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MIPS Improvement Activity +
Earn ABIM MOC Credit

Missed Diagnosis and Misdiagnosis:

Optimizing Management of Diabetic Gastroparesis

Monday, May 20, 2019

Dinner: 6:00 pm | Symposium: 6:30 pm

Features Interactive 3-D Animation

This program is not affiliated with Digestive Disease Week®.

Provided by: CME Outfitters

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Rochester, MN

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Learning Objective 1

Review the signs, symptoms, and diagnostic tests for diabetic gastroparesis

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Case Study

- A 47-year-old female teacher with 3-year history of postprandial nausea, intermittent vomiting, fullness, early satiety, and epigastric pain
- She has lost 15 pounds in weight over three years
- Was prescribed PPIs and H2 blockers − no response
- EGD x 3 & H. Pylori test were normal
- CAT scan x 2 & U/S scan were normal

47-Year-Old Teacher With Nausea and Vomiting

- Due to lack of relief, 6 months after onset of pain and nausea, she had a HIDA scan
  - 40% ejection fraction
- She underwent a cholecystectomy
- Symptoms persisted
- Failed metoclopramide, 2 PPIs, on prochlorperazine and hyoscyamine prn
  - No relief
- What Next?

Audience Response

What is your differential diagnosis?

A. Functional dyspepsia
B. Gastroparesis
C. Unexplained nausea/vomiting
D. Small intestinal pseudo-obstruction
E. Biliary dyskinesia
F. Not sure

Gastroparesis Cardinal Symptom Index Daily Diary (GCSI-DD)

	None	Mild	Moderate	Severe	Very Severe
Nausea	0	1	2	3	4
Vomiting	0	1	2	3	4
Post-prandial Fullness	0	1	2	3	4
Early Satiety	0	1	2	3	4
Weight Loss	0	1	2	3	4
Abdominal Pain	0	1	2	3	4

Revicki DA, et al. *J of Patient Rep Outcomes* 2018;2(1):61.

47-Yr-Old School Teacher
GCSI – Symptom Profile Score

- Nausea: 4
- Vomiting: 3
- Postprandial fullness: 3
- Early satiety: 3
- Abdominal pain: 3
- Bloating: 4

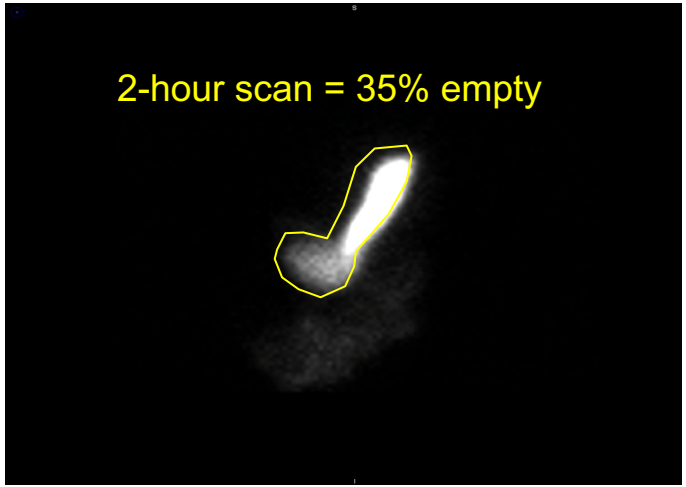
Total GCSI Score = 20/24

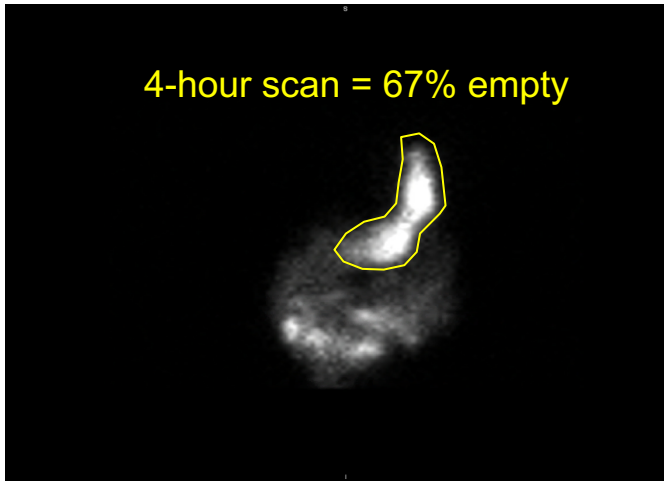
Audience Response

What is your next step in the evaluation of this patient?

A. Gastric emptying test (nuclear scintigraphy) − 2 hours
B. Gastric Emptying Test − 4 hours
C. Wireless motility capsule test
D. ^{13}C-spirulina or ^{13}C-octanoic acid breath test
E. Water load test or nutrient drink test
F. Gastric SPECT scan
G. Not sure

The Importance of 4h GE Scintigraphy





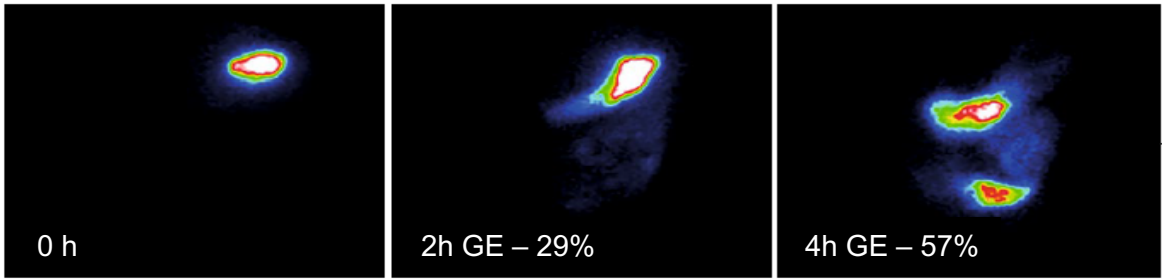
Normal values (median, 5th-95th percentile)	Males (n = 105)	Females (n = 214)
GE2h	60, 28%-82%	47, 25%-71%
GE4h	98, 77%-100%	95, 76%-100%

Kolar G, et al. *Neurogastroenterol Motil.* 2014;26:31-38.

