GHAPP

Gastroenterology & Hepatology
Advanced Practice Providers

2021 Fourth Annual National Conference

September 9-11, 2021

Red Rock Hotel – Las Vegas, NV

Jointly provided by the Annenberg Center for Health Sciences at Eisenhower
and Gastroenterology and Hepatology Advanced Practice Providers.

GHAPP
Gastroenterology & Hepatology
Advanced Practice Providers

Gastroesophageal Reflux Disease

versus

Functional Dyspepsia

versus

Gastroparesis

Monica Nandwani, DNP, RN, FNP-BC

Disclosures

All individuals in control of the content of continuing education activities provided by the Annenberg Center for Health Sciences at Eisenhower are required to disclose to the audience any real or apparent commercial financial affiliations related to the content of the presentation or enduring material. Full disclosure of all commercial relationships must be made in writing to the audience prior to the activity. All staff at the Annenberg Center for Health Sciences at Eisenhower and the Gastroenterology and Hepatology Advanced Practice Providers have no relationships to disclose.

Disclosures

Monica Nandwani, DNP, RN, FNP-BC

Advisory Board: Phathom Pharmaceuticals, Clinical Area- H. pylori

Objectives

Define gastroesophageal reflux disease (GERD), functional dyspepsia (FD), and gastroparesis (GP)

Discuss the overlap of symptoms and pathophysiology of GERD, FD, and GP

Review treatment options for GERD, FD, and GP

Definitions

GERD	• Reflux of stomach contents causing **troublesome** symptoms and/or complications[1]
FD	• **One or more** of the following: a. Bothersome postprandial fullness b. Bothersome early satiation c. Bothersome epigastric pain d. Bothersome epigastric burning AND **no evidence of structural disease** (including at upper endoscopy) that is likely to explain the symptoms
GP	• **Delayed gastric emptying** of solid food in the **absence of** a mechanical **obstruction** of the stomach[3]

1. Vakil N et al. *Am J Gastroenterol*. 2006;101(8):1900-20;
2. Stanghellini et al. *Gastroenterology*. 2016;150(6):1380-92
3. Camilleri M et al. *Nat Rev Dis Primers*. 2018; 4(1):41

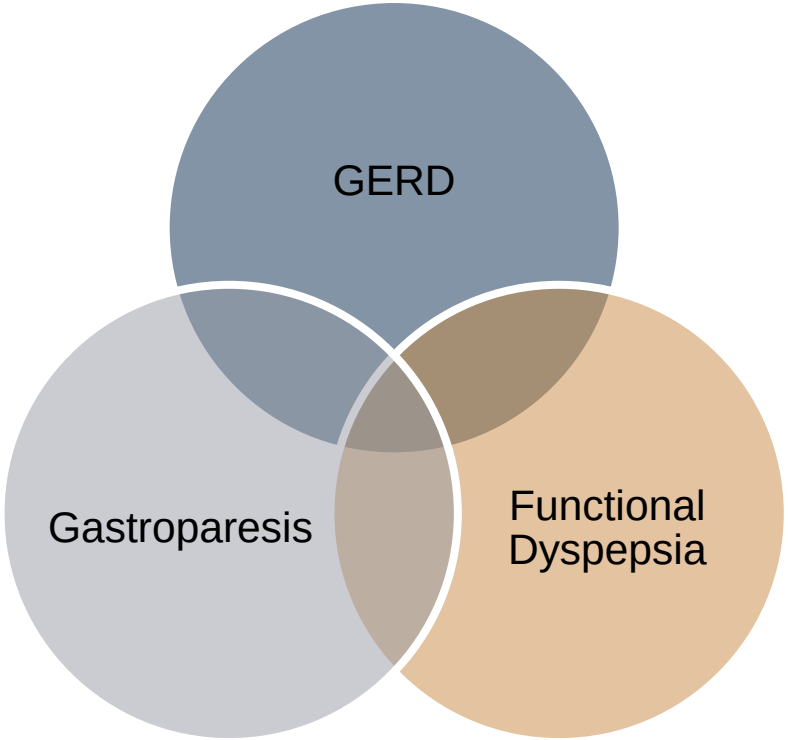
Is It GERD, FD, or GP?

Epigastric burning

Epigastric pain

Post-prandial fullness

Early satiety



Belching

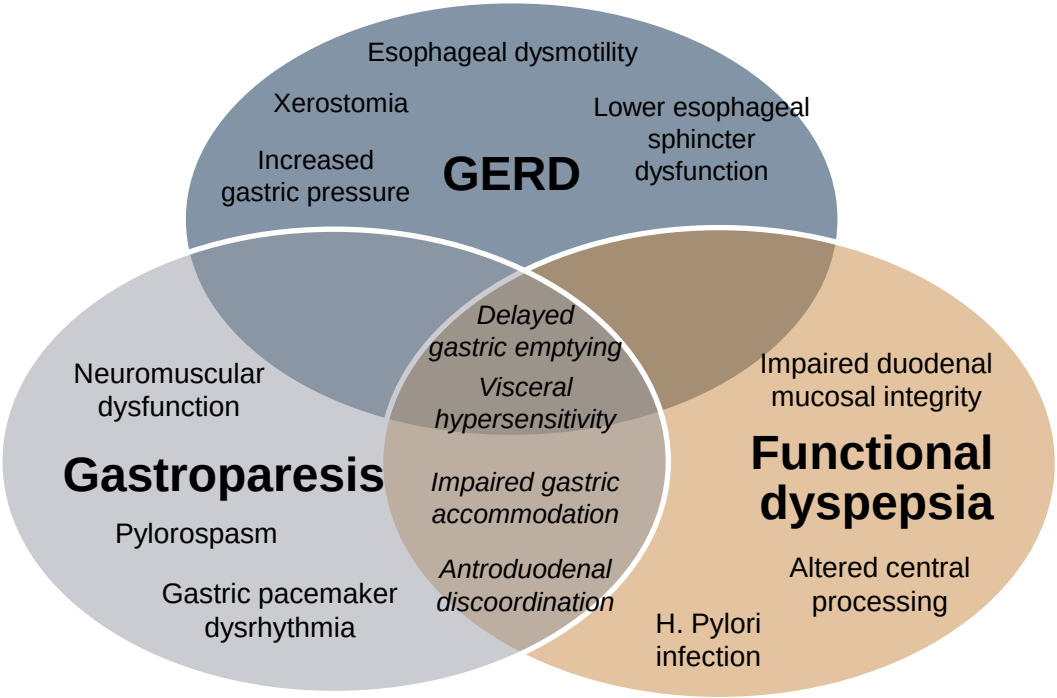
Upper abdominal bloating

Heartburn

Nausea and/or Vomiting

Maret-Ouda J, Markar SR, Lagergren J. *JAMA.* 2020; 324(24), 2536–2547.
Tack J, Camilleri M. *Curr Opin Pharmacol*. 2018;43:111-117.

