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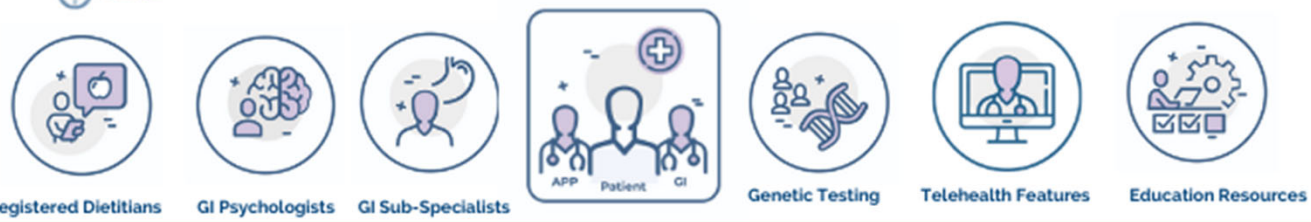

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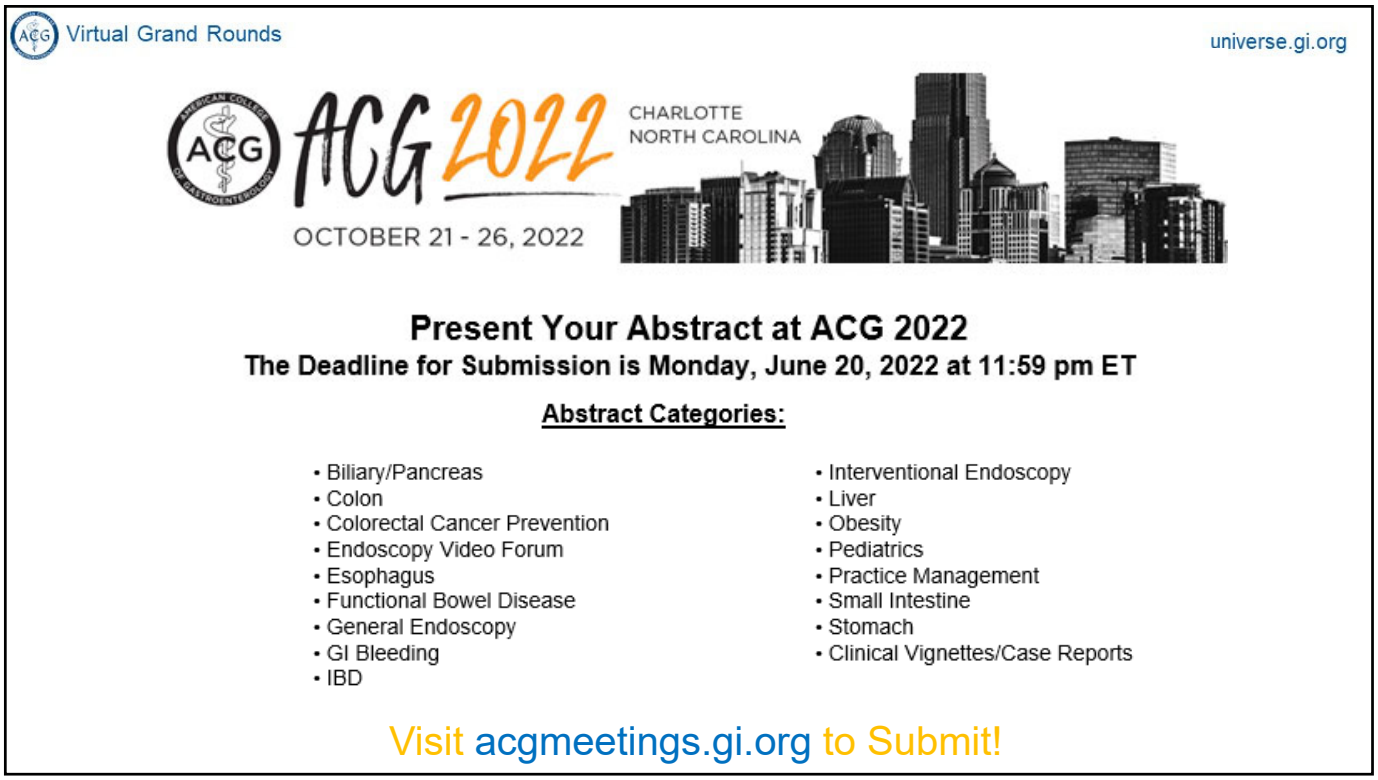
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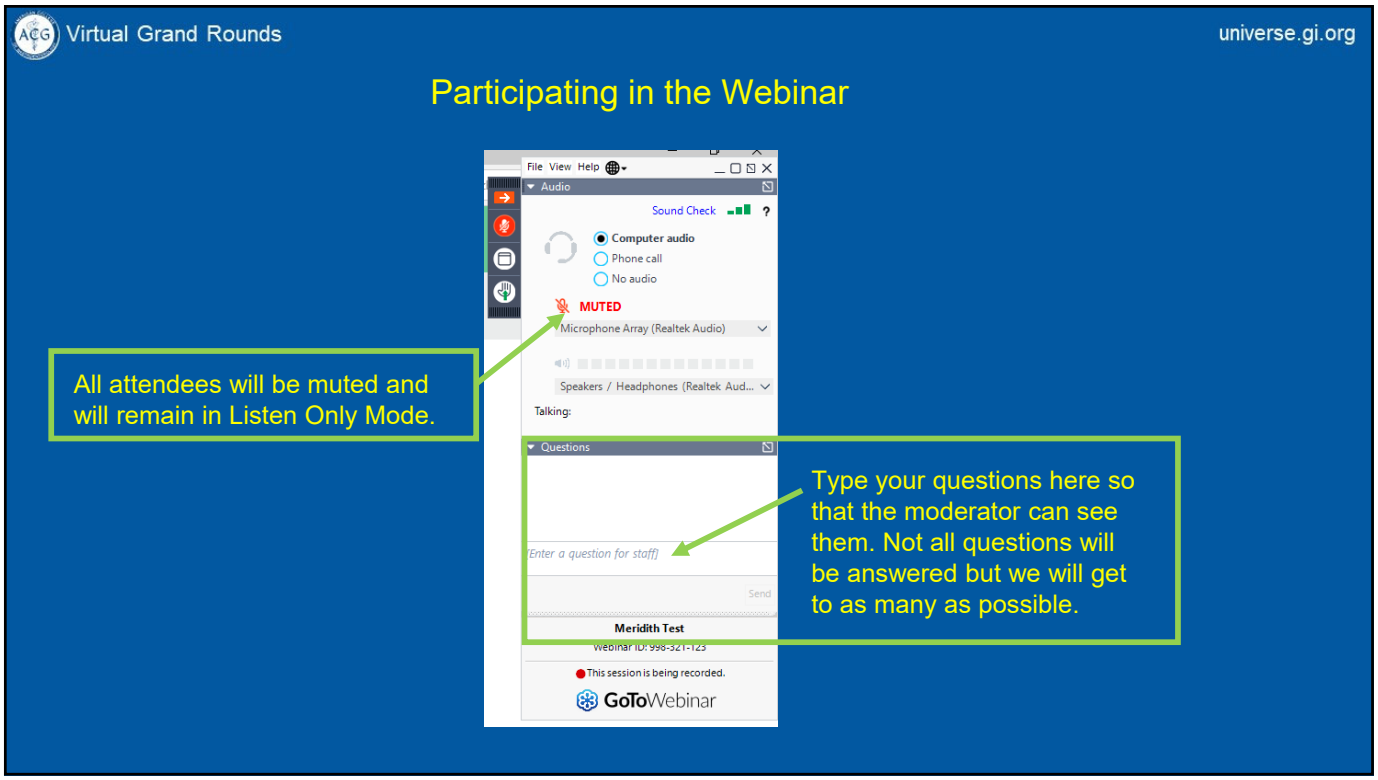
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ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