320 kcal, 30% fat, real eggs meal

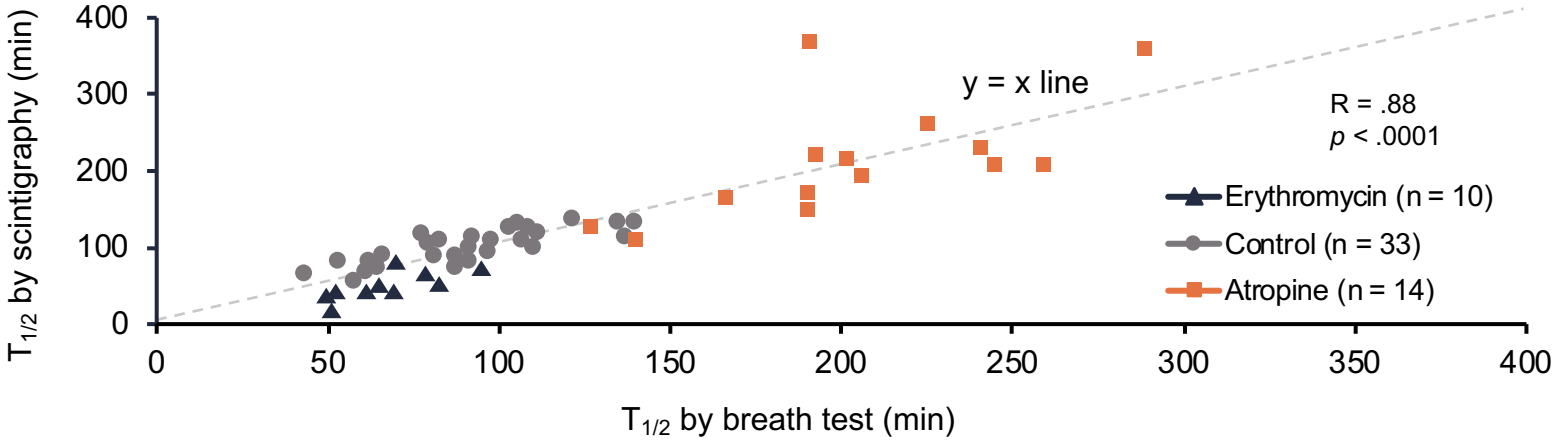
Measurement of Gastric Emptying

Scintigraphy, ^{13}C-spirulina GEBT



Stomach

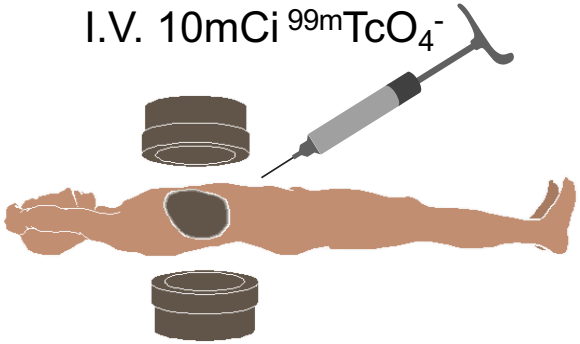
Small intestine

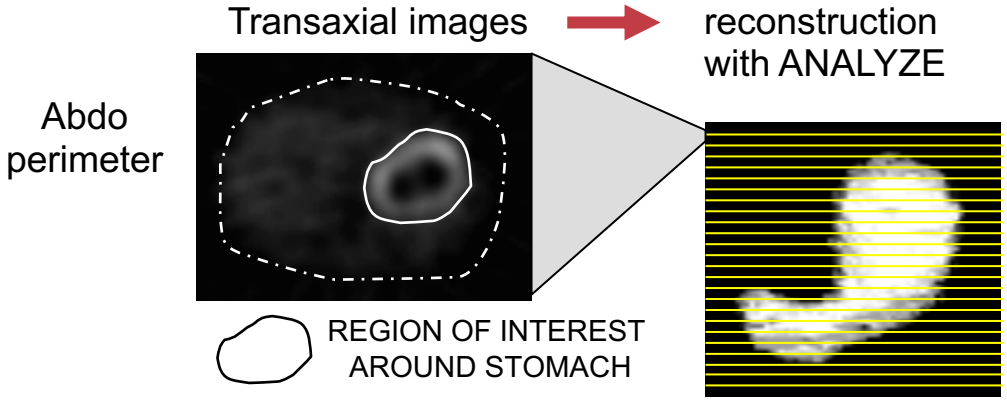


Camilleri M, et al. *Nat Rev Dis Primers*. 2018;4(1):41.

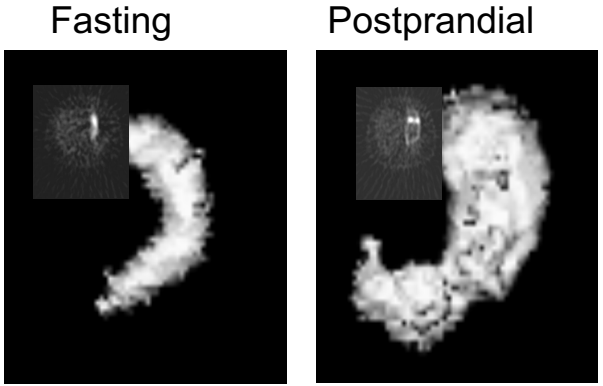
SPECT Method to Measure Gastric Volumes

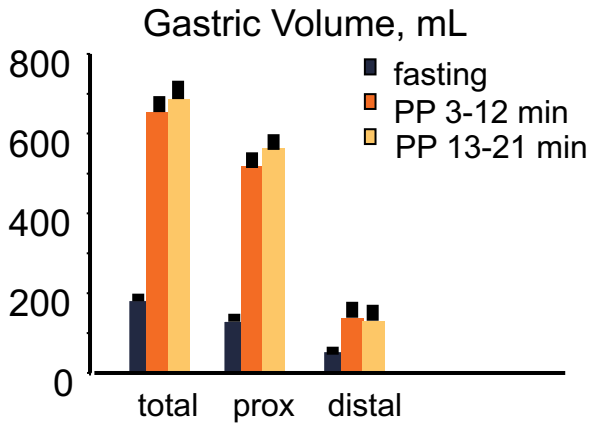
Fasting and Postprandial





SPECT camera to measure gastric volume

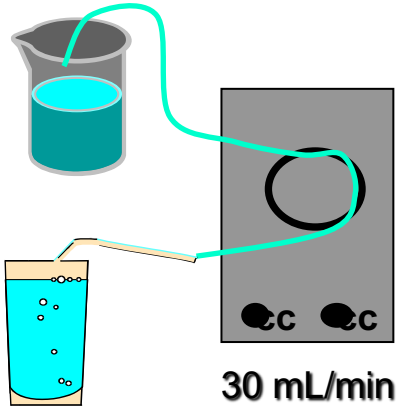




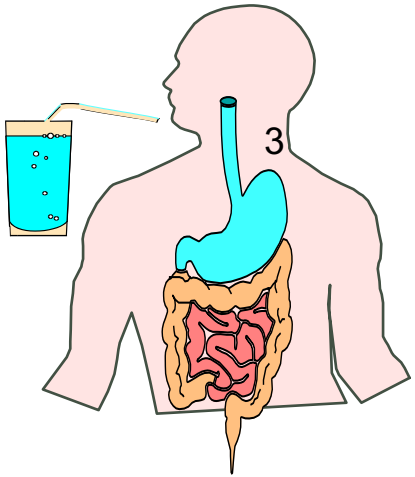
Bouras EP, et al. *Gut.* 2002;51:781-786.