Pathophysiology



Camilleri M. UpToDate. 2021; Camilleri M et al. *Nat Rev Dis Primers*. 2018; 4(1):41; Cangemi DJ, Lacy BE. *Curr Opin Gastroenterol*. 2020;36(6):509-517; Kim BJ, Kuo B. *J Neurogastroenterol Motil*. 2019;25(1):27-35; Sharma P, Yadlapati R. Ann N. *Y Acad Sci*. 2021;1486(1):3-14; Savarino E et al. *Nat Rev Gastroenterol Hepatol.* 2018;15(5), 323; Tack J, Camilleri M. *Curr Opin Pharmacol*. 2018;43:111-117. Wauters et al. United European Gastroenterol J. 2021;9(3):307-331.

GHAPP
Gastroenterology & Hepatology
Advanced Practice Providers

GERD

GERD

1 in 5 Americans experience GERD ≥1x/week[1]

One of the most common diseases encountered by gastroenterologists[2]

US annual direct cost estimated at over $10 billion[3]

Up to 40% of patients with suspected GERD have inadequate symptom relief despite PPI therapy[4]

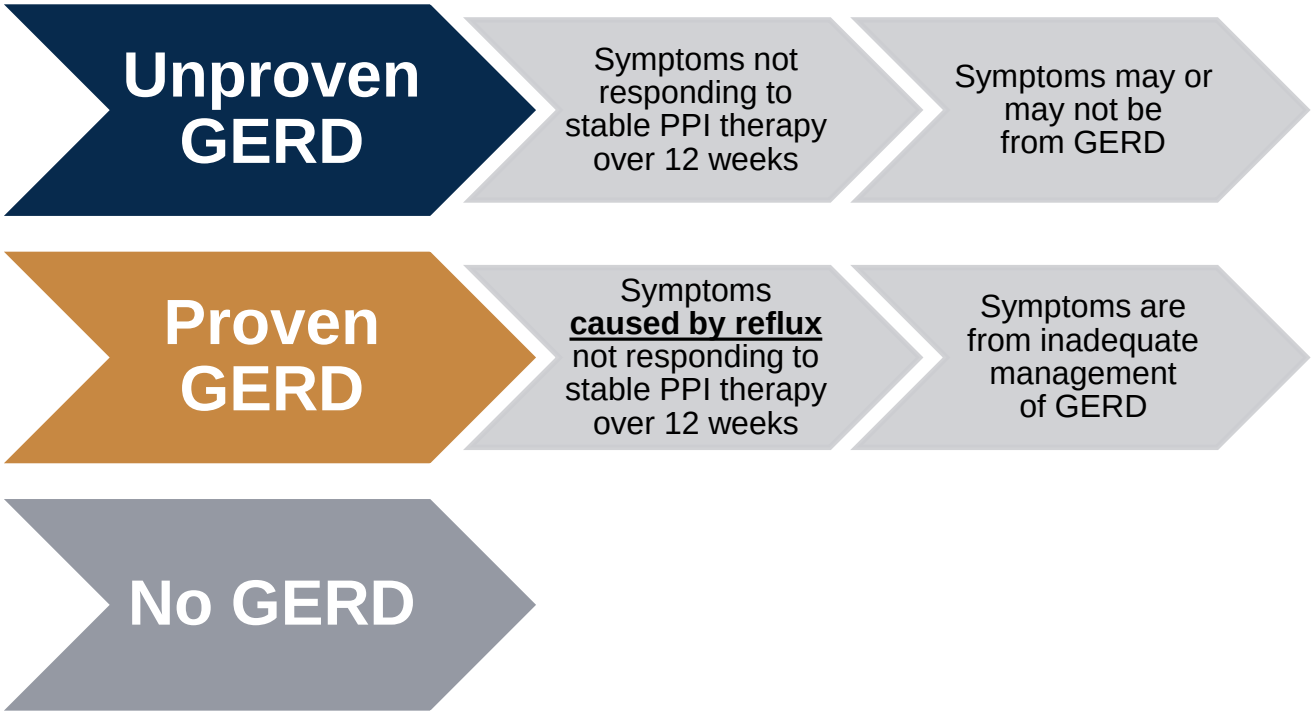
1. US Department of Health and Human Services 2014; 2. Katz PO, Gerson LG, Vela MF. *Am J Gastroenterol.* 2013; 108: 308 – 328;
3. Gyawali CP et al. *Gut*. 2018; 67: 1351– 1362; 4. Yadlapati R, DeLay K. *Med Clin North Am*. 2019; 103(1), 15–27.

GERD – The Lyon Consensus

	ENDOSCOPY	pH or pH-IMPEDANCE	HIGH RESOLUTION ESOPHAGEAL MANOMETRY
CONCLUSIVE **EVIDENCE FOR** PATHOLOGIC REFLUX	LA grades C&D esophagitis Long segment Barrett's mucosa (≥3 cm) Peptic esophageal stricture	AET >6%	
BORDERLINE OR **INCONCLUSIVE** EVIDENCE	LA grades A & B esophagitis	AET 4 – 6% Reflux episodes 40 – 80	ADJUNCTIVE OR SUPPORTIVE EVIDENCE Hypotensive EGJ Hiatal hernia Esophageal hypomotility
EVIDENCE AGAINST PATHOLOGIC REFLUX		AET <4% Reflux episodes <40	

Gyawali CP et al. *Gut*. 2018;67;1351– 1362.