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.

7

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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*Overcoming the **Challenges & Mitigating the Disparities in Our LGBTQI+ Patients: A Digestive Diseases Health Perspective***
Sonali Paul, MD, MS
June 9, 2022 at Noon Eastern and *NEW!* **8pm Eastern!**

Week 24 – June 16, 2022
Hereditary Pancreatic Cancers: What Should We Screen and How?
Yasmin G. Hernandez-Barco, MD
June 16, 2022 at Noon Eastern and *NEW!* **8pm Eastern!**

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Disclosures

Philip O. Katz, MD, MACG
Sebela Pharmaceuticals: Consultant
Phathom Pharmaceuticals: Consultant
AstraZeneca: Advisory Board Member

Rena H. Yadlapati, MD, MSHS, FACG
Medscape: Consultant
Phathom Pharmaceuticals: Consultant
RJS Mediagnostix: Advisory Board
Ironwood Pharmaceuticals: Consultant, Research Grant (institution)
Medtronic: Consultant (institution)
StatLink MD: Consultant (institution)

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

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ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease

Philip O. Katz, MD, MACG
Professor of Medicine
Jay Monahan Center for Gastrointestinal Health
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12

Co Authors

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- Felice Schnoll-Sussman MD
- Katarina Greer MD (Grade methodologist)
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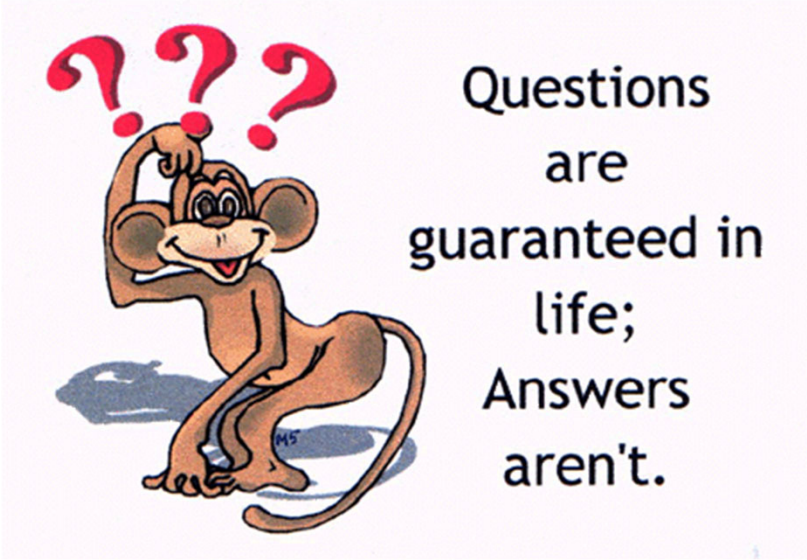

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Today's Talk will address key features of ACG GERD Guidelines 2022

- Definition of GERD
- Diagnostic Approach including Extraesophageal and Refractory GERD
- Therapy
- PPI Adverse Events

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What has changed since the 2013 ACG Guidelines?

- New data on pathogenesis of erosive esophagitis
- Increased acceptance of prolonged telemetry capsule monitoring for GERD
- Improved imaging technology
- Widespread availability and use of HRM and impedance/pH monitoring
- Lyon Consensus

- HRM, high resolution manometry
- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

16

What has changed since the 2013 ACG Guidelines? (continued)

- Clearer understanding and definition of "refractory GERD"
- Level 1 evidence for laparoscopic fundoplication, magnetic sphincter augmentation and TIF success.
- Major change in approach to PPI use
- Wealth of data on PPI adverse events

- TIF, transoral incisionless fundoplication
- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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GERD Defined

GERD is a condition in which the reflux of gastric contents into the esophagus results in symptoms and/or complications

GERD is objectively defined by the presence of characteristic mucosal injury seen at endoscopy and/or abnormal esophageal acid exposure demonstrated on a reflux monitoring study.