Maximum Tolerable Volume and Symptoms

Nutrition Meal Product



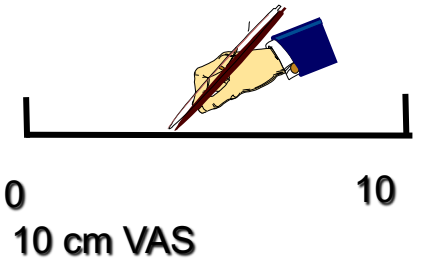
Satiety score every 5 minutes



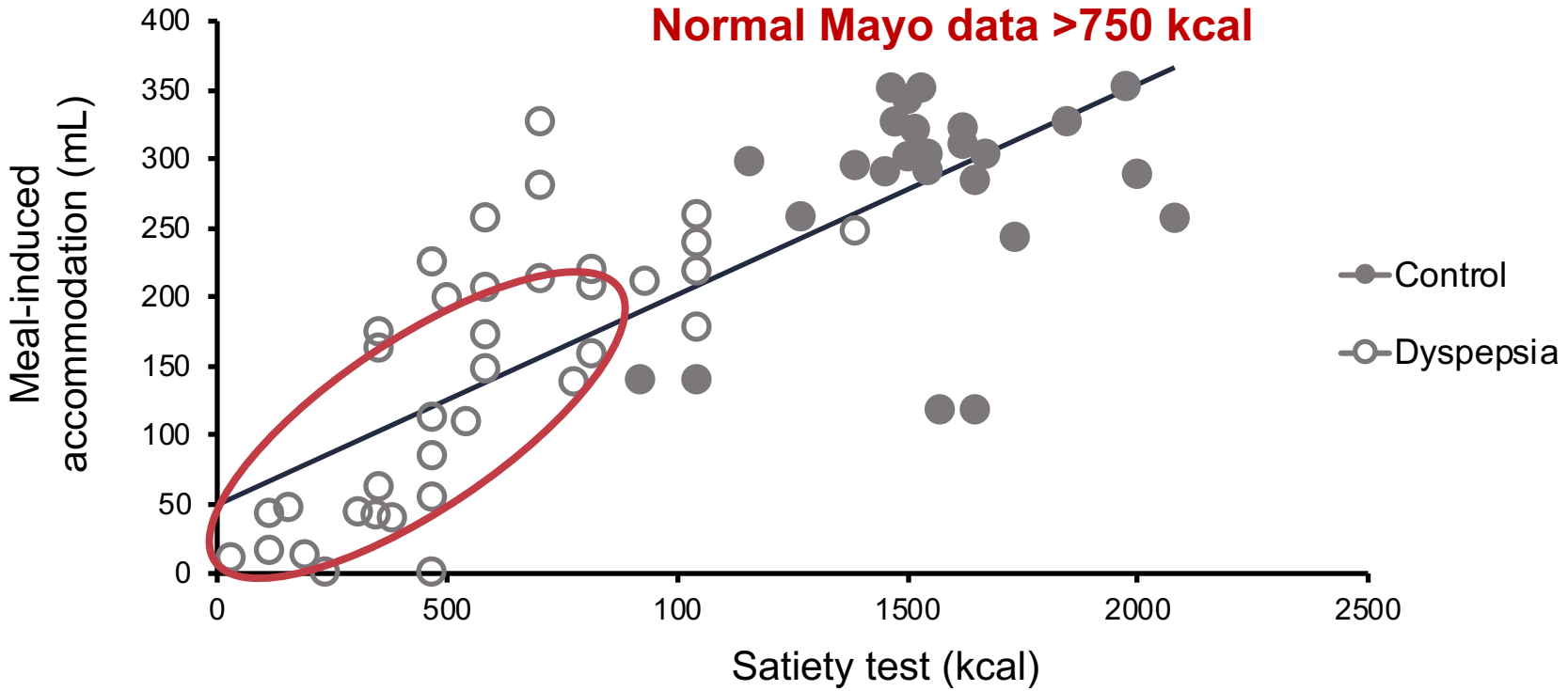
Postprandial symptoms

30 min

- Nausea
- Bloating
- Fullness
- Pain

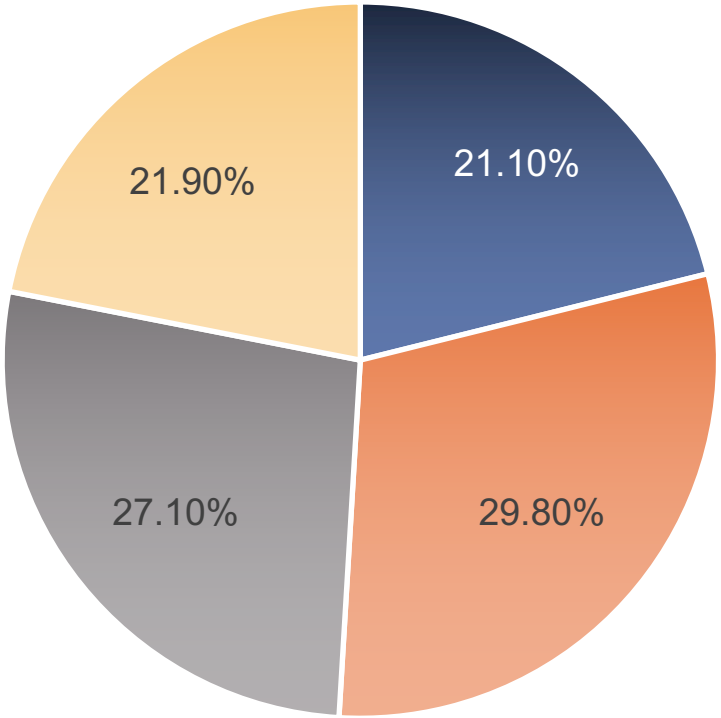


Is There a Surrogate Test for Gastric Accommodation and Sensation?



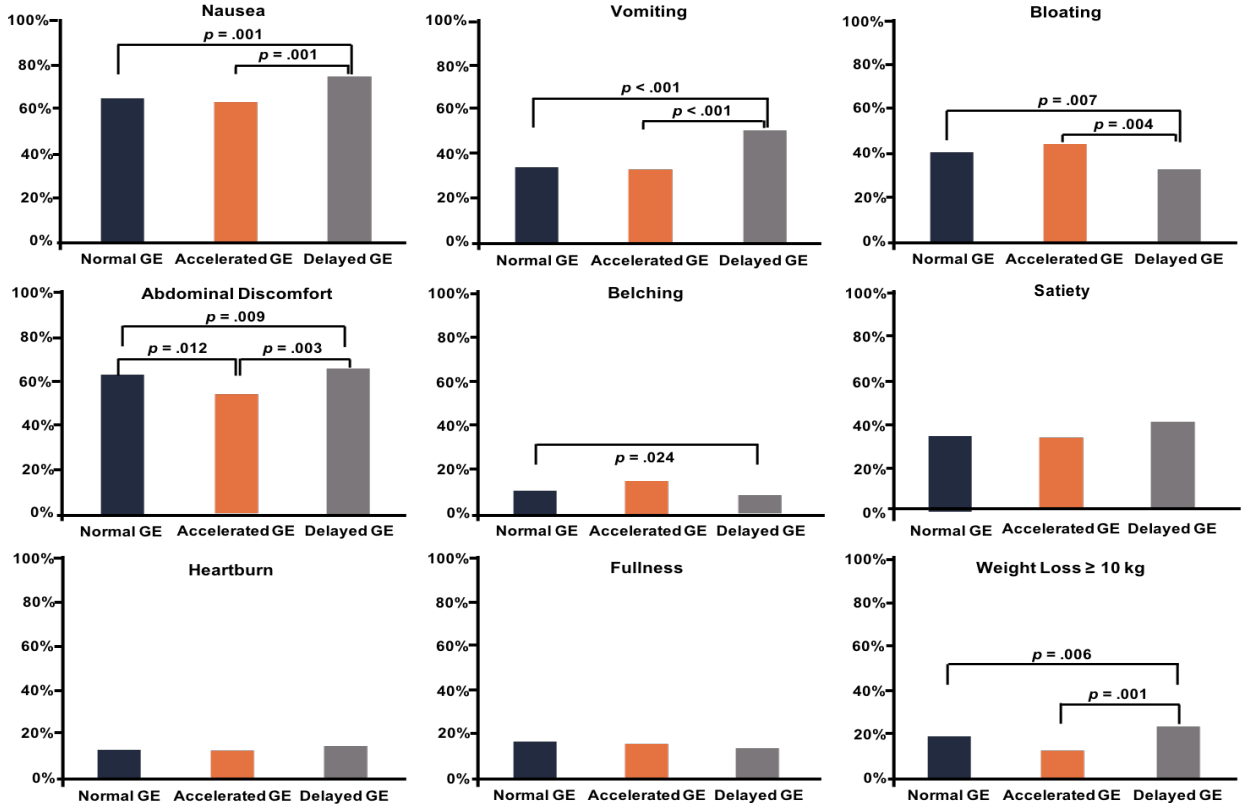
Tack J, et al. *Gut*. 2003;52:1271–1277.

Gastric Motor Dysfunction in 1287 Patients With Functional Gastroduodenal Symptoms



Park SY, et al. *Am J Gastroenterol*. 2017;112:1689-1699.

Gastric Motor Dysfunction in 1287 Patients With Functional Gastroduodenal Symptoms



Park SY, et al. *Am J Gastroenterol*. 2017;112:1689-1699.

Learning Objective 2

Analyze the role of ghrelin in promoting GI motility associated with diabetic gastroparesis

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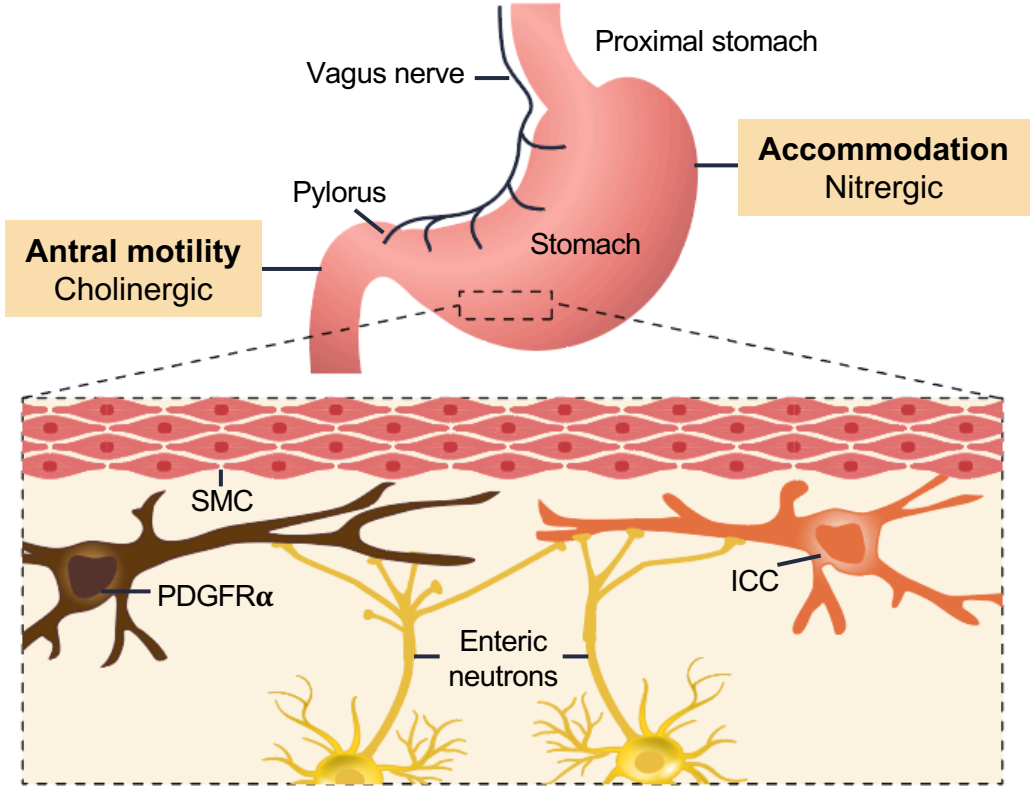
Pathophysiology of Gastroparesis



Camilleri M, et al. *Nat Rev Dis Primers.* 2018;4(1):41.