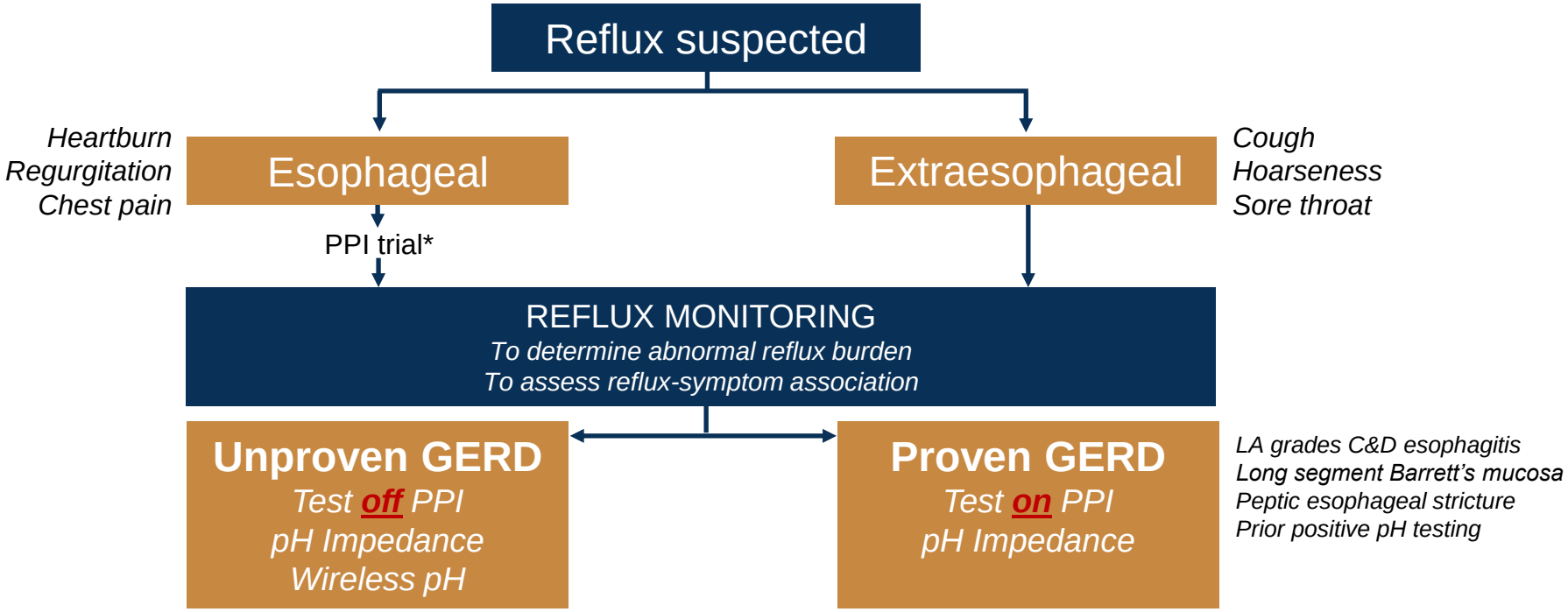
Defining GERD Symptoms



Adapted from ACG Virtual Grand Rounds by C. Prakash Gyawali on 7.29.2021.

Testing ON Versus OFF PPI Therapy

Endoscopy to evaluate for mucosal or mechanical processes



*If not performed earlier

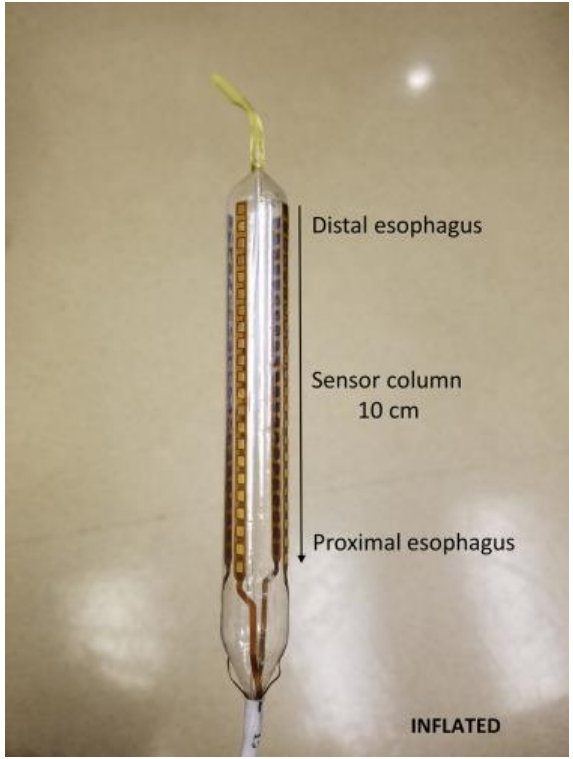
Gyawali et al. *Am J Gastroenterol*. 2020;115(9):1412-1428.

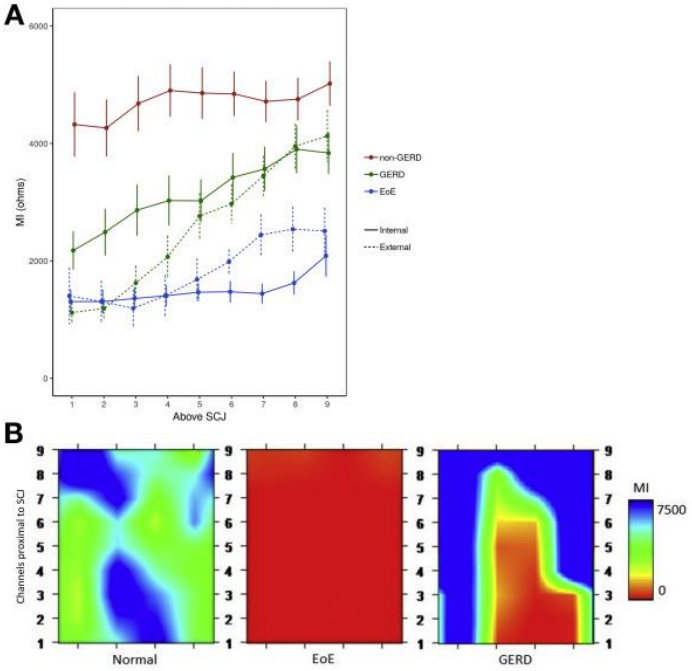
Mucosal Impedance

Novel balloon catheter with 36 channels that measures esophageal mucosal integrity via impedance

May predict GERD and EoE

FDA Approved in December 2019





Patel et al. *Gastroenterology*. 2019;156(6):1617-1626.e1.

GERD Phen

Not all GERD is the same

- NERD
- Reflux hypersensitivity
- Functional heartburn
- Erosive esophagitis, low grade
- Erosive
- Reflux chest pain syndrome
- Regurgitation-dominant reflux disease
- Laryngopharyngeal reflux
- Chronic cough

Katzka DA, Pandolfino JE, Kahrilas PJ. *Clin Gastroenterol Hepatol*. 2020;18(4):767-776.

Treatment of GERD

Lifestyle Modification	Pharmacologic Therapy	Endoscopic Management	Surgical Management	Alternative Therapies
• Selective dietary avoidance • Small meal size • Weight loss • Smoking Cessation • Alcohol avoidance • HOB elevation • Avoiding post-prandial recumbency	• Acid suppression – H2RAs – PPIs – PCABs • Reflux inhibition – Baclofen* – Prokinetics* • Neuromodulators* • Alginates and surface acting compounds	• Transoral incisionless fundoplication (TIF) • Radiofrequency ablation (RFA) • Anti-reflux Mucosectomy (ARMS) • Injectables	• Magnetic sphincter augmentation (MSA) • Roux-en-Y Gastric bypass • Fundoplication (Nissen, Toupet, Dor)	• Melatonin • Herbal Therapies (STW5, Rikkunshito) • Acupuncture • Diaphragmatic breathing

***Denotes off-label use**

Ahuja A, Ahuja NK. Curr Gastroenterol Rep 2019; 10: 1 – 8; Gyawali CP, Fass R. Gastroenterology, 2018;154(2), 302–318; Katzka DA, Kahrilas PJ. BMJ. 2020;371:m3786; Kushner et al. Ann N Y Acad Sci. 2020;1482(1):121-129.

