
In patients with gastroparesis, use of antiemetic agents is suggested for improved symptom control, however, these medications do not improve gastric emptying.	Low	Conditional
Central neuromodulators are NOT recommended for management of gastroparesis.	Moderate	Strong
Current data do NOT support the use of ghrelin agonists for management of gastroparesis.	Moderate	Strong
Current data do NOT support the use of haloperidol for treatment of gastroparesis.	Low	Conditional

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Efficacy of antiemetics and central neuromodulators in gastroparesis

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Medication/ trial design	N, Etiology	Dose	Duration	Efficacy	Reference
Aprepitant PC, PG, DB, RCT	126 pts with at least moderate chronic nausea and vomiting	p.o. 125mg /day	4-weeks	Aprepitant did not reduce symptoms of nausea (primary outcome measure) but significantly reduced secondary outcomes: in symptom severity for nausea, vomiting and overall symptoms. Adverse events (mild or moderate severity) commoner in aprepitant (35%) vs placebo (17%).	Pasricha 2018, ref. 103
Tradipitant PC, PG, DB, RCT	152 adults with IG (91) or DG (61)	p.o. 85 mg bid	4 weeks	Significant decrease in nausea score (reduction of 1.2) at week 4; significant increase in nausea-free days at week 4 with even greater effects in patients with nausea and vomiting at baseline (n = 101). A >1-point improvement in GCSI score in 46.6% on tradipitant compared with 23.5% on placebo.	Carlin 2021, ref. 104
Nortriptyline PG, PC, DB RCT	130 IG	dose escalation at 3-week intervals (10, 25, 50, 75 mg) to 75 mg at 12 weeks	15 weeks	No difference in primary outcome measure (decrease from the patient's baseline GCSI score of at least 50% on 2 consecutive 3-week GCSI assessments during 15 weeks of treatment); more treatment cessation in nortriptyline group (29%) than placebo group (9%); numbers of adverse events not different.	Parkman 2013, ref. 105
Haloperidol PC, RCT	33 Emergency Dept. patients with acute exacerbation of diagnosed gastroparesis	5mg vs. placebo both + conventional therapy (selected by treating MD)	Single dose	One hour after therapy, the mean pain and nausea scores in the haloperidol group were 3.13 and 1.83 compared to 7.17 and 3.39 in the placebo group (symptoms on 10-point scale). No adverse events were reported.	Roldan 2017, ref. 106
STW5 or STW5-11 vs. cisapride DB, double dummy, RCT	186 dysmotility type of FD	NA	NA	The lower limit of the confidence interval for both herbal preparations was above the pre-defined lower limit of the equivalence border and hypothesis of non-inferiority was proven for STW 5 & STW 5-II.	Rosch 2002, ref. 107
STW 5 PC, PG, DB, RCT	103 patients with FD and gastroparesis	20 drops tid	4 weeks	Improvement of the GIS (P=0.08) and the proportion of patients with a treatment response (P=0.03) were more pronounced in the STW 5 group compared to placebo. No effect on GEBT.	Braden 2009, ref. 108
Survey question-naire of treatment of nausea in clinical practice	102 patients: GP43.1%, FD 27.5%, PSG 8.8%, other 2.0%, undeter-mined multiple 10.8%.			Patient-reported best treatments were marijuana, ondansetron, and promethazine. Least effective treatments were erythromycin, diphenhydra-mine, buspirone, gabapentin, pregabalin, acupuncture, and Iberogast. Promethazine was more effective in patients with a higher GCSI.	Zikos 2018, ref. 109

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Recommendation	GRADE Level of Evidence	Strength of Recommendation
Management		
Gastric electric stimulation (GES) may be considered for control of gastroparesis (GP) symptoms as a humanitarian use device (HUD)	Low	Conditional
Acupuncture alone or acupuncture combined with prokinetic drugs may be beneficial for symptom control in patients with diabetic gastroparesis. Acupuncture cannot be recommended as beneficial for other etiologies of gastroparesis.	Very Low	Conditional
Herbal therapies such as Rikkunshito or STW5 (Iberogast) should NOT be recommended for treatment of gastroparesis.	Low	Conditional