Case Results

Scintigraphy and WMC

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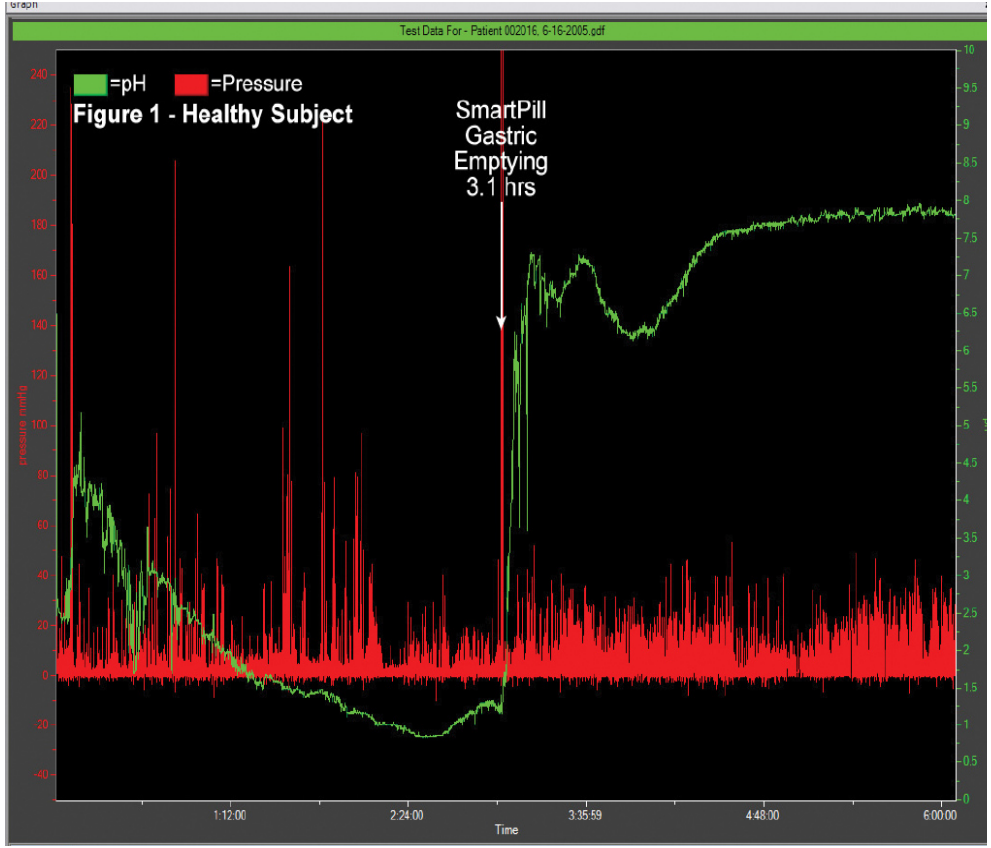
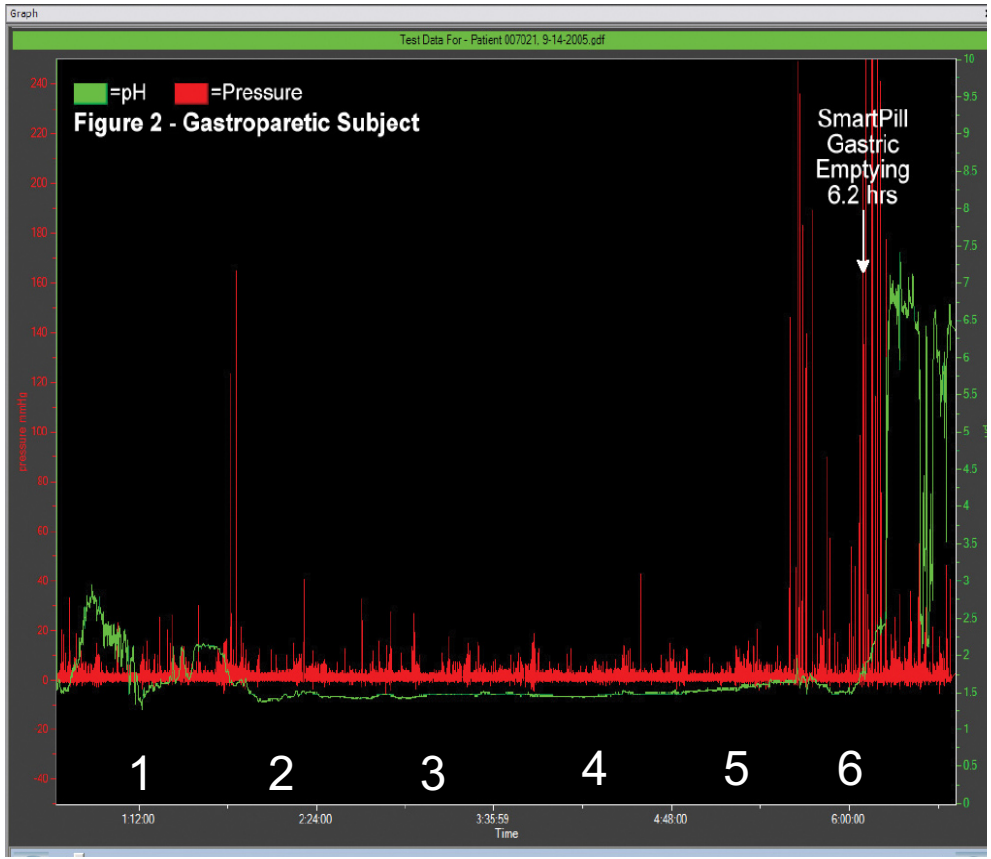
Normal Subject GET