GHAPP
Gastroenterology & Hepatology
Advanced Practice Providers

Functional Dyspepsia

Dyspepsia

Functional dyspepsia refers to patients where diagnostic testing has ruled out organic pathology

~20% of global population has symptoms of dyspepsia

More common in women, smokers and on NSAIDs

Estimated cost of >$18B per annum

Moayyedi PM et al. *Am J Gastroenterol*. 2017;112(7):988-1013.

Functional Dyspepsia

Rome IV Criteria PDS

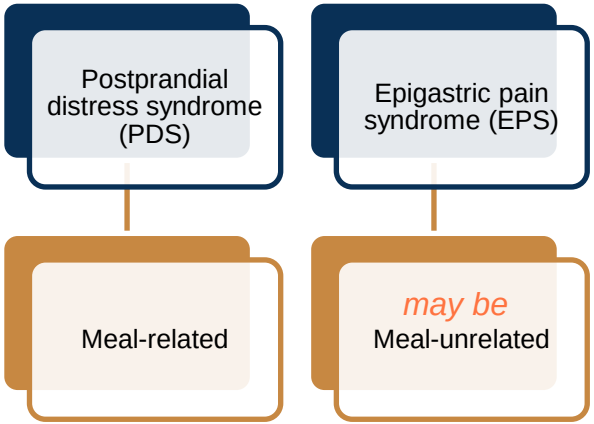
Must include one or both of the following at least 3 days a week:*

1. Bothersome post-prandial fullness
2. Bothersome early satiation

Supportive Criteria:

- Postprandial epigastric pain or burning, epigastric bloating, excessive belching, and nausea can also be present
- Vomiting warrants consideration of another disorder
- Heartburn is not a dyspeptic symptoms but may often co-exist
- Symptoms that are relieved by evacuation of feces or gas should generally not be considered as part of dyspepsia

Other individual digestive symptoms or groups of symptoms (from GERD and IBS) may co-exist with PDS



Rome IV Criteria EPS

Must include one or both of the following at least 1 day a week:*

1. Bothersome epigastric pain
2. Bothersome epigastric burning

Supportive Criteria:

1. Pain may be induced by ingestion of a meal, relieved by ingestion of a meal, or may occur while fasting
2. Postprandial epigastric bloating, belching, and nausea can also be present
3. Persistent vomiting likely suggests another disorder
4. Heartburn is no a dyspeptic symptom but may often coexist
5. The pain does not fulfill biliary pain criteria
6. Symptoms that are relieved by evacuation of feces or gas should not be considered as part of dyspepsia

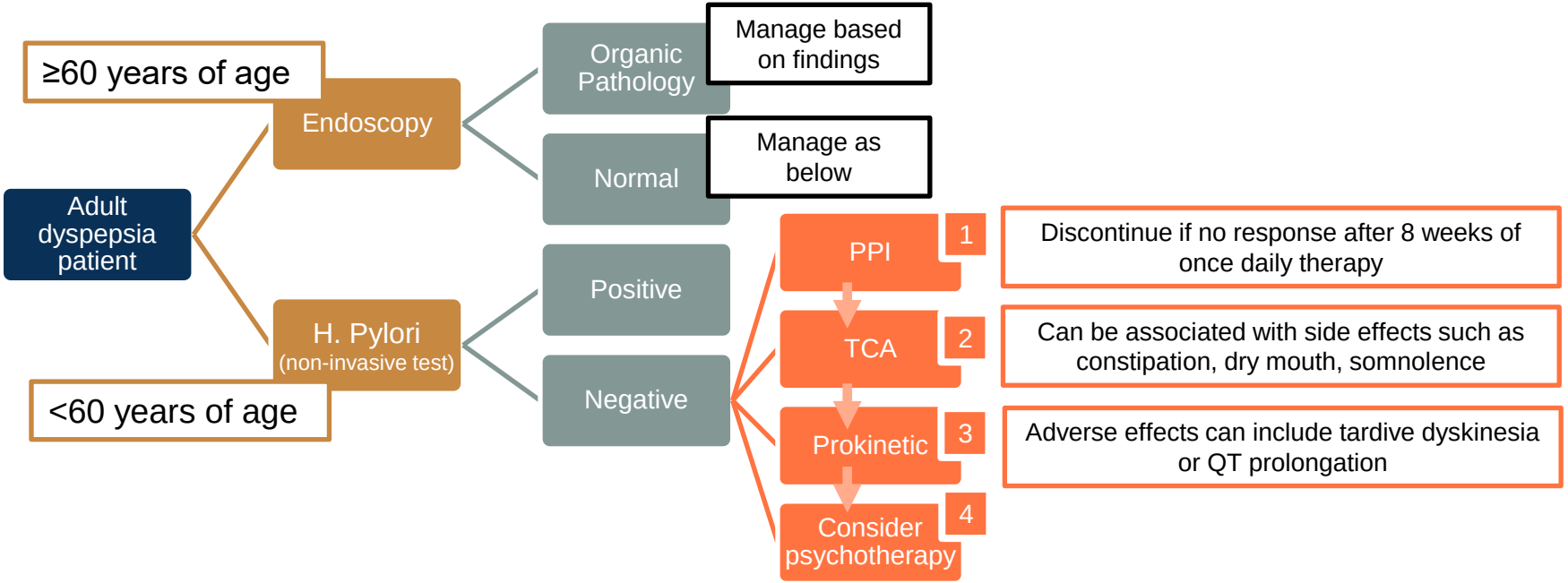
Other individual digestive symptoms or groups of symptoms (from GERD and IBS) may co-exist with PDS

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

Stanghellini et al. *Gastroenterology*. 2016;150(6):1380-92; Tack J, Camilleri M. *Curr Opin Pharmacol*. 2018;43:111-117.