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Efficacy of several bioelectric therapies in gastroparesis

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Device/trial design	Patients	Efficacy	Reference
Vagal Stimulation			
Open-label pilot study: short-term noninvasive cervical vagal nerve stimulation in patients with drug-refractory gastroparesis	23 patients with gastroparesis for 3 weeks and 7 of these for 6 weeks.	Response rates were 35% at 3 weeks and 43% for 3-6 weeks. Improvements in mean total GCSI and subscales were noted.	Paulon 2017, ref. 117
Open-label pilot study: noninvasive vagal nerve stimulation for 4 wks improves symptoms and gastric emptying in patients with IG	15 patients with mild to moderate IG	Improvement in total GCSI symptom scores and three sub-scales, with 40% participants meeting primary endpoint; therapy also associated with a reduction in GE T1/2.	Gottfried-Blackmore 2020, ref. 118
Spinal Cord Stimulation			
Open-label study of spinal stimulation in patients with abdominal pain, with the majority having gastroparesis	23 patients, 96% Caucasian and 79% women, with gastroparesis in 63%	After 12 months of 10-KHZ spinal cord stimulation, 78% of patients had >50% reduction in pain and 64% remitted in pain. Other outcomes improved in most patients.	Kapural 2020, ref. 119
Meta-analyses Assessing Effectiveness of Gastric Electrical Stimulation			
NICE Guidance on GES for gastroparesis	Several studies reviewed, 2 metanalysis, 2 RCT, XO	Diabetics with severe symptoms may benefit from therapy.	Kong 2015, ref. 129
SRMA 13 studies, 12 lacked controls and 1 blinded and randomized	13 studies, 12 lacked controls and 1 blinded and randomized	Following GES, improvements in TSS score (3/13 studies), vomiting severity (4/13), nausea severity (4/13), SF-36 physical composite score (4/13), SF-36 mental composite score (4/13), requirement for enteral or parenteral nutrition (8/13), and 4-h gastric emptying (5/13). Weight gain (in 3/13) did not reach overall significance, Device removal or reimplantation rate was 8.3%. Beneficial in improving symptoms in patients with gastroparesis	O'Grady 2009, ref. 130
SRMA 5 studies randomly allocated patients to periods with or without GES	5 randomized trials 16 open-label studies	TSS scores did not differ between these periods with or without GES in randomized trials. Open-label studies showed a significant decrease in TSS scores, which was also shown with medical therapy or placebo arms, or botulinum toxin. Meta-regression analysis showed that significant differences in baseline TSS ratings impacted TSS ratings during treatment. Argues against the use of GES outside of strict clinical trials as viable treatment option.	Levinthal 2017, ref. 131
SRMA	21 studies	GES appears to offer significant improvement in symptom control in a subset of patients.	Lal 2015, ref.-132
SRMA	10 studies	GES is an effective modality for treating gastroparesis refractory to less invasive treatment.	Chu 2012, ref. 133

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Recommendation	GRADE Level of Evidence	Strength of Recommendation
Management		
In patients with gastroparesis, EndoFLIP evaluation may have a role in characterizing pyloric function and predicting treatment outcomes following peroral pyloromyotomy.	Very Low	Conditional
Intrapyloric injection of botulinum toxin is not recommended for patients with gastroparesis based on randomized controlled trials.	Moderate	Strong
In patients with gastroparesis with symptoms refractory to medical therapy, we suggest pyloromyotomy over no treatment for symptom control.	Low	Conditional

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EndoFLIP for Selection of Patients for Pyloromyotomy or Pyloric Botulinum Toxin Injection