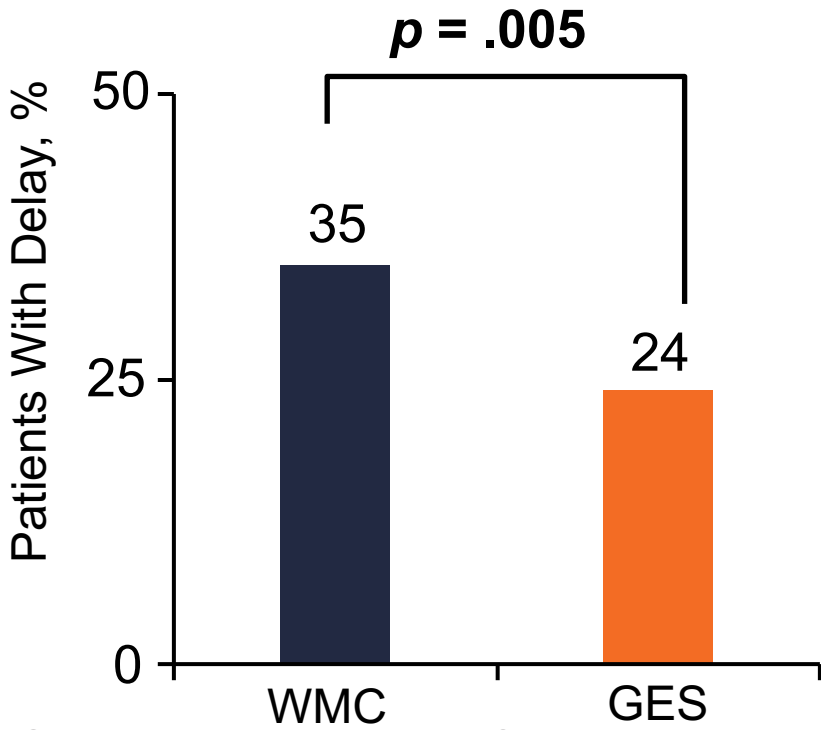


47-Yr-Old Teacher

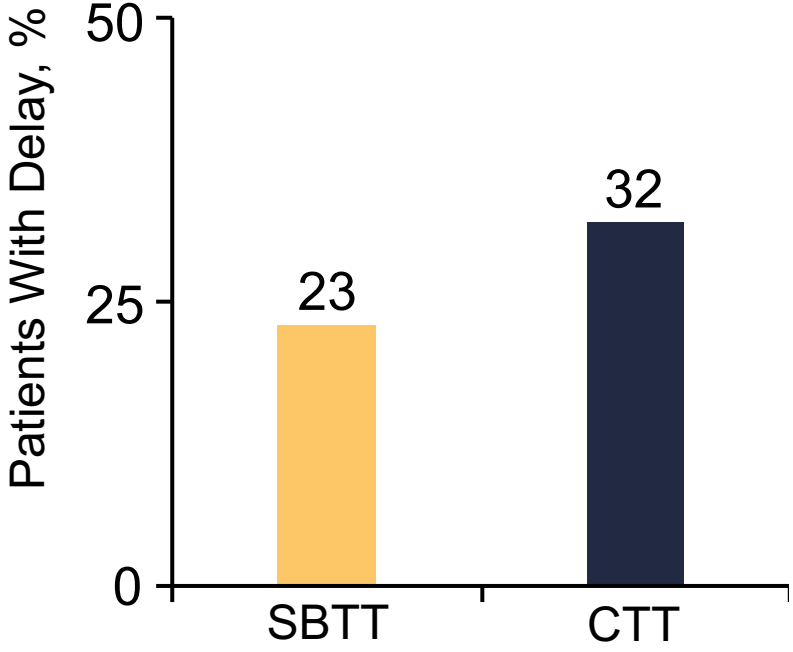


Wireless Motility Capsule (WMC) vs. Gastric Emptying Scintigraphy (GES)

Delayed gastric emptying

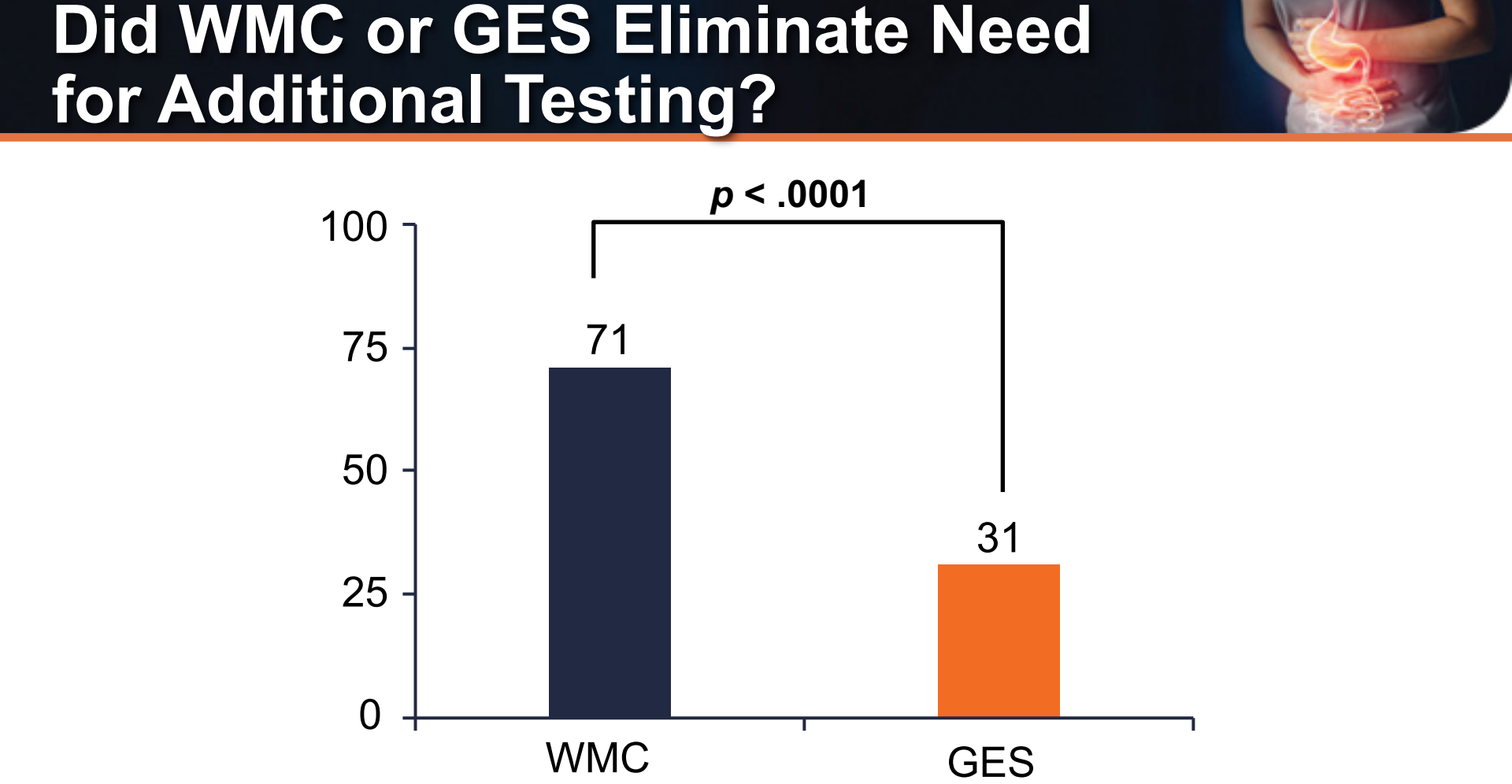


Delayed regional transit time



SBTT = small bowel transit time; CTT = colonic transit time. Hasler W, et al. Presented at: ACG 2017. P801.

Did WMC or GES Eliminate Need for Additional Testing?



Hasler W, et al. Presented at: ACG 2017. P801.

Learning Objective 3

Evaluate the clinical efficacy and safety profiles of current and emerging agents for the management of diabetic gastroparesis

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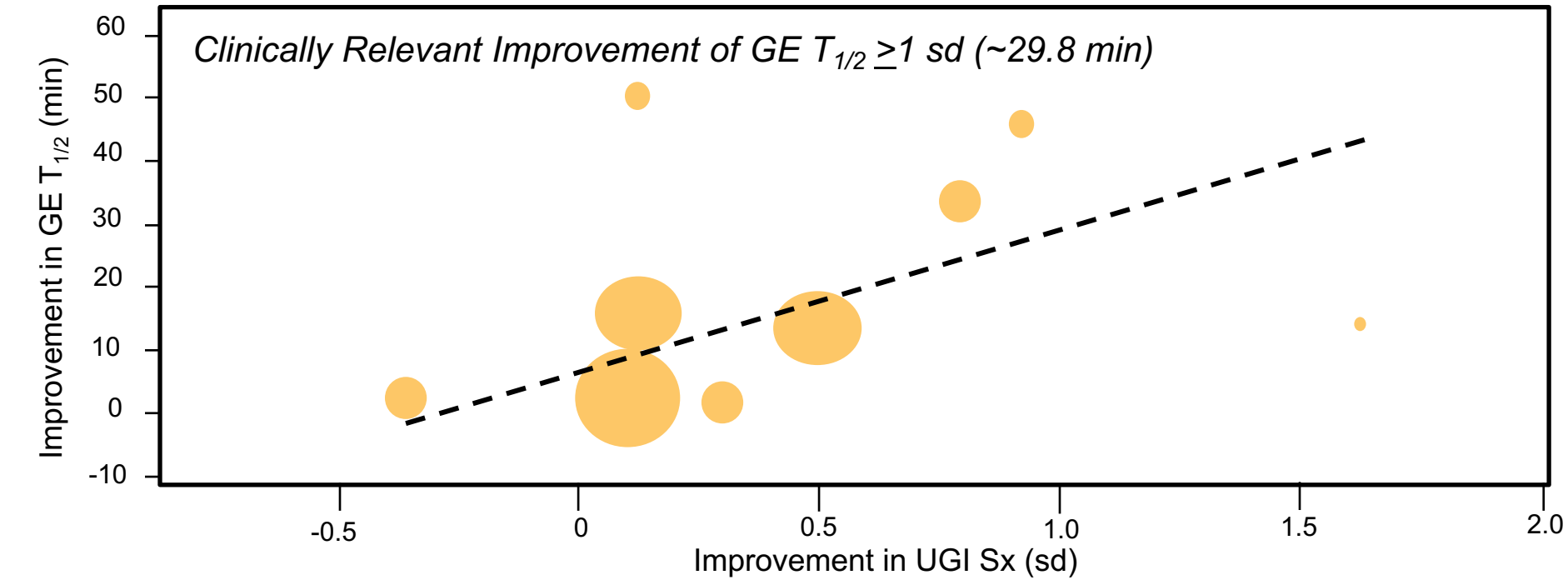
Influence of Promotility Agents on Both Gastric Emptying and Symptoms

A Systematic Review and Meta-Analysis



Various scales or symptoms were utilized in the different trials; the difference in the changes (post – pretreatment) between drug and placebo was converted to a standardized mean difference:
An acceleration of GE by 20.4 minutes resulted in a meaningful improvement in UGI Sx.