Katz, Dunbar, Schnoll, Spechler AJG 2022

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Pathophysiology of GERD

- Poorly functioning esophagogastric junction: antireflux barrier composed of the lower esophageal sphincter and crural diaphragm
- Impaired esophageal clearance and alterations in esophageal mucosal integrity.
- Decreased salivary production
- Delayed gastric emptying, and
- Esophageal hypersensitivity
- Reflux esophagitis develops when refluxed gastric juice is sufficient to trigger the release of cytokines and chemokines that attract inflammatory cells

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GERD Symptoms: Typical/Classic

- Heartburn
- Regurgitation
- Chest Pain
- No symptom is exclusive to GERD

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Extraesophageal: Symptoms/Associations

- Hoarseness, Throat Clearing: ENT symptoms
- Cough
- Asthma symptoms
- Dyspepsia
- Nausea
- Pneumonia, Bronchitis, Interstitial Lung Disease

- Typical symptoms may or may not be present: if not do not treat empirically

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Alarm Symptoms: Mandates Work up prior to therapeutic trial

- Dysphagia
- Weight loss
- Bleeding

22

Case

- 44 yr old male/Caucasian female 3 years now daily substernal burning, mostly post prandial. Notes daily regurgitation of undigested food 10-15 minutes after eating, rarely in between meals, never has nausea, rare belching presents for evaluation. Halitosis for 20 years. Rare OTC, no longer helpful does not want to take PPI because of seizure medicine (Lamotrigine). Wakes from sleep once or twice a month. No dysphagia, weight loss or bleeding.
- Has attempted to avoid acidic trigger foods, late night eating
- BMI 33
- Family history of esophageal cancer in grandfather
- No other medical problems

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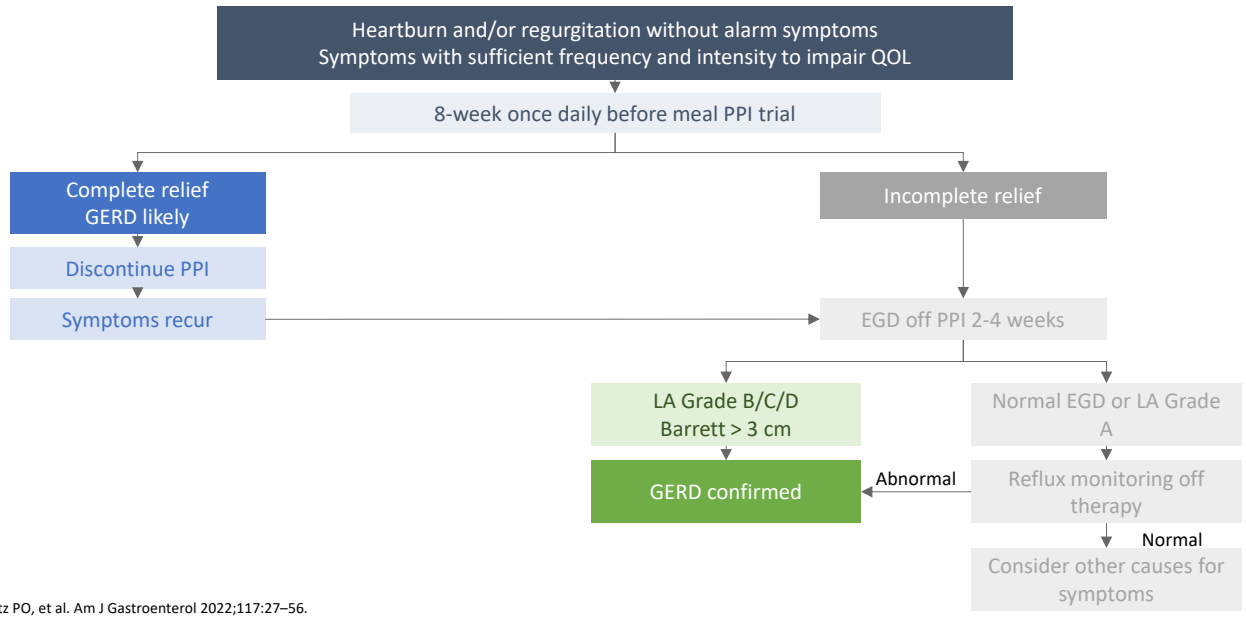
ACG GERD Guidelines: Diagnostic Algorithm



- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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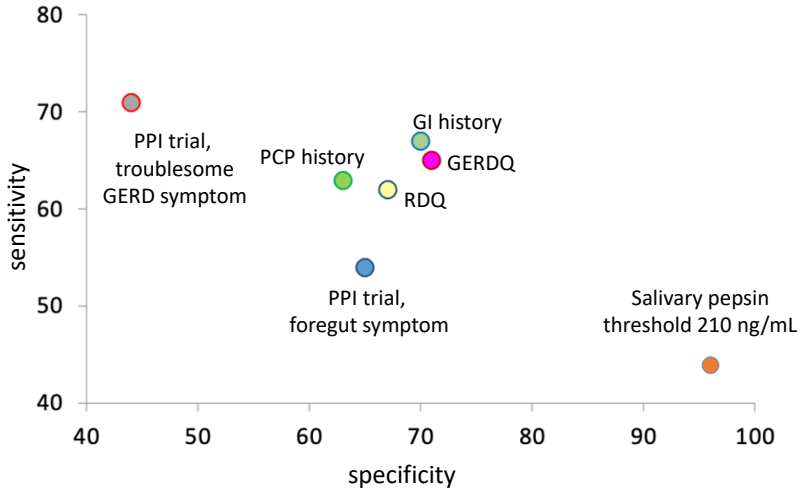
Office Based Clinical Diagnosis: How often do you want to be right?