Dyspepsia Management Algorithm

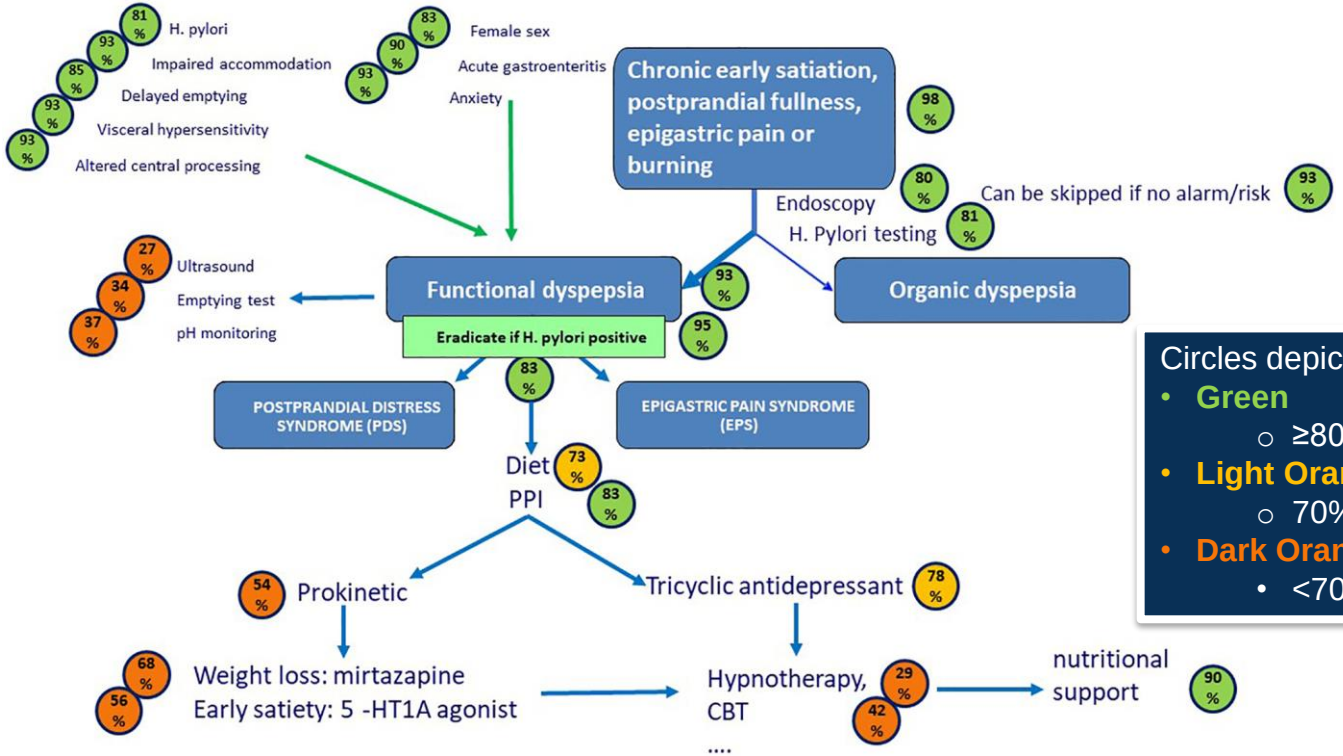
Based on American College of Gastroenterology (ACG) And Canadian Association of Gastroenterology (CAG) Guidelines



TCA = Tricyclic antidepressant.

Moayyedi PM et al. *Am J Gastroenterol*. 2017;112(7):988-1013.

United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) Consensus on Functional Dyspepsia

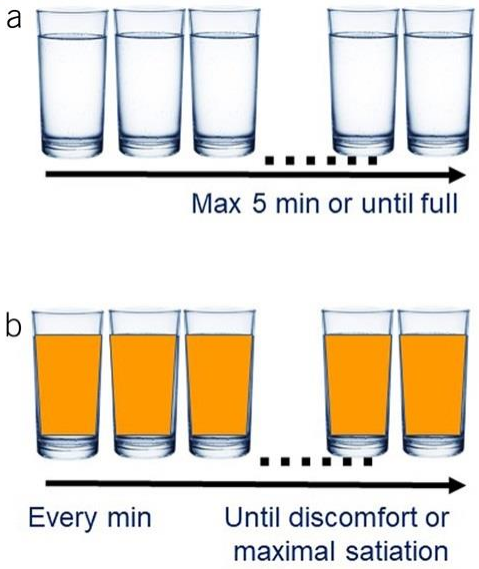


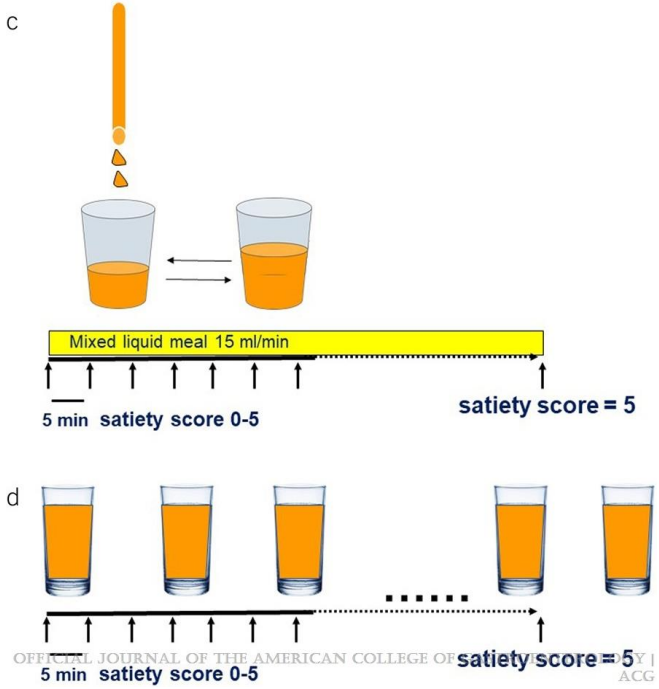
Circles depict % agreement:

- **Green**
  - ≥80% consensus
- **Light Orange**
  - 70% - 80% consensus
- **Dark Orange**
  - <70% consensus

Wauters et al. United European Gastroenterol J. 2021;9(3):307-331.

Drink Tests Used In Functional Dyspepsia





a) Rapid water drink test or water load test
b) Rapid nutrient drink test
c) Satiety drinking test
d) Slow nutrient drink test

Scarpellini et al. *Am J Gastroenterol*. 2021;116(7):1387-1395.

GHAPP
Gastroenterology & Hepatology
Advanced Practice Providers

Gastroparesis

Gastroparesis

Epidemiology

Incidence

- 2.4 per 100,000 in men
- 9.8 per 100,000 in women

Prevalence

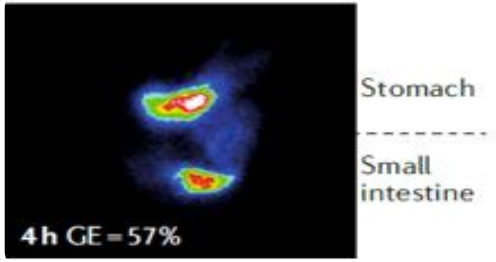
- 9.8 per 100,000 men
- 37.8 per 100,000 women

Etiology

- Idiopathic
- Diabetes
- Iatrogenic
- Neurologic disorders
- Post-viral infection
- Autoimmune

Camilleri et al. *Nature Reviews.* 2018;4(1):1-19.