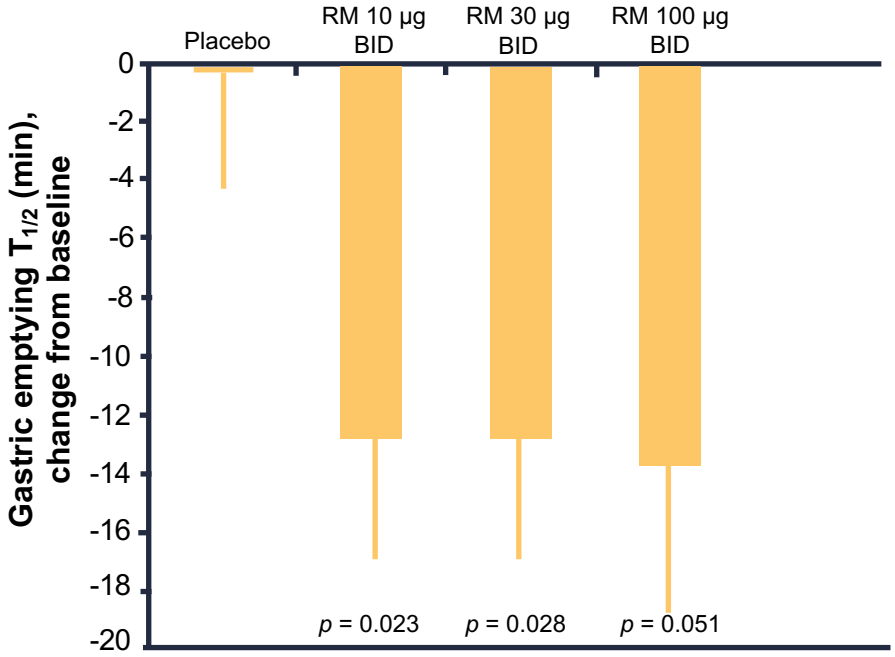
Vijayvargiya P, et al. *Gastroenterology.* 2019;156:1650-1660.

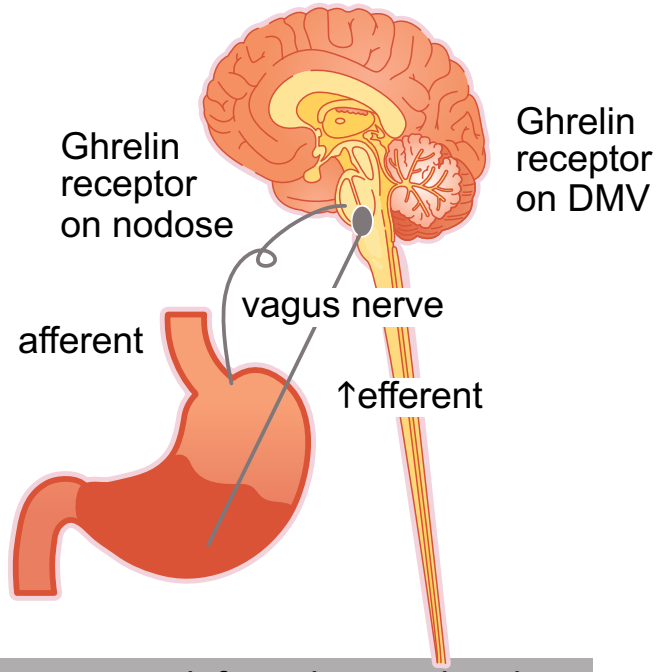
Audience Response

What is your approach for the management of our patient with gastroparesis?

A. Metoclopramide
B. Erythromycin
C. Domperidone
D. Prucalopride
E. Gastric Electrical Stimulation (Enterra)
F. Anti-nausea treatment (prochlorperazine, CBD oil, others)
G. Not sure

Relamorelin: Impact on Gastric Emptying in Phase 2B Study



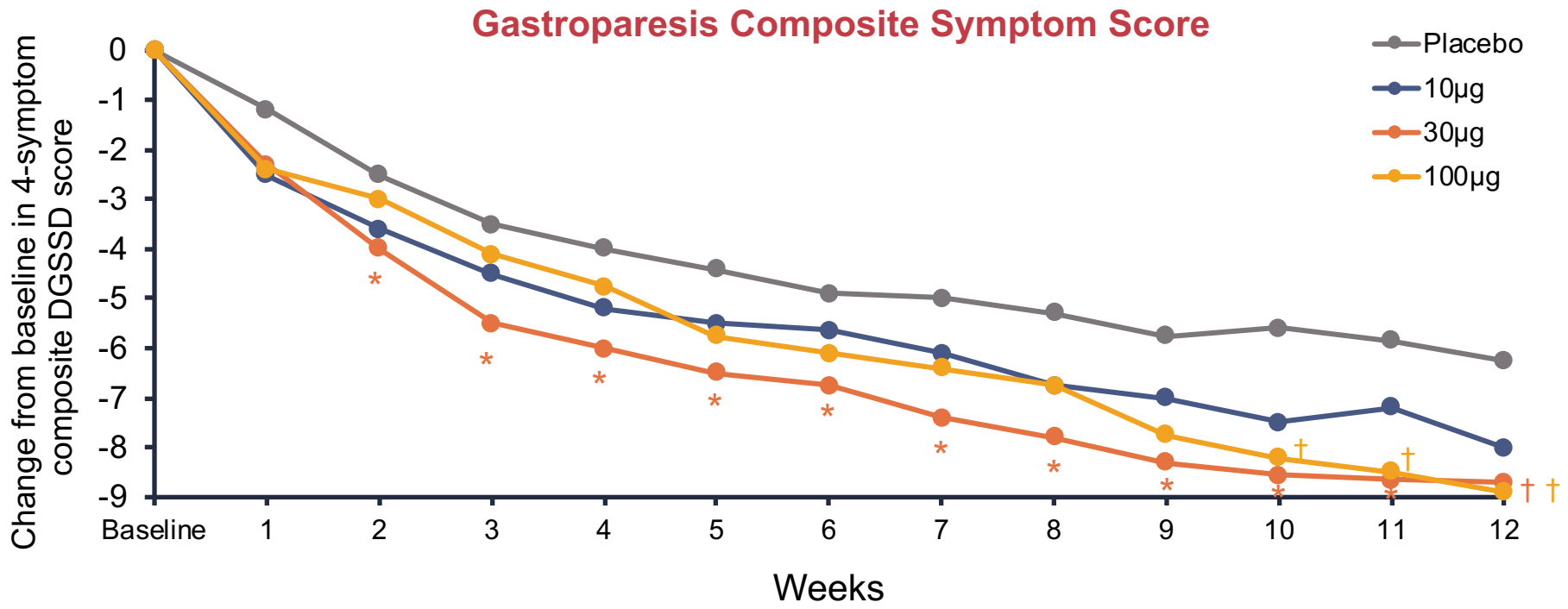


Relamorelin was generally safe; postprandial hyperglycemia may result from the acceleration of gastric emptying and enhanced nutritional intake achievable with relamorelin treatment.

DMV = dorsal motor nucleus of the vagus.

Camilleri M, et al. *Gastroenterology.* 2017;153:1240-1250.