Gold Standard

-Esophagitis on endoscopy
-Acid exposure time (AET) > 6%
-Symptom association probability >95%
-AET 4-6% & symptom improvement

Gold Standard

-Acid exposure time (AET) >4.2%
-Symptom association probability >95%

Hayat JO et al. Gut 2015;64:373-80
Jones R et al. APT 2009;30:1030-8
Dent J et al. Gut 2010;59:714-21
Bolier EA et al. Dis Esophagus 2015;28:105-20

25

PPI trial as a diagnostic test

- Practical, simple but has danger of giving and continuing a medicine for the wrong disease
- Pooled sensitivity of 78% and specificity of only 54% (using endoscopy and pH monitoring as the reference standard)
- As such its use should be limited to classic symptoms, the absence of warning signs
- Step up therapy offers no long-term advantage over a PPI trial
- Continuing an unsuccessful PPI trial beyond 8-12 weeks cannot be justified. Adjustment or ideally a workup is strongly recommended.

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Case

- Patient agrees to try PPI as she prefers to not have EGD (sedation) after discussion of potential interactions with her seizure medications
- PPI once daily, taken 30 minutes before breakfast for 8 weeks, misses next appointment.
- Returns for video visit 2 months later, reports PPI was helpful with heartburn (90% gone), not as good for regurgitation and no help with halitosis.
- Stopped PPI on her own, symptoms returned slowly and returned to baseline.

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Guidelines 2022: Endoscopy

Recommended

- Diagnostic endoscopy if classic GERD symptoms do not respond adequately to 8-week empiric trial of PPIs or symptoms return when PPIs are discontinued
- Performed off PPI, ideally for 2-4 weeks
- 1 week minimum for intended pH testing if endoscopy is negative
- Mandatory off therapy ≥ 1 week if biopsy planned for normal mucosa (EoE cannot be ruled out if biopsy on PPI)

Not supported compared to the left

- Increasing the dose or switching before a work-up

- EoE, eosinophilic esophagitis
- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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Endoscopy

- For diagnosis if PPI trial unsuccessful or patient relapses
- For any patient with dysphagia, anemia, weight loss
- Should be performed off PPI for at least a week, ideally 2-4 weeks
- Mucosal abnormality <50% of patients with heartburn, lower when extraesophageal symptoms are reason for exam
- Normal endoscopy mandates a reflux monitoring study for diagnosis

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Endoscopy/Biopsy

- Biopsy should NOT be performed to make a diagnosis of GERD
- Biopsy of the gastroesophageal junction is not recommended
- Biopsy of a reflux erosion is not necessary
- Eosinophilic Esophagitis cannot be ruled out if the patient is on a PPI

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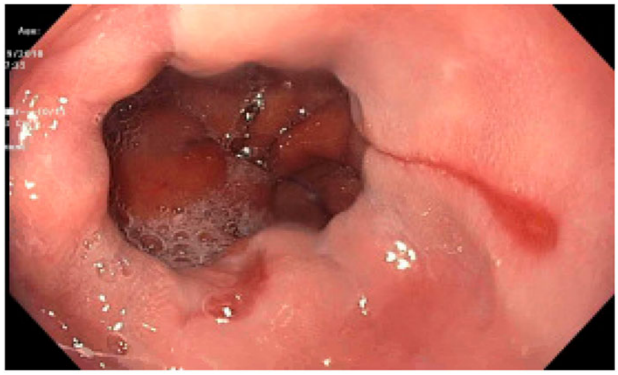
Endoscopy performed



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2022 Guidelines: Reflux Monitoring

Recommended

- Should be performed off therapy for all patients who do not have a clear endoscopic diagnosis (Grade B, C or D, Barrett, clear peptic stricture)
- On therapy with impedance/pH if GERD previously objectively documented and optimized PPI not effective

- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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Reflux Monitoring

- Only test to evaluate for reflux over time
- Can be 24-96 hours, catheter or telemetry capsule
- Weakly or non-acidic contents can be assessed
- Can evaluate belching
- Should be done in all patients who do not have EE or Barrett's and those who fail PPI before an operation

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A Normal EGD and Reflux Monitor Makes it Highly Unlikely GERD is Responsible for Symptoms

The best way to make decisions on long term PPI use

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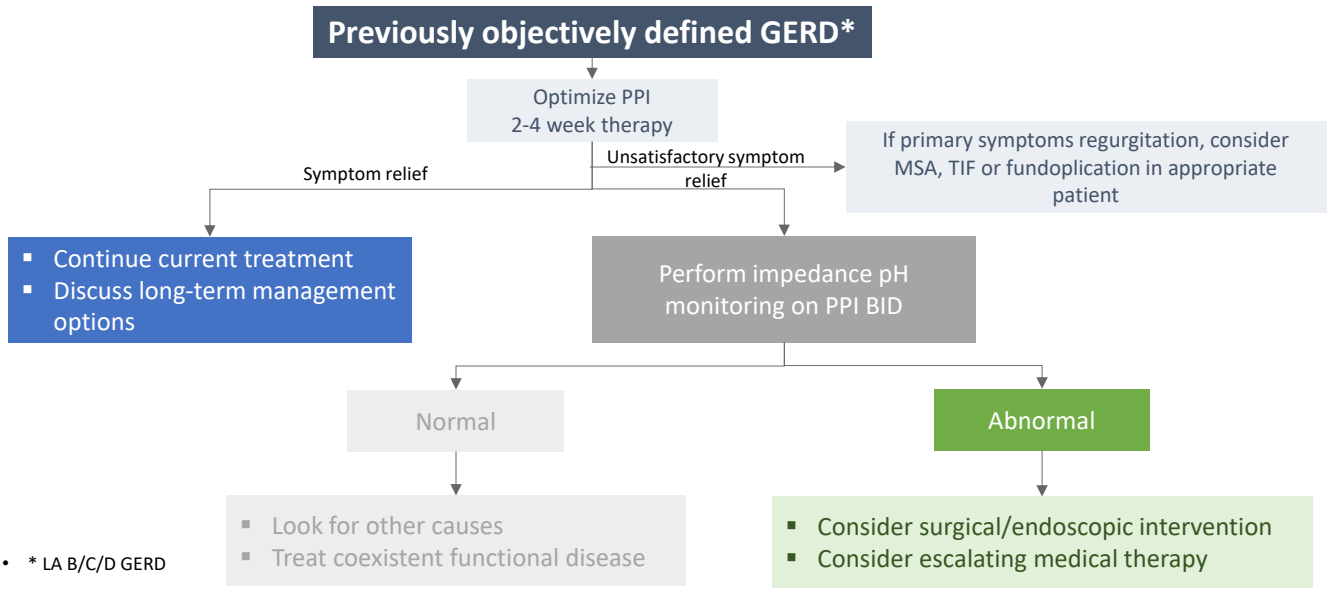
ACG Guidelines 2022: Management of Refractory GERD