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Patients	Measurement	Results	Reference
21 HC, 27 patients with gastroparesis and 5 patients with esophagectomy	Fasting pyloric pressure and compliance	Fasting pyloric compliance 25.2±2.4 mm/mmHg in HV, 16.9±2.1 mm/mmHg in gastroparesis (P <0.05) and 10.9±2.9 mm/mmHg in patients with esophagectomy (; P <0.05). Pyloric dilation in 10 gastroparesis patients with low fasting pyloric compliance increased compliance from 7.4±0.4 to 20.1±4.9 mm/mmHg (P <0.01) and improved the GIQLI score.	Gourcerol 2015, ref. 155
54 patients (39 IG, 15 DG)	Fasting pyloric diameter, CSA, pressure, length, DI	Wide range seen in diameter (5.6-22.1 mm) and distensibility (1-55 mm^2/mmHg) of the pylorus. Symptoms of early satiety and postprandial fullness were inversely correlated with pyloric sphincter diameter and CSA.	Malik 2015, ref. 156
47 DG patients and 67 IG patients with nausea and vomiting	Sleeve manometry and EndoFLIP performed sequentially during the same endoscopy	Basal pyloric pressure was elevated (>10 mmHg) in 34 patients (42% of patients with delayed emptying); significant decrease in distensibility in patients with gastric retention (>20% at 4 h) compared with patients with normal gastric retention (<10%).	Snape 2016, ref. 157
30 IG patients and 14 DG patients	Fasting pyloric diameter, CSA, and DI	Greater gastric retention tended to correlate with decreased CSA and pyloric DI. Greater pyloric compliance at baseline correlated with greater improvement in early satiety and nausea at 8 weeks and greater pyloric DI correlated with improvement in upper abdominal pain.	Saadi 2018, ref. 158
37 patients with refractory gastroparesis	Fasting CSA, balloon pressure, and DI	Post-G-POEM CSA and DI were significantly higher in the clinical success group and improvement in gastric emptying.	Vosoughi 2020, ref. 159
20 patients with refractory gastroparesis	Fasting pyloric diameter and DI before and after G-POEM	G-POEM increased mean and maximum pyloric diameters and mean and maximum pyloric DI on 50 mL EndoFLIP inflation; therapy enhances pyloric opening but may not impair pyloric closure. The clinical success of G-POEM using EndoFLIP inflated to 50mL had specificity of 100% and sensitivity of 72.2% (area under the curve 0.72) at a distensibility threshold of 9.2 mm^2/mmHg.	Watts 2020, ref. 160
35 patients with gastroparesis: 11 DG, 6 PSG, 17 IG	Fasting pyloric diameter and distensibility before BOTOX	19/35 patients with reduced (<10 mm^2/mm Hg) pyloric distensibility) had benefits: TSS decreased at 3 months and gastric fullness, bloating and GIQLI score and gastric emptying $T_{1/2}$ all improved; no such benefit in those with normal distensibility.	Desprez 2019, ref. 161

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Efficacy of G-POEM for gastroparesis based on open-label studies.