Tests for Gastric Emptying



Gastric emptying scintigraphy (GES)

Wireless motility capsule (WMC)

Gastric emptying breath test

Camilleri et al. *Nature Reviews.* 2018;4(1):1-19.

Endoscopic Functional Lumen Imaging Probe

Figure 1 Endoscopic image of the pylorus during EndoFLIP®, showing catheter through the pylorus with 40 cc balloon distension.

EndoFLIP

- Measures the stiffness or compliance at the pylorus
- May help guide selection of patients for pyloric interventions

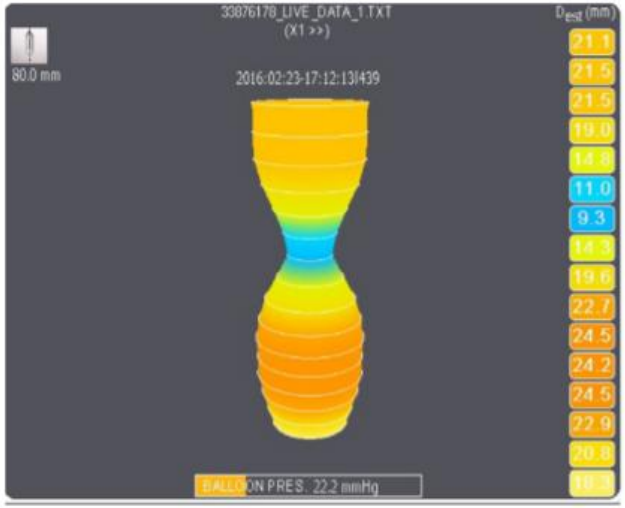


Figure 2 EndoFLIP® image of the pylorus at 40 cc balloon volume distension.

Camilleri et al. *Nature Reviews.* 2018;4(1):1-19; Saadi et al. *Rev Gastroenterol Mexico.* 2018;83(4),375–384.

Gastroparesis Treatment Options

Dietary Modification

- Low fat, low (insoluble) fiber diet
- Small, frequent meals
- Homogenized meals if unable to tolerate solids
- Avoid carbonated beverages, smoking, and alcohol
- Enteral and parenteral supplementation for refractory symptoms

Medication Therapy

- Glycemic control
- Prokinetics
  - Metoclopramide
  - Domperidone
  - Cisapride
  - Prucalopride*
  - Bethanechol*
  - Pyridostigmine*
- Macrolide antibiotics
  - Erithromycin*
  - Azithromycin*
- Antiemetics
- Neuromodulators
  - Nortriptyline*
  - Mirtazapine*
  - Buspirone*

Endoscopic Therapy

- Intrapyloric botulinum toxin injection
- Feeding tubes
- Transpyloric stenting
- Gastric per-oral endoscopy myotomy (G-POEM)

***Denotes off-label use**

Acosta, A & Camilleri, M. *Gastroenterol Clin North Am*. 2015;44(1):97-111; Camilleri. UpToDate. 2021; Camilleri et al. *Am J Gastroenterol*. 2013;108:18–37; Quigley, EMM. *J Neurogastroenterol Motil*. 2015; 21(3):330–336; Reddymasu, SC & McCallum, RW. *Expert Opin Pharmacother*. 2009;10(3):469-84; Tack, J & Camilleri, M. *Curr Opin Pharmacol.* 2018; 43:111-117.

Gastroparesis Treatment Options

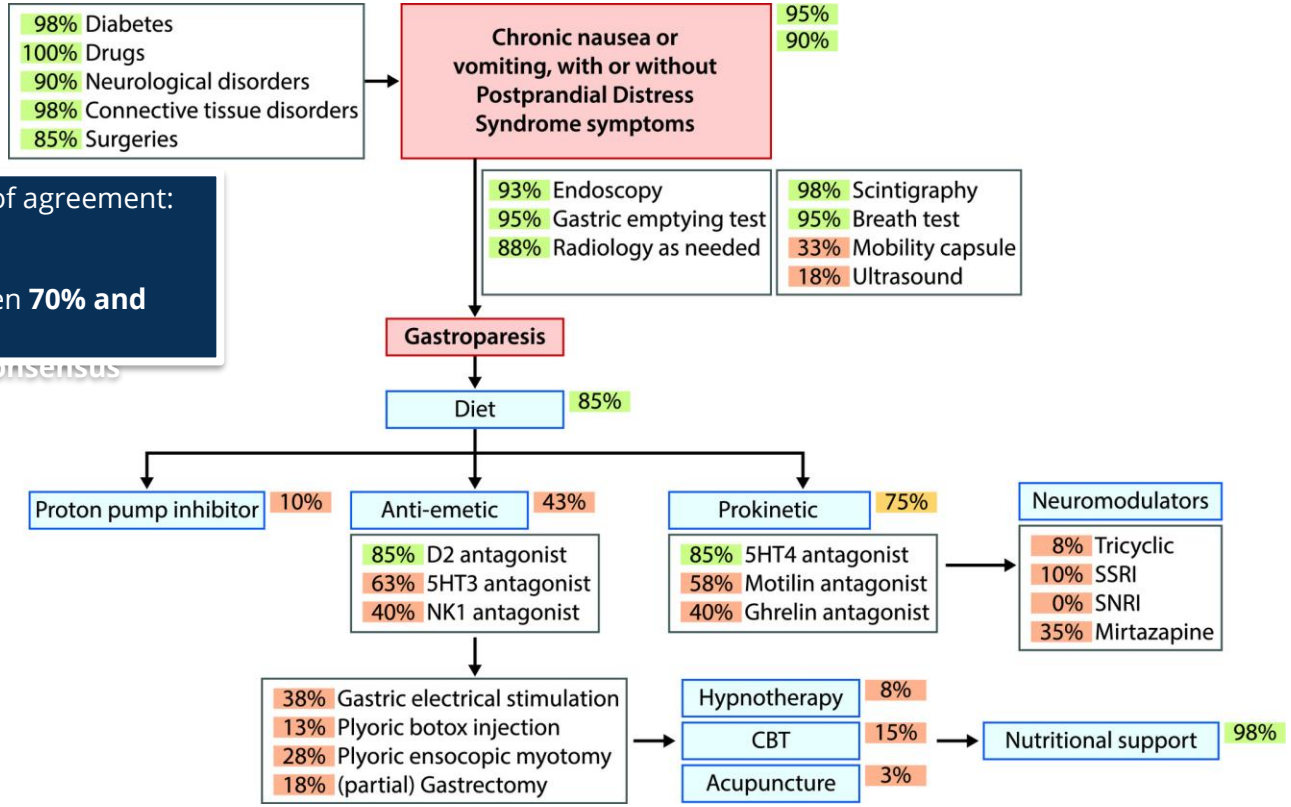
Surgical Therapy	Alternative Therapy	Future Options
• Gastric electrical stimulation (GES) • Pyloroplasty • Gastrectomy	• Ginger • Herbal preparations (STW5, peppermint) • Acupuncture • Non-invasive Vagal Nerve Stimulator (nVNS)	• Relamorelin (ghrelin agonist) • Acotiamide (acetylcholinesterase inhibitor) • Tradipitant (NK-1R antagonist) • TAK-906 (D2/D3 antagonist) • Velusetrag (5-HT4 agonist)