- * LA B/C/D GERD
- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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Treatment

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Food: Diet

- Weight loss in overweight and obese patients for improvement of GERD symptoms
- Suggest avoiding meals within 2–3 hours of bedtime
- Suggest avoidance of "trigger foods" for GERD symptom control (conditional recommendation, low level of evidence).
- Suggest elevating head of bed for nighttime GERD symptoms

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Lifestyle Changes: The Evidence is Generally Weak

Lifestyle modification	Strength of scientific evidence	Pathophysiologically conclusive?	Recommendable?
Avoid fatty meals	Equivocal	Equivocal	Yes
Avoid carbonated beverages	Moderate	Yes	Yes
Select decaffeinated beverages	Equivocal	Equivocal	Not generally
Avoid citrus	Weak	Yes	Yes, if citrus triggers symptoms
Eat smaller meals	Weak	Yes	Yes
Lose weight	Equivocal	Equivocal	Yes[a]
Avoid alcoholic beverages	Weak	Mechanisms not understood; different alcoholic beverages have different effects	Not generally
Stop smoking	Weak	Yes	Yes[a]
Avoid excessive exercise	Weak	Yes	Yes
Sleep with head elevated	Equivocal	Equivocal	Yes
Sleep on the left side	Unequivocal	Yes	Yes

[a]Obesity and smoking seem to be risk factors for cancer of the distal esophagus.

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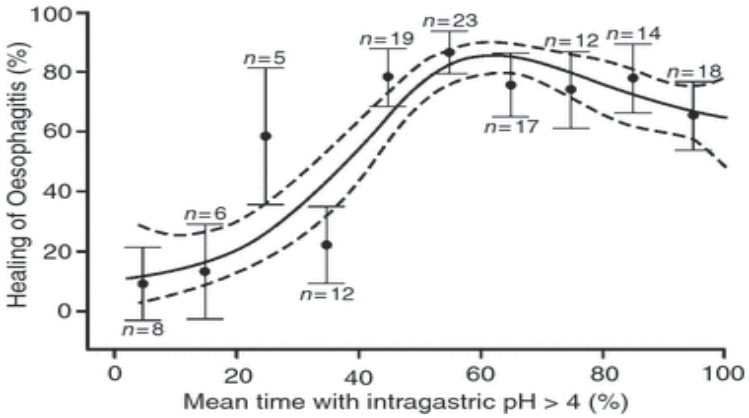
General Principle: Healing (Symptom improvement) Related to Acid Control



Katz P et al, APT 2007

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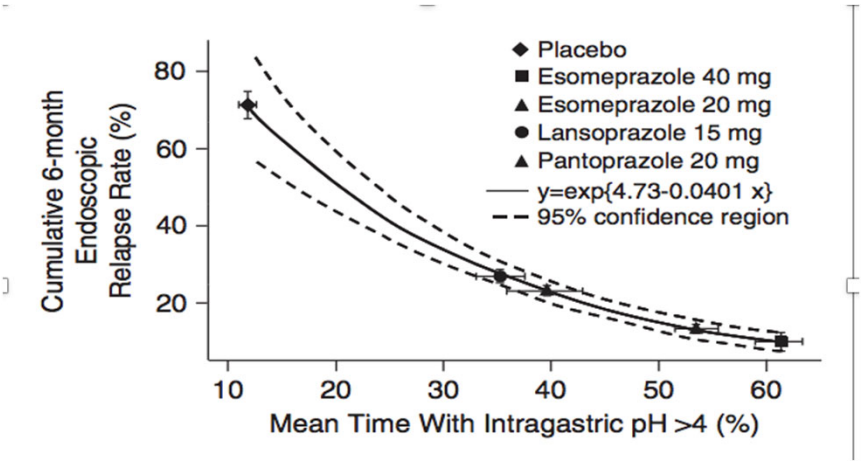
Acid Control Reduces Relapse



Johnson DA, Katz P
J Clin Gastro 2010

40

PPIs are the BEST drugs currently available

- Block terminal step of acid secretion
- Require active proton pump to be effective
- Block 70% of active pumps
- Half-life short, half-life of pump long so 5-7 days to reach steady state
- Pumps regenerate so MUST take drug daily
- PUMPS ACTIVATED by FOOD
- PPI absorption may be diminished by FOOD