# Pts	Types of gastroparesis pts	Changes in GE	Changes in symptoms	Follow up	Adverse events	Ref. #
29	DG=7; IG= 15;PSG=5 scleroderma=2	70% Normalized	79% at 3 months; 69% at 6 months. GCSI improved from 3.5 to 0.9 at 3 months	3 and 6 months	17% (2/12) Pneumoperitoneum requiring decompression	Gonzalez 2017, ref. 163
16	DG=9; IG=5; PSG=1 post-infectious = 1	75% normalized, 25% improved	81% improvement. GCSI improved from baseline of 3.4 to 1.46 12 months later	12 months	None	Dacha 2017, ref. 164
47	DG=12; IG=27 PSG=8	4h retention improved: from 37.2 to 20.4%	GCSI improved from 4.6 to 3.3	3 months (follow-up in 31/47 pts)	1 death (unrelated)	Rodriguez 2017, ref. 165
30	DG=11; IG=7 PSG=12	47% Normalized	No validated outcome measure available	6 months	2/30 (6%): 1 pre-pyloric ulcer and 1 capnoperitoneum	Khashab 2017, ref. 166
13	DG=1; IG=4 PSG=8	4/6 improved; % retention at 4h improved from 49 to 33%	In 11: 4 considerably better, 4 somewhat better, 1 no Δ, 2 worse	3 months	3 accidental mucosotomy closed with clips; 1 pulmon. embolism	Malik 2018, ref. 167
16	DG=3 PSG=13	Mean % retention (radiolabeled bread) at 2h from 69.3 to 33.4%	Mean total symptom score from 24.25 to 6.37; 13/16 substantial improvement	3 months	1 pyloric stenosis at day 45	Xu 2018, ref. 168
20	DG=10 non-diabetic=10	% retention at 4h improved from 57.5 to 15%; and 30% normal	GCSI improved from 3.5 to 1.3; QOL improved	3 months	3 mild hemorrhage, 3 gastric perforation, 1 moderate dyspepsia	Jacques 2019, ref. 169
40	DG=15 Nondiabetic=25 (of which 18 were IG)	% retention at 4h reduced by 41.7%	Improved GCSI, nausea/vomiting, not bloating	median 15 months	1 tension capnoperitoneum, 1 worse COPD; 1 (Ehlers-Danlos syndrome) disrupted mucoso-tomy + ulcer	Mekaroonkamol 2019, ref. 170
22	DG=8, IG=14, all with GES and most with diverse other procedures	In 7/11 with post-G-POEM, GE was normal	GCSI improved (reduction 1.63 points); improved all sub-scores	1 and 3 months	1 laparoscopy for pain due to capnoperitoneum and adhesions	Strong 2019, ref. 171
38	PSG (76% for fundoplication or hiatal hernia repair)	% retention at 4h improved from 46.4 to 17.9%; 50% normalized	GCSI improved (mean reduction 1.29 points); improved all sub-scores	1 month	2 readmissions: 1 melena; 1 dehydration	Strong 2019, ref. 172
80	IG (41.3%), PSG (35%) and DG (23.8%).	GE scintigraphy improvement in 64.2% and normalized in 47.2% (of 53 cases with test) at 3 mo.	Decrease in total GCSI >1 + >25% decrease in at least two of the subscales in 66.6% at 12 months	3 months GES, 12 months clinical	3 symptomatic capno-peritoneum, 1 mucosotomy; 1 thermal mucosal injury	Vosoughi 2021, ref. 173
9	5 PSG, 2 DG, 1 IG, and 1 PSG and diabetic		Mean GSCI decreased from 3.16 to 0.86 (3 months), 0.74 (6 months), 1.07 (12 months) and 1.31 (24 months [ns]) after the procedure. GIQLI improved from baseline at 12 mo.; not at 24 mo.	median follow-up was 23 (range 12-31) months	1 delayed bleeding from gastric ulcer	Hustak 2020, ref. 174
76	Gastroparesis with median duration 48 months; median gastric retention at 4h 45% and median GCSI 3.6	High rate of gastric retention at 4h was significantly associated with clinical failure	Clinical success in 65.8% of patients at 1 year, with median of reduction in GCSI score of 41%; high preop GCSI satiety score predicted clinical success	At least 1 y		Ragi 2021, ref. 175

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Efficacy of G-POEM vs. surgical pyloroplasty for gastroparesis based on open-label studies

# Pts	Types of gastroparesis pts	Changes in GE	Changes in symptoms	Follow up	Adverse events	Ref. #
Laparoscopic pyloroplasty compared to G-POEM procedure						
60	Retrospective comparison lap pyloroplasty (LP) vs. G-POEM, Single-center, 30 per group (19 IG, 6 PSG, 5 DG), matched by propensity scoring	LP and G-POEM both resulted in similar, significant improvements in GCSI scores (overall and each of 3 subscales) with no differences between treatment groups	LP and G-POEM both resulted in similar, significant improvements in objective GE with no differences between treatment groups	1-month outcome (28 G-POEM, 22 LP) 3-month outcome (25 G-POEM, 21 LP)	Longer length of stay, operative time, more estimated blood loss and complications in the LP group (surgical site infection, pneumonia, and unplanned ICU admission	Landreneau 2019, ref. 180
SRMA	G-POEM (332 in 11 studies) vs. surgical pyloroplasty (375 in 7 studies	4h GE scintigraphy success results: G-POEM 85.1% (95% CI 68.9-93.7) and surgical pyloroplasty 84% (95% CI 64.4-93.8) with no significant difference	Clinical success, based on GCSI score: G-POEM 75.8% (95% CI 68.1-82.1) and surgical pyloroplasty 77.3% (95% CI 66.4-85.4), with no significant difference		Overall adverse events were comparable	Mohan 2020, ref. 181