Camilleri et al. *Am J Gastroenterol.* 2013;108:18–37; Camilleri et al. *Nature Reviews*. 2018;4(1):1-19; Gottfried-Blackmore et al. *Neurogastroenterol Motil*. 2020;32(4); Khashab et al. *Gastrointest Endosc*. 2015; 82(6), 1106–1109; Parkman H. *ACG Virtual Grand Rounds*; Tack, J & Camilleri, M. *Curr Opin Pharmacol.* 2018;43:111-117.

United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) Consensus on Gastroparesis

The highlights depict the percentage of agreement:

- **green color** for **≥80% consensus**
- **light orange** for consensus between **70% and 80%**
- **dark orange** for lower levels of consensus



Schol et al. Neurogastroenterol Motil. 2021;33(8):e14237.

Functional Dyspepsia and Gastroparesis in Tertiary Care are Interchangeable Syndromes With Common Clinical and Pathologic Features

Pankaj J. Pasricha,[1] Madhusudan Grover,[2] Katherine P. Yates,[1] Thomas L. Abell,[3] Cheryl E. Bernard,[2] Kenneth L. Koch,[4] Richard W. McCallum,[5] Irene Sarosiek,[5] Braden Kuo,[6] Robert Bulat,[1] Jiande Chen,[7] Robert J. Shulman,[8] Linda Lee,[9] James Tonascia,[9] Laura A. Miriel,[9] Frank Hamilton,[10] Gianrico Farrugia,[2] and Henry P. Parkman,[11] for the National Institute of Diabetes and Digestive and Kidney Diseases/National Institutes of Health Gastroparesis Clinical Research Consortium

[1]Johns Hopkins University School of Medicine, Baltimore, Maryland; [2]Mayo Clinic, Rochester, Minnesota; [3]University of Louisville, Louisville, Kentucky; [4]Wake Forest University, Winston-Salem, North Carolina; [5]Texas Tech University, El Paso, Texas; [6]Massachusetts General Hospital, Boston, Massachusetts; [7]University of Michigan, Ann Arbor, Michigan; [8]Baylor College of Medicine, Houston, Texas; [9]Johns Hopkins University, Baltimore, Maryland; [10]National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland; and [11]Temple University, Philadelphia, Pennsylvania

Pasricha et al. *Gastroenterology.* 2021;160:2006–2017.

Functional Dyspepsia and Gastroparesis in Tertiary Care Are Interchangeable Syndromes With Common Clinical And Pathologic Features

944 patients enrolled during a 12-year period

76% gastroparesis

24% functional dyspepsia

Pasricha et al. *Gastroenterology.* 2021;160:2006–2017.

Functional Dyspepsia and Gastroparesis in Tertiary Care Are Interchangeable Syndromes With Common Clinical And Pathologic Features

944 patients enrolled during a 12-year period

76% gastroparesis

24% functional dyspepsia

48-week clinical outcome similar

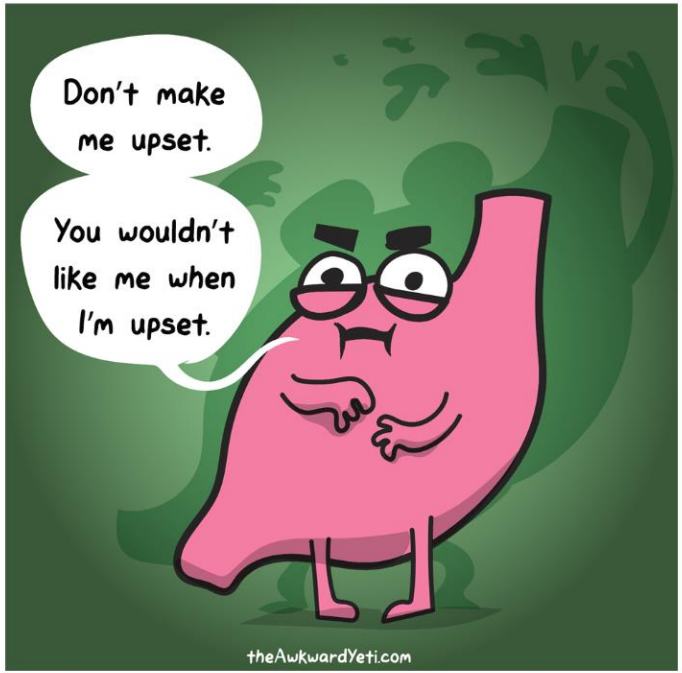
42% of patients with GP were reclassified as FD

37% of patients with FD were reclassified as GP

"Future improvements in diagnostic ability may reveal subtle differences between these 2 syndromes but for now it is reasonable to conclude that FD and GP are part of the same spectrum…"

Pasricha et al. *Gastroenterology.* 2021;160:2006–2017.

Take Home Points



GERD, functional dyspepsia, and gastroparesis symptoms and pathophysiology can overlap

A good clinical history is critical and can direct diagnostic investigation and treatment

Therapy should be patient specific based on symptoms and underlying mechanisms

Research continues to explore pathophysiologic mechanisms, diagnostic testing, and novel therapeutic options