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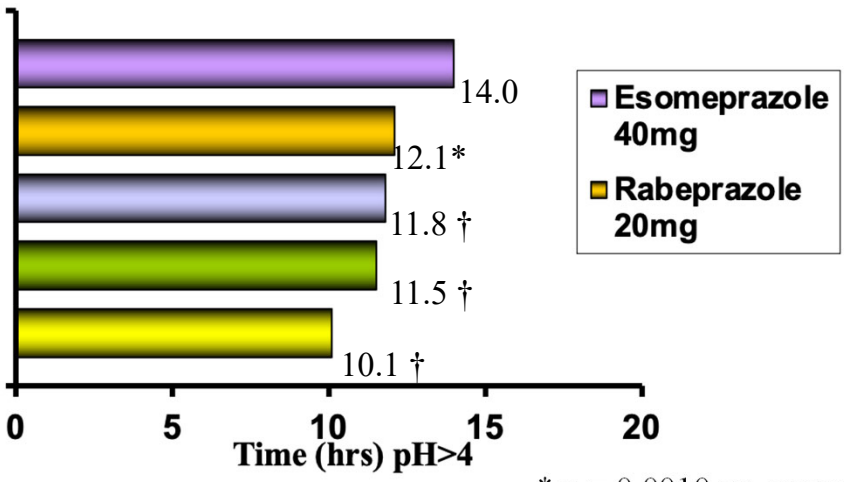
Intragastric pH control with once daily PPI)



* p = 0.0010 vs. esomeprazole
† p ≤ 0.0001 vs. esomeprazole

Miner PB, Katz PO et al. *Am J Gastro*. 2003

42

2022 Guidelines: Surgery/Endoscopic Treatment

Recommended

- PPI indefinitely or surgery in patients with C or D erosive esophagitis (or clear Barrett esophagus)
- Consider early intervention for patients with regurgitation as primary symptom, objective evidence for GERD
- Surgery: option for long term management of objectively proven GERD
- Refractory regurgitation: MSA, laparoscopic hernia repair plus fundoplication or TIF
- If patient does not wish to have surgery: TIF if non-erosive, A, B, Hill 1 or 2 and axial HH 2 cm or less

- MSA, magnetic sphincter augmentation; TIF, transoral incisionless fundoplication
- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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A second dose increases time pH>4 by 5 hours

Pantoprazole is the weakest PPI and used the most as it is on most formulary due to cost

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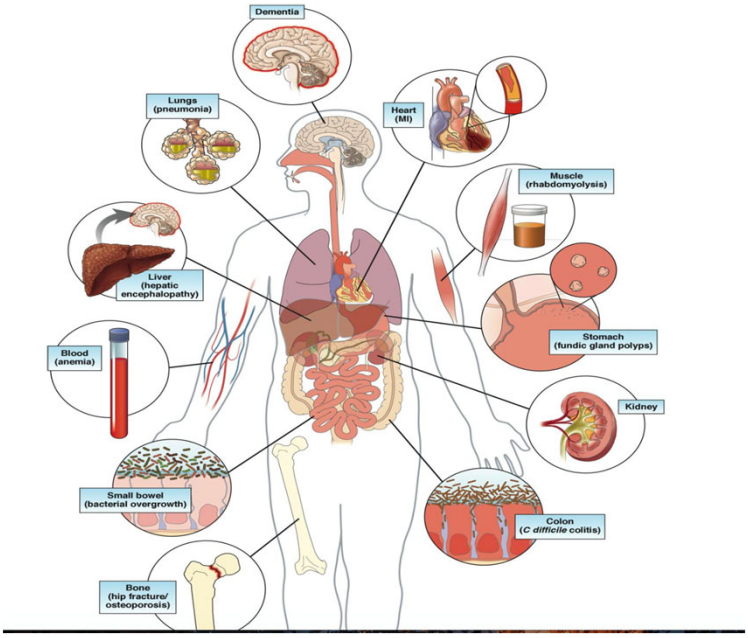
Adverse Events Associated with PPIs



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The longest running Risks of "Concern"

- Fractures (FDA Class warning 2010, revised 2011)
- Clopidogrel interaction (FDA warning 2009, different PPI labels)
- *Clostridium difficile* (FDA Class warning 2012)
- Pneumonia (No class Warning)
- Magnesium Deficiency (Class Warning)

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Other Potential PPI "Risks"

- Interstitial Nephritis
- Cardiac Disease (adjudicated by FDA in past)
- Small Intestinal Bacterial Overgrowth
- Bacterial Peritonitis
- Traveller's Diarrhea
- Iron Deficiency Anemia
- Rhabdomyolysis
- Cardiac Defects when used in pregnancy

47

The Latest most talked about "Worries"

- Myocardial Infarction
- Chronic Kidney Disease
- Dementia
- Ischemic stroke
- Early death

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What are the possible mechanisms of PPI adverse events

1. Infectious consequences of hypochlorhydria
2. Non-infectious consequences of hypochlorhydria
3. Dysbiosis
4. Consequences of hypochlorhydria on electrolyte and nutrition absorption

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Proposed Effects/ Concerns of Long-Term PPI Therapy

1. Bone consequences (Ca absorption)
2. Dementia (Amyloid in mice, B12)
3. Renal Disease (AIN, idiosyncratic)

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Results of Studies

- Results expressed as Hazard Ratios or Odds Ratios rather than NNT or NNH
- Increased likelihood of an unlikely event still unlikely
- Relative Risk increased
- Absolute Risk Variable
- Prospective studies though smaller all show no harms or reported events

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Examining the Data: Methodology of studies

- Retrospective Cohort
- Database Reviews using ICD-9/10 codes
- Meta analysis
- Few RCT's or prospective cohort studies