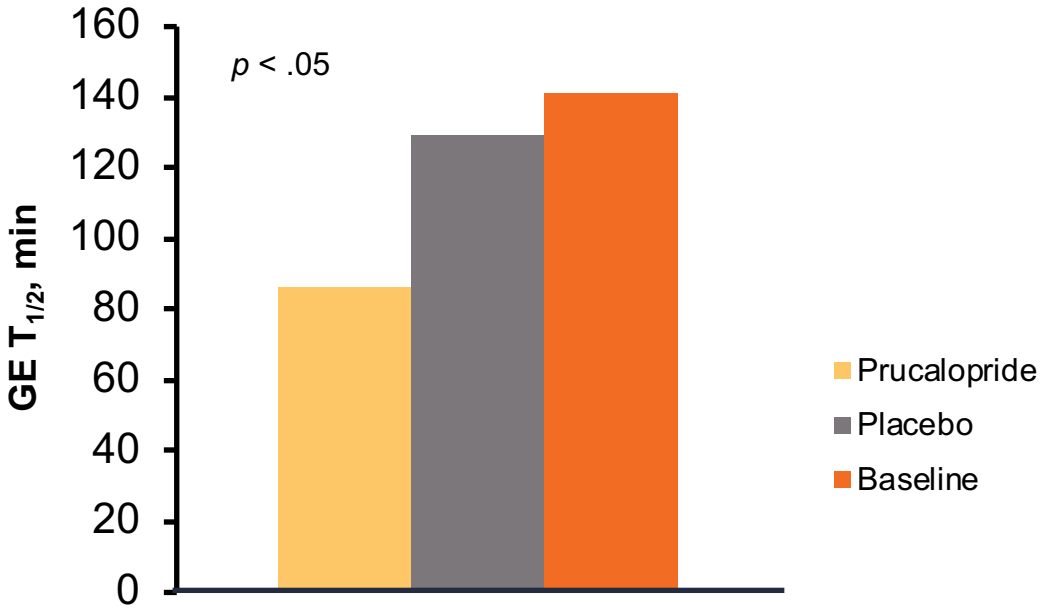
Relamorelin: Impact on Composite DGSSD Score in Phase 2b Study



*$p < .05$; † $.05 \leq p \leq .10$; DGSSD = Diabetic Gastroparesis Symptom Severity Diary.

Camilleri M, et al. *Gastroenterology*. 2017;153:1240-1250.

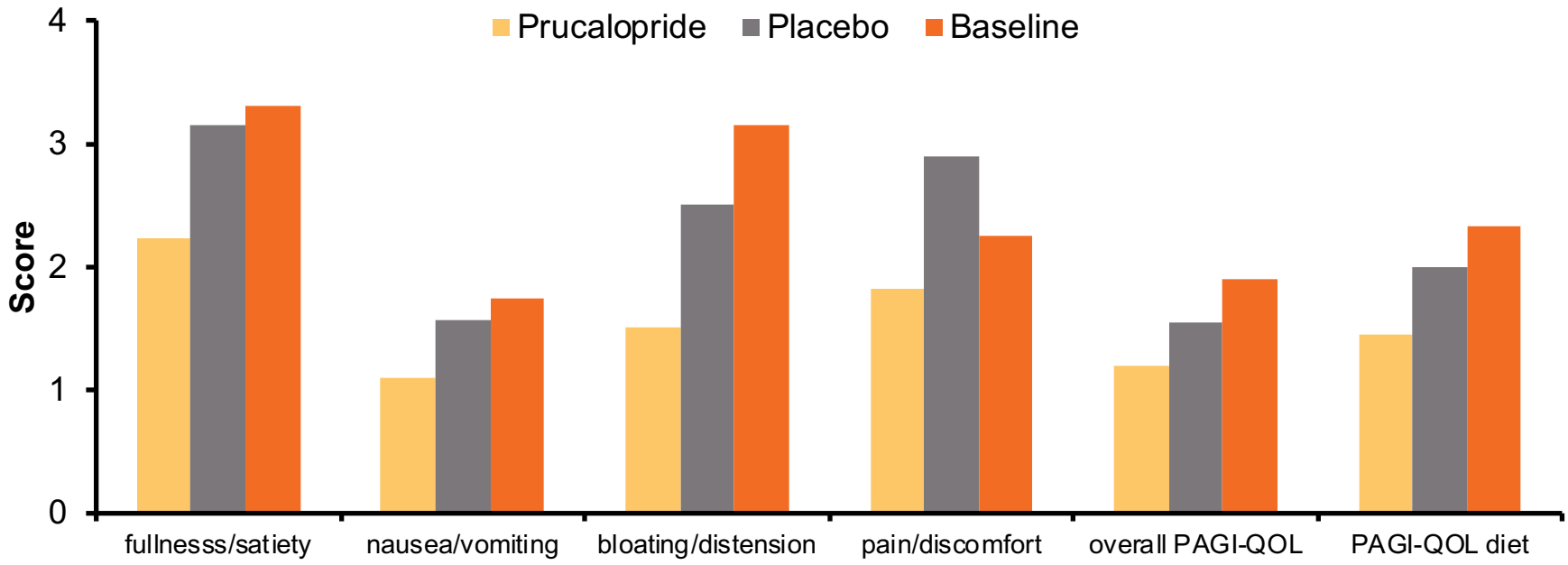
Prucalopride: Impact on Gastric Emptying in Idiopathic Gastroparesis in Placebo-Controlled Crossover Study



- 28 pts w/ idiopathic gastroparesis (7 men, age 42.3 ± 2.6) underwent a ^{13}C-octanoic acid solid GEBT, and symptom severity assessment by GCSI at run-in and at end of 4 wk blinded cross-over treatment periods with placebo or prucalopride 2 mg q.d., separated by 2 weeks wash-out.

Carbone F, et al. *Gastroenterology*. 2016:150:S213-S214.

Prucalopride: Impact on GCSI Subscales in Idiopathic Gastroparesis in Placebo-Controlled Crossover Study



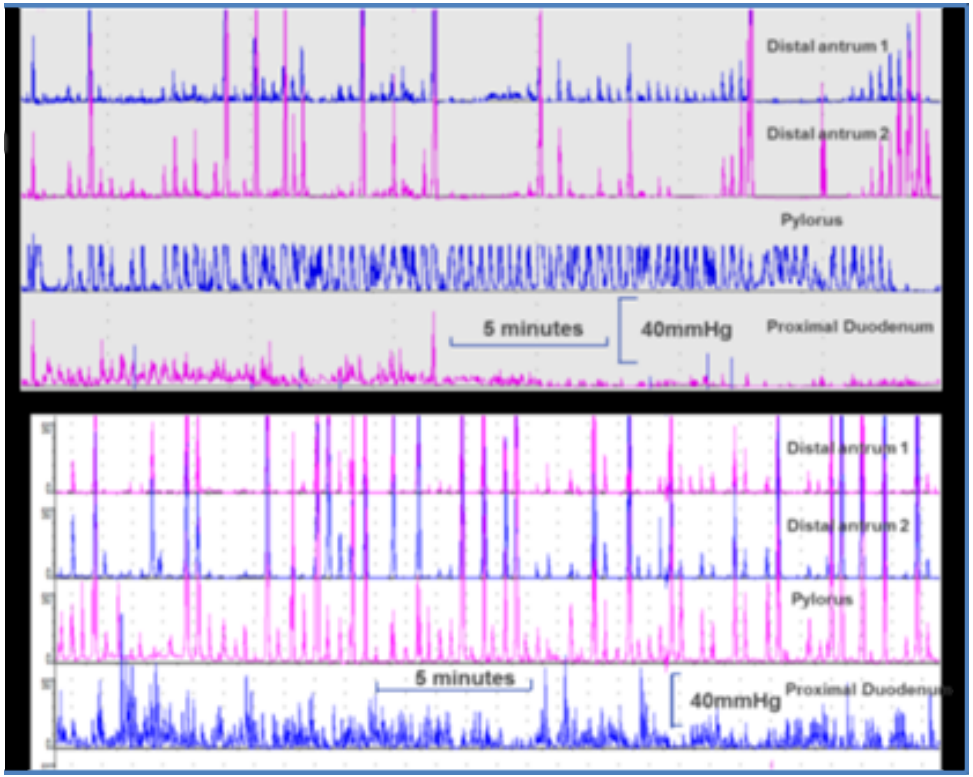
One serious AE occurred (small bowel volvulus in the prucalopride group), and 3 pts dropped out because of nausea and headache (all prucalopride).

Carbone F, et al. Gastroenterology. 2016:150:S213-S214.

Antroduodenal Motility Tracings in the Postprandial Period With Sensors 1 cm Apart

Pylorospasm

Normal Antro-Pyloro-Duodenal coordination



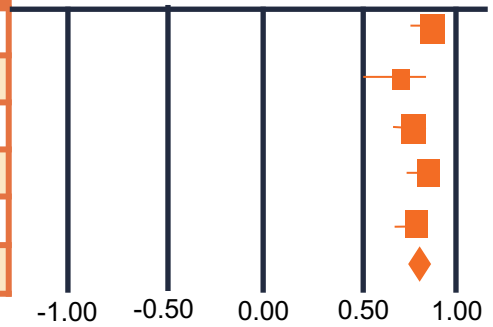
Camilleri M. *Clin Gastroenterol Hepatol*. 2016;14:1072-1080.