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ENDOSCOPIC PYLOROMYOTOMY FOR THE TREATMENT OF SEVERE AND REFRACTORY GASTROPARESIS: A PILOT, RANDOMIZED, SHAM-CONTROLLED TRIAL

- **Objective/Design:** Prospective RCT compared Endoscopic pyloromyotomy (G-POEM) with a sham procedure in patients with severe gastroparesis.
- **Primary outcome** was the proportion of patients with treatment success (defined as a decrease in GCSI by at least 50%) at 6 months. Pts randomized to sham group with persistent symptoms were offered cross-over G-POEM.
- **Interim Analysis**: The enrolment was stopped after the interim analysis by the Data and Safety Monitoring Board prior to reaching the planned sample of 86 patients. A total of 41 patients (17 diabetic, 13 post-surgical, 11 idiopathic; 46% male) were randomized (21 G-POEM, 20-sham)
- **Treatment success rate:** 71% (95%CI: 50-86) after G-POEM vs 22% (8-47) after sham (p=0.005).
- **"Cross-over" group**: 12 patients, who did not have treatment success after the sham procedure and agreed with a cross-over G-POEM, underwent the procedure and were followed up for another 6 months

Martinek J, Hustak R, Mares J, Vackova Z, Spicak J, Kieslichova E, Buncova M, Pohl D, Amin S, Tack J Gut. 2022 Apr 25: gutjnl-2022-326904.

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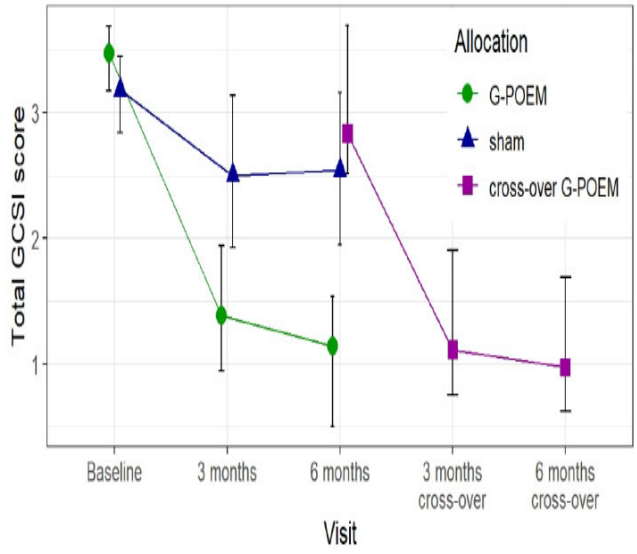
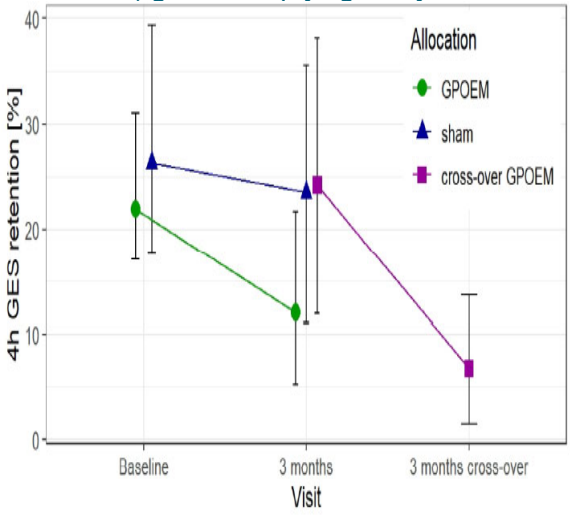
Evolution of Total GCSI