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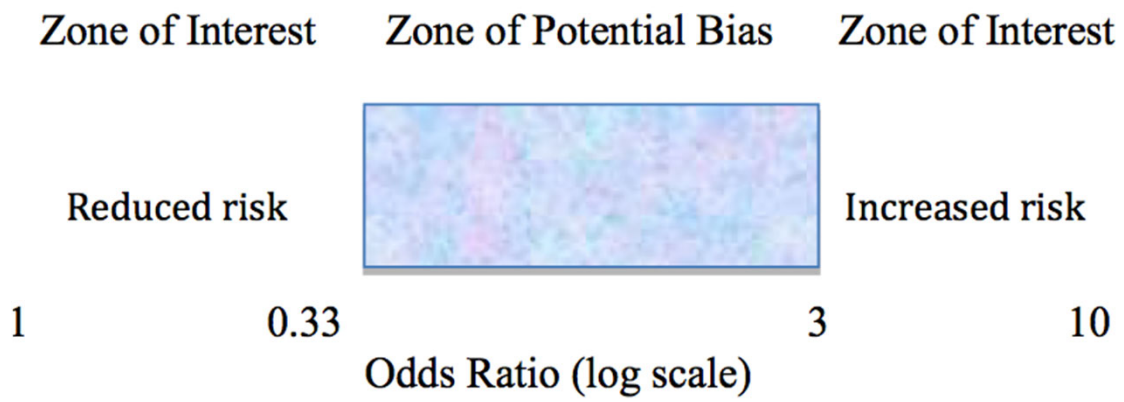
Dealing with Strength of Odds Ratios



Grimes DA, 2012

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Criteria for Judging a Study of Association

- Strength of the Association: Is the association of high magnitude
- Consistency: Is the association reproducible
- Specificity: Is the effect directly attributed to (in this case) PPIs
- Temporality: Does the use of the PPI precede the outcome
- Biologic gradient: Direct relationship between dose and or duration
- Biologic plausibility: Any logical reason for the outcome
- Coherence: Conflict with what is known about the disease in question
- Experiment: Are the results based on an experiment
- Analogy: Any similarity to associations that are deemed causal

Hill, 1965

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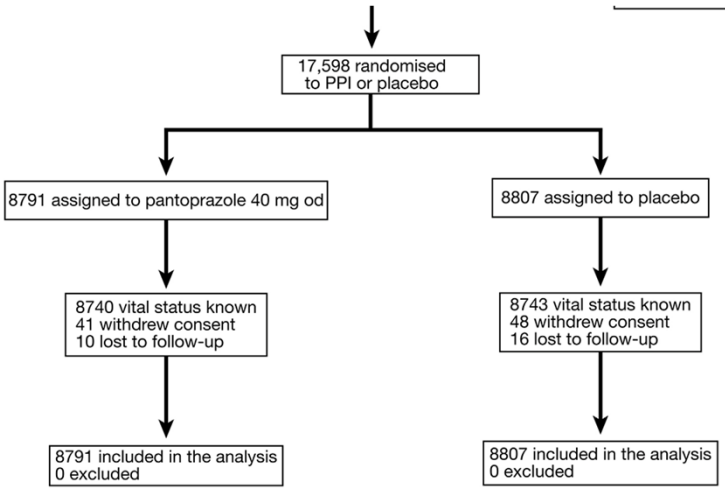
Randomized Trial: Panto v placebo: 53K patient years of follow-up



Moayyedi, 2019

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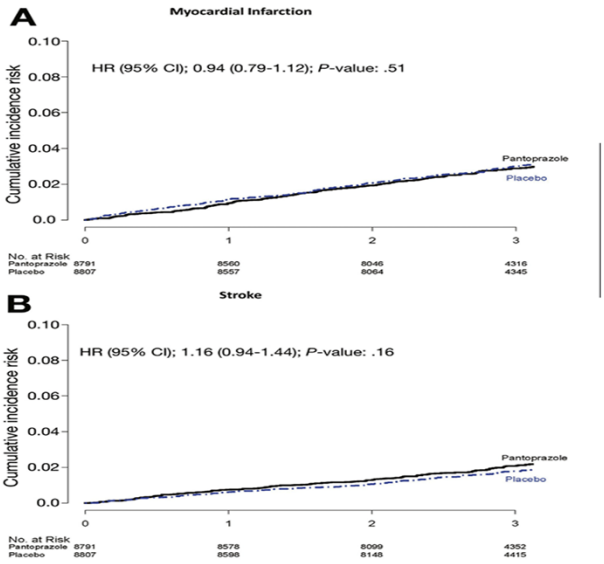
MI/Stroke



Moayyedi, 2019

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Other Outcomes

Outcome	Incident events, n (%)		Pantoprazole, 40 mg od, vs placebo	
	Pantoprazole, 40 mg od (n = 8791)	Placebo (n = 8807)	OR (95% CI)	*P* value
Gastric atrophy	19 (0.2)	26 (0.3)	0.73 (0.40–1.32)	.30
Clostridium difficile	9 (0.1)	4 (<0.1)	2.26 (0.70–7.34)	.18
Other enteric infection	119 (1.4)	90 (1.0)	1.33 (1.01–1.75)	.04
Chronic kidney disease	184 (2.1)	158 (1.8)	1.17 (0.94–1.45)	.15
Dementia	55 (0.6)	46 (0.5)	1.20 (0.81–1.78)	.36
Pneumonia	318 (3.6)	313 (3.6)	1.02 (0.87–1.19)	.82
Fracture	203 (2.3)	211 (2.4)	0.96 (0.79–1.17)	.71
COPD	146 (1.7)	124 (1.4)	1.18 (0.93–1.51)	.17
Diabetes mellitus	513 (5.8)	532 (6.0)	0.96 (0.85–1.09)	.56

Moayyedi, 2019

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Association Never Proves Casuality

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Guideline Statement Regarding PPI Safety

Regarding the safety of long-term PPI usage for GERD, we suggest that patients should be advised as follows: "PPIs are the most effective medical treatment for GERD. Some medical studies have identified an association between the long-term use of PPIs and the development of numerous adverse conditions including intestinal infections, pneumonia, stomach cancer, osteoporosis-related bone fractures, chronic kidney disease, deficiencies of certain vitamins and minerals, heart attacks, strokes, dementia, and early death. Those studies have flaws, are not considered definitive, and do not establish a cause-and-effect relationship between PPIs and the adverse conditions. High-quality studies have found that PPIs do not significantly increase the risk of any of these conditions except intestinal infections. Nevertheless, we cannot exclude the possibility that PPIs might confer a small increase in the risk of developing these adverse conditions. For the treatment of GERD, gastroenterologists generally agree that the well-established benefits of PPIs far outweigh their theoretical risks."