References

- Acosta, A., & Camilleri, M. Prokinetics in gastroparesis. *Gastroenterology Clinics of North America*. 2015 44(1), 97–111. https://doi.org/10.1016/j.gtc.2014.11.008
- Ahuja A, Ahuja NK. Popular Remedies for Esophageal Symptoms: a Critical Appraisal. *Curr Gastroenterol Rep*. 2019;21(8):39. Published 2019 Jul 10. doi:10.1007/s11894-019-0707-4
- Camilleri, M. *Gastroparesis: Treatment of gastroparesis*. In: UpToDate, Talley, NJ (Ed), UpToDate, Waltham, MA, 2021.
- Camilleri, M. *Pathogenesis of delayed gastric emptying*. In: UpToDate, Talley, NJ (Ed), UpToDate, Waltham, MA, 2021.
- Camilleri, M., Chedid, V., Ford, A. C., Haruma, K., Horowitz, M., Jones, K. L., Low, P. A., Park, S. Y., Parkman, H. P., & Stanghellini, V. Gastroparesis. Nature reviews. *Disease primers*. 2018. 4(1), 41. https://doi-org.laneproxy.stanford.edu/10.1038/s41572-018-0038-z
- Camilleri, M., Parkman, H. P., Shafi, M. A., Abell, T. L., & Gerson, L. *Clinical Guideline: Management of Gastroparesis: American Journal of Gastroenterology*. 2013. 108(1), 18–37. https://doi.org/10.1038/ajg.2012.373
- Gottfried-Blackmore, A., Adler, E. P., Fernandez-Becker, N., Clarke, J., Habtezion, A., & Nguyen, L. Open-label pilot study: Non-invasive vagal nerve stimulation improves symptoms and gastric emptying in patients with idiopathic gastroparesis. *Neurogastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society*. 2020. 32(4), e13769. https://doi.org/10.1111/nmo.13769
- Gyawali CP, Carlson DA, Chen JW, Patel A, Wong RJ, Yadlapati RH. ACG Clinical Guidelines: Clinical Use of Esophageal Physiologic Testing. *Am J Gastroenterol*. 2020;115(9):1412-1428. doi:10.14309/ajg.0000000000000734
- Gyawali CP, Fass R. Management of Gastroesophageal Reflux Disease. *Gastroenterology*. 2018;154(2):302-318. doi:10.1053/j.gastro.2017.07.049 Gyawali CP, Kahrilas PJ, Savarino E, et al. Modern diagnosis of GERD: the Lyon Consensus. *Gut*. 2018;67(7):1351-1362. doi:10.1136/gutjnl-2017-314722
- Katz, P. O., Gerson, L. B., & Vela, M. F. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol. 2013.* 108(3), 308-328. doi:10.1038/ajg.2012.444
- Katzka DA, Kahrilas PJ. Advances in the diagnosis and management of gastroesophageal reflux disease. *BMJ*. 2020;371:m3786. Published 2020 Nov 23. doi:10.1136/bmj.m3786
- Katzka DA, Pandolfino JE, Kahrilas PJ. Phenotypes of Gastroesophageal Reflux Disease: Where Rome, Lyon, and Montreal Meet. *Clin Gastroenterol Hepatol*. 2020; 18(4):767-776. doi:10.1016/j.cgh.2019.07.015
- Khashab, M. A., Besharati, S., Ngamruengphong, S., Kumbhari, V., El Zein, M., Stein, E. M., Clarke, J. O. Refractory gastroparesis can be successfully managed with endoscopic transpyloric stent placement and fixation (with video). *Gastrointestinal Endoscopy*. 2015. 82(6), 1106–1109. https://doi.org/10.1016/j.gie.2015.06.051
- Kim BJ, Kuo B. Gastroparesis and Functional Dyspepsia: A Blurring Distinction of Pathophysiology and Treatment. *J Neurogastroenterol Motil*. 2019;25(1):27-35. doi:10.5056/jnm18162
- Kushner BS, Awad MM, Mikami DJ, Chand BB, Wai CJ, Murayama KM. Endoscopic treatments for GERD. *Ann N Y Acad Sci.* 2020;1482(1):121-129. doi:10.1111/nyas.14511

References

- Maret-Ouda J, Markar SR, Lagergren J. Gastroesophageal Reflux Disease: A Review. *JAMA*. 2020;324(24):2536-2547. doi:10.1001/jama.2020.21360
- Moayyedi P, Lacy BE, Andrews CN, Enns RA, Howden CW, Vakil N. ACG and CAG Clinical Guideline: Management of Dyspepsia [published correction appears in *Am J Gastroenterol*. 2017 Sep;112(9):1484]. *Am J Gastroenterol*. 2017;112(7):988-1013. doi:10.1038/ajg.2017.154
- Patel DA, Higginbotham T, Slaughter JC, et al. Development and Validation of a Mucosal Impedance Contour Analysis System to Distinguish Esophageal Disorders. *Gastroenterology*. 2019;156(6):1617-1626.e1. doi:10.1053/j.gastro.2019.01.253
- Pasricha PJ, Grover M, Yates KP, et al. Functional Dyspepsia and Gastroparesis in Tertiary Care are Interchangeable Syndromes With Common Clinical and Pathologic Features. *Gastroenterology*. 2021;160(6):2006-2017. doi:10.1053/j.gastro.2021.01.230
- Quigley, E. M. M. Prokinetics in the Management of Functional Gastrointestinal Disorders. *Journal of Neurogastroenterology and Motility*. 2015. 21(3), 330–336. https://doi.org/10.5056/jnm15094
- Reddymasu, S. C., & McCallum, R. W. Pharmacotherapy of gastroparesis. *Expert Opinion on Pharmacotherapy*. 2009.10(3), 469–484. https://doi.org/10.1517/14656560902722505
- Savarino E, Bredenoord AJ, Fox M, et al. Advances in the physiological assessment and diagnosis of GERD. *Nat Rev Gastroenterol Hepatol*. 2018;15(5):323. doi:10.1038/nrgastro.2018.32
- Scarpellini E, Van den Houte K, Schol J, et al. Nutrient Drinking Test as Biomarker in Functional Dyspepsia. *Am J Gastroenterol*. 2021;116(7):1387-1395. doi:10.14309/ajg.0000000000001242
- Schol J, Wauters L, Dickman R, et al. United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on gastroparesis. *Neurogastroenterol Motil*. 2021;33(8):e14237. doi:10.1111/nmo.14237
- Sharma, P., & Yadlapati, R. Pathophysiology and treatment options for gastroesophageal reflux disease: looking beyond acid. *Annals of the New York Academy of Sciences*. 2001. 1486(1), 3–14. https://doi-org.laneproxy.stanford.edu/10.1111/nyas.14501
- Stanghellini V, Chan FK, Hasler WL, et al. Gastroduodenal Disorders. *Gastroenterology*. 2016;150(6):1380-1392. doi:10.1053/j.gastro.2016.02.011
- Tack J, Camilleri M. New developments in the treatment of gastroparesis and functional dyspepsia. *Curr Opin Pharmacol.* 2018;43:111-117. doi:10.1016/j.coph.2018.08.015
- U.S. Department of Health and Human Services. (2014). Digestive diseases statistics for the United States.
- Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R; Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol*. 2006;101(8):1900-1943. doi:10.1111/j.1572-0241.2006.00630.x
- Wauters L, Dickman R, Drug V, et al. United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on functional dyspepsia. *United European Gastroenterol J*. 2021;9(3):307-331. doi:10.1002/ueg2.12061
- Yadlapati, R., & DeLay, K. Proton Pump Inhibitor-Refractory Gastroesophageal Reflux Disease. *The Medical Clinics of North America.* 2019. 103(1), 15–27.