Forest Plot Displaying Weighted Pool Rate for Clinical Success of G-POEM in Refractory Gastroparesis

Clinical Success

Study Name	N	WPR	Lower Limit	Upper Limit
Khashab	30	0.867	0.694	0.949
Malik	13	0.727	0.414	0.910
Gonzalez	29	0.793	0.610	0.904
Kahaleh	33	0.848	0.684	0.935
Mekaroonkamol	30	0.800	0.621	0.907
Mean		0.816	0.740	0.874

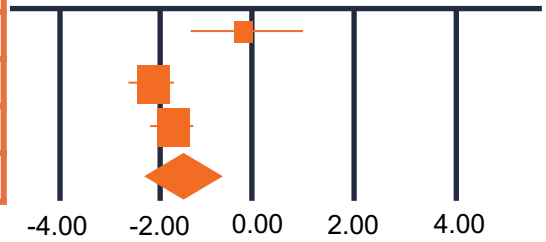
WPR and 95% CI



GCSI before and 5 days after procedure

Study Name	Statistics for each study			
	Difference in means	Lower limit	Upper limit	*p value*
Malik	-0.200	-1.418	1.018	0.748
Xue	-2.090	-2.492	-1.688	0.000
Mekaroonkamol	-1.700	-2.117	-1.283	0.000
Mean	-1.574	-2.259	-0.890	0.000

Difference in means and 95% CI

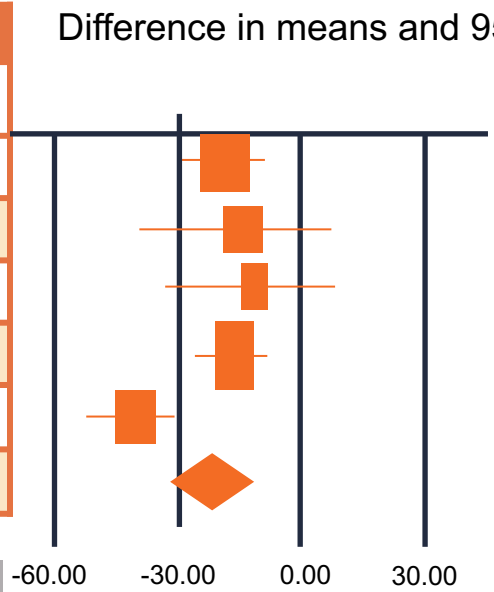


Meybodi MA, et al. *Endosc Int Open*. 2019;7:E322-E329.

Forest Plot Displaying Weighted Pool Rate for Clinical Success of G-POEM in Refractory Gastroparesis

Gastric retention 4 hours after solid meal on GES before and after the procedure

Study Name	Statistics for each study			
	Difference in means	Lower limit	Upper limit	*p value*
Khashab	-20.000	-30.000	-9.974	0.000
Malik	-16.000	-38.182	6.182	0.157
Gonzalez	-12.000	-32.527	8.572	0.252
Rodriguez	-16.800	-27.152	-6.448	0.001
Mekaroonkamol	-40.800	-52.424	-29.176	0.000
	-22.308	-32.944	-11.671	0.000



Conclusion: G-POEM is promising
Sham-controlled trials are needed

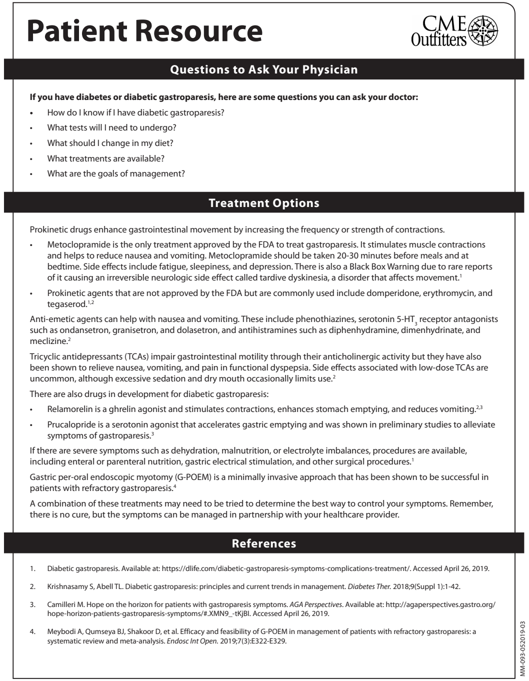
Meybodi MA, et al. *Endosc Int Open*. 2019;7:E322-E329.

SMART Goals

Specific, **M**easurable, **A**ttainable, **R**elevant, **T**imely

- Symptoms of DG overlap with those of other gastrointestinal disorders, and it is important to distinguish among them.
- Ghrelin has an important role in the regulation of gastric motility.
- New treatments for DG that can improve outcomes for patients are on the horizon.

Resources to Use With Your Patients



Patient Resource

CME Outfitters

Questions to Ask Your Physician

If you have diabetes or diabetic gastroparesis, here are some questions you can ask your doctor:

- How do I know if I have diabetic gastroparesis?
- What tests will I need to undergo?
- What should I change in my diet?
- What treatments are available?
- What are the goals of management?

Treatment Options

Prokinetic drugs enhance gastrointestinal movement by increasing the frequency or strength of contractions.

- Metoclopramide is the only treatment approved by the FDA to treat gastroparesis. It stimulates muscle contractions and helps to reduce nausea and vomiting. Metoclopramide should be taken 20-30 minutes before meals and at bedtime. Side effects include fatigue, sleepiness, and depression. There is also a Black Box Warning due to rare reports of it causing an irreversible neurologic side effect called tardive dyskinesia, a disorder that affects movement.[1]
- Prokinetic agents that are not approved by the FDA but are commonly used include domperidone, erythromycin, and tegaserod.[1,2]

Anti-emetic agents can help with nausea and vomiting. These include phenothiazines, serotonin 5-HT_3 receptor antagonists such as ondansetron, granisetron, and dolasetron, and antihistamines such as diphenhydramine, dimenhydrinate, and meclizine.[2]

Tricyclic antidepressants (TCAs) impair gastrointestinal motility through their anticholinergic activity but they have also been shown to relieve nausea, vomiting, and pain in functional dyspepsia. Side effects associated with low-dose TCAs are uncommon, although excessive sedation and dry mouth occasionally limits use.[2]

There are also drugs in development for diabetic gastroparesis:

- Relamorelin is a ghrelin agonist and stimulates contractions, enhances stomach emptying, and reduces vomiting.[2,3]
- Prucalopride is a serotonin agonist that accelerates gastric emptying and was shown in preliminary studies to alleviate symptoms of gastroparesis.[3]

If there are severe symptoms such as dehydration, malnutrition, or electrolyte imbalances, procedures are available, including enteral or parenteral nutrition, gastric electrical stimulation, and other surgical procedures.[1]

Gastric per-oral endoscopic myotomy (G-POEM) is a minimally invasive approach that has been shown to be successful in patients with refractory gastroparesis.[4]

A combination of these treatments may need to be tried to determine the best way to control your symptoms. Remember, there is no cure, but the symptoms can be managed in partnership with your healthcare provider.

References

1. Diabetic gastroparesis. Available at: https://dlife.com/diabetic-gastroparesis-symptoms-complications-treatment/. Accessed April 26, 2019.
2. Krishnasamy S, Abell TL. Diabetic gastroparesis: principles and current trends in management. *Diabetes Ther.* 2018;9(Suppl 1):1-42.
3. Camilleri M. Hope on the horizon for patients with gastroparesis symptoms. *AGA Perspectives*. Available at: http://agaperspectives.gastro.org/hope-horizon-patients-gastroparesis-symptoms/#.XMN9_-tKjBI. Accessed April 26, 2019.
4. Meybodi A, Qumseya BJ, Shakoor D, et al. Efficacy and feasibility of G-POEM in management of patients with refractory gastroparesis: a systematic review and meta-analysis. *Endosc Int Open.* 2019;7(3):E322-E329.

MM-093-052019-03

www.CMEOutfitters.com/gastrohub

Questions & Answers

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  (If you are claiming ABIM MOC, Dental, or Pharmacy credit, add your identification number on this survey)
- **Complete the evaluation** displayed during Q&A
- CME Outfitters will **email your certificate** after the symposium

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1. Be sure to fill in your **ABIM ID number** and **DOB** (MM/DD) on the initial survey, so we can submit your credit to ABIM.
2. Actively participate in the discussion by **responding to ARS** and/or **asking the faculty questions**

   (It's ok if you miss answering a question or get them wrong; you can still claim MOC)
3. Complete your post-test and evaluation at the conclusion of the live meeting

Resources

Today's presentation slides and resources will be available for download at:
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