Evolution of gastric retention at 4 hours after meal ingestion on a standardized ^{99m}Tc- sulphur colloid solid-phase (Egg-Beaters meal, 2% fat, 200kcal) gastric emptying study



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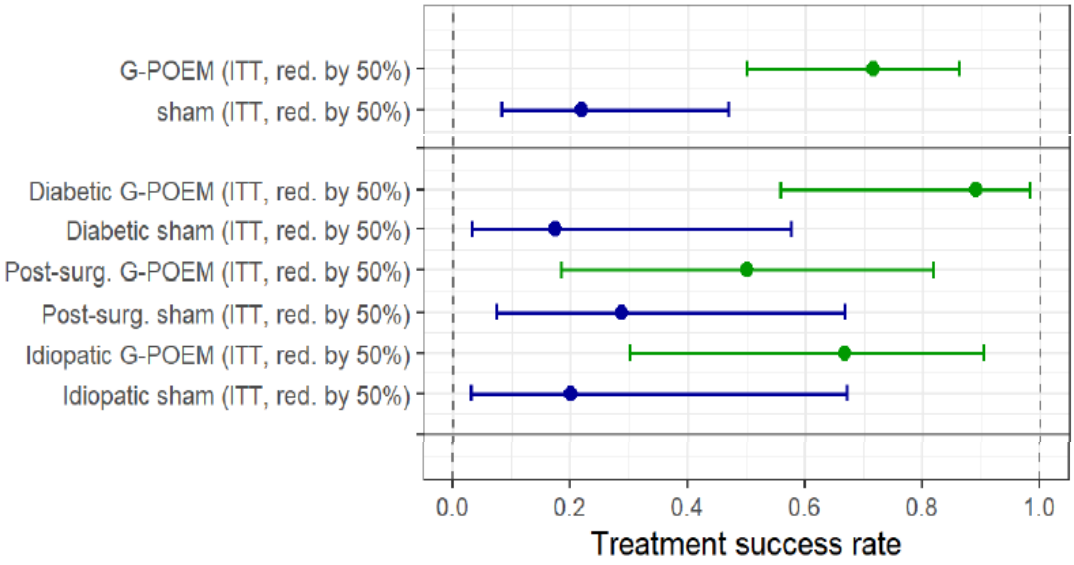
Treatment success at 6 months

Treatment success at 6 months after the assigned procedure (main outcome) (upper panel) and in sub-groups by etiology of gastroparesis (lower panel): Note lack of efficacy in idiopathic and post-surgical groups.



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Supplement: histological and molecular studies of full thickness biopsy of stomach

1. **Cellular basis for the development of gastroparesis**

- Experimental models of gastroparesis show a reduction in the number of interstitial cells of Cajal (ICC) in the deep muscle plexus with secondary effects in gastric muscles because of the lack of trophic factors (such as stem cell factor)
- Depletion of ICCs may have prognostic significance regarding the efficacy of GES.

2. **Morphological and transcriptomics evidence from human gastric biopsies**

(i). Neural, pacemaker and muscular elements:

(ii). Inflammatory elements: Loss of anti-inflammatory macrophages and increased expression of genes associated with pro-inflammatory macrophages have been reported in full-thickness gastric biopsies from patients with gastroparesis. However, there may be differences in the morphological abnormalities in diabetic and idiopathic gastroparesis in the different studies reported to date. In contrast, genes associated with M1 (pro-inflammatory) macrophages were increased in idiopathic gastroparesis samples compared to their controls. Finally, innate immune mechanisms in diabetic gastroparesis seem to be associated with reduced expression of inflammatory markers on transcriptomics and paradoxically they are associated with M2 macrophage deficiency, which would be expected to be pro-inflammatory in diabetic gastroparesis. There were higher numbers of mast cells on full-thickness gastric biopsy in idiopathic compared to diabetic gastroparesis (17).

- **Section summary**:
- Although full thickness biopsies have helped to shed light onto the pathogenesis of gastroparesis, to date, the biopsies have yet to help guide management. Therefore, similar to the European Society of Neurogastroenterology and Motility consensus statement (21), **we do not recommend the routine use of full thickness biopsies**

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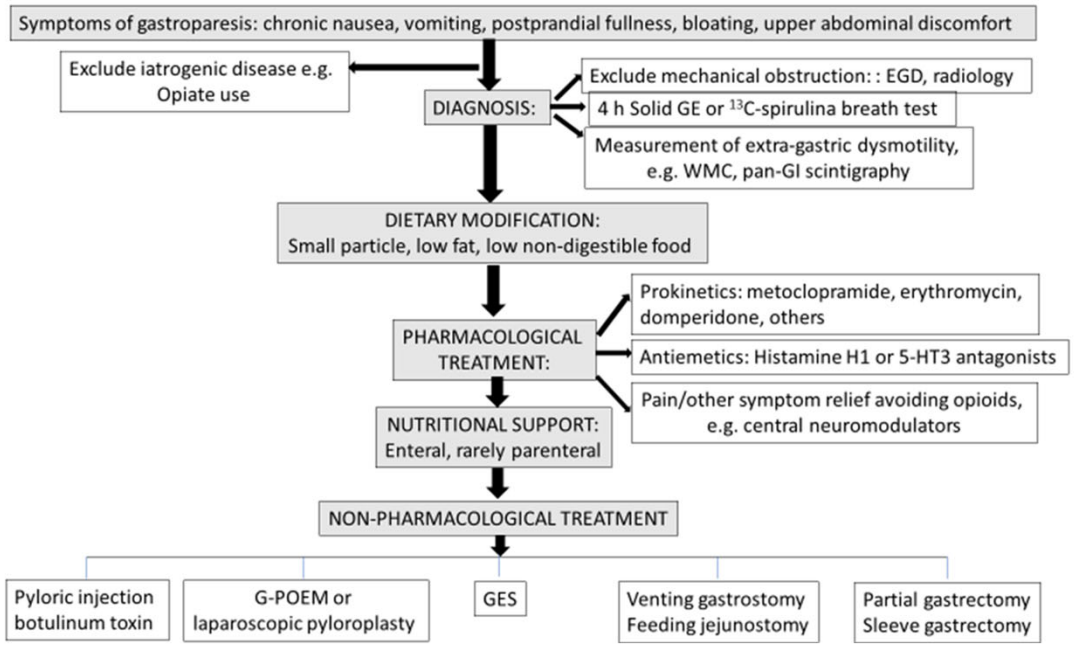

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Information for Patients, Parents, and Caregivers: Understanding the ACG Clinical Guidelines

The guidelines summarize the risk factors, diagnosis, and management of gastroparesis in adults, including dietary, pharmacological, device, and interventions directed at the pylorus

- **"What are they key takeaways in these guidelines for patients?"**
  - The best way to diagnose gastroparesis is with a gamma camera test or a breath test where the meal is labeled with special substances
  - A small particle diet increases symptom relief
  - Several medications are superior to no treatment but evidence of efficacy is weak
  - A gastric electrical stimulation device may be considered for symptom control
  - Cutting of the pylorus (outflow valve) is superior to no treatment; botulinum toxin injection is not recommended
  - In people with diabetes, optimal blood glucose control reduces risk of gastroparesis
- **"Based on these guidelines, what questions should patients ask their physicians about their care?"**
  - Is my stomach emptying test normal?
  - What treatment for the gastroparesis would be recommended based on my nutritional state?
- **•"What warning signs or alarm symptoms should never be ignored?"**
  - Significant weight loss and recurrent dehydration

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Questions?

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