Katz, et al. AJG 2022

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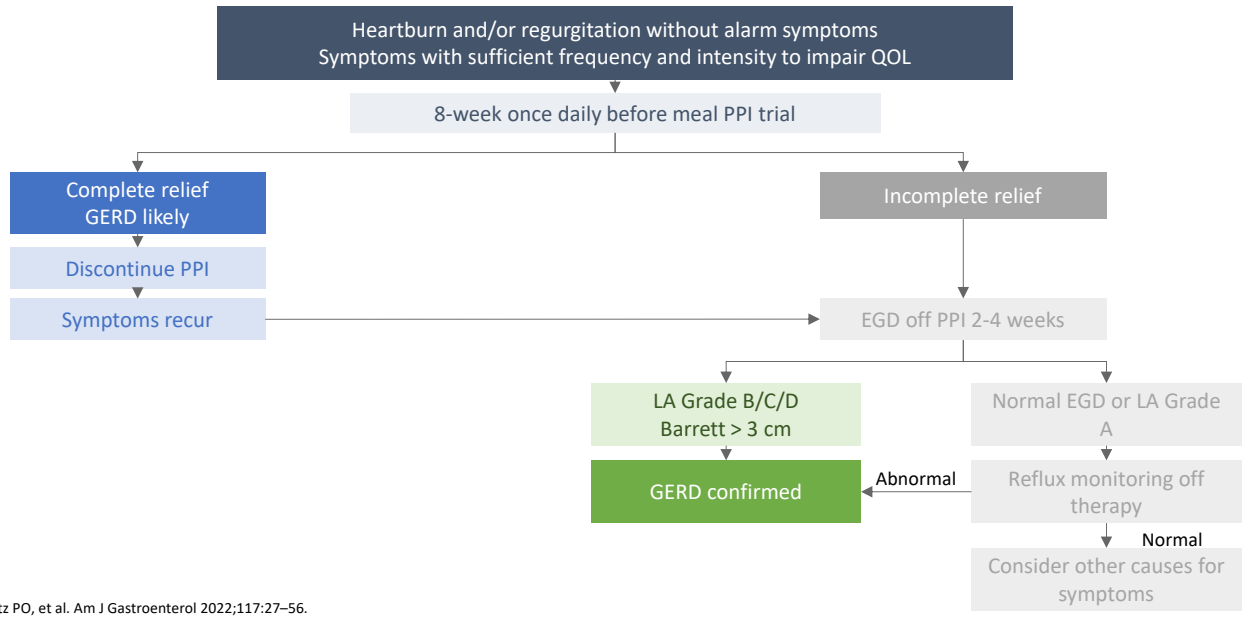
ACG GERD Guidelines: Diagnostic Algorithm



- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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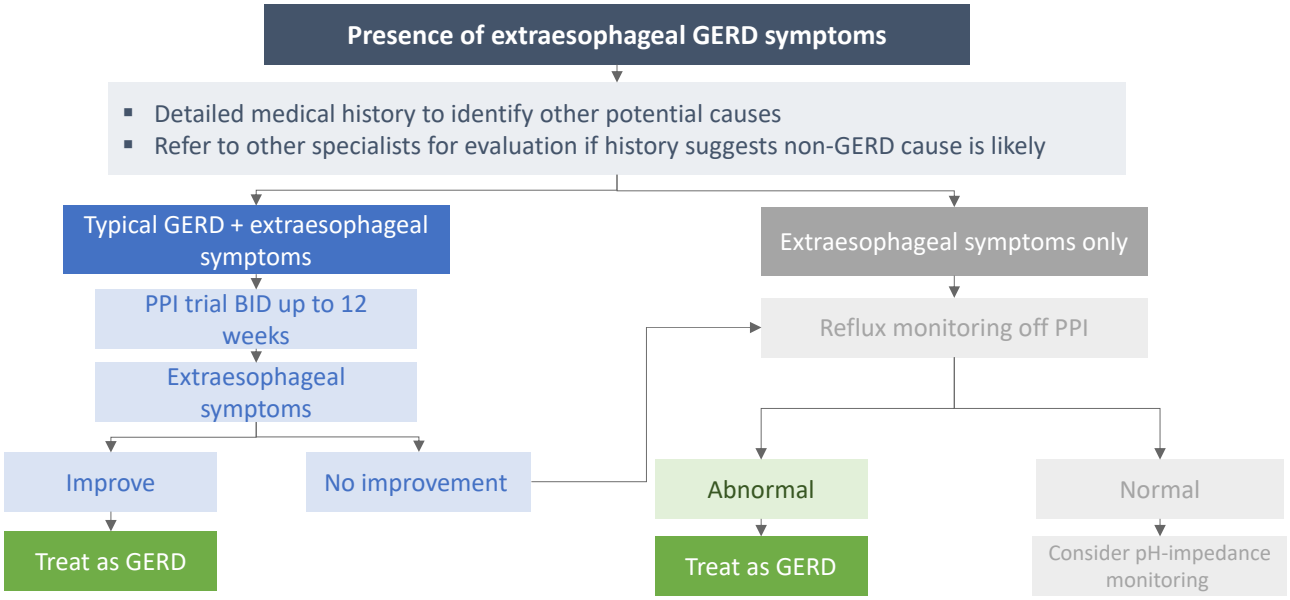
ACG Guidelines 2022: Management of Extraesophageal GERD



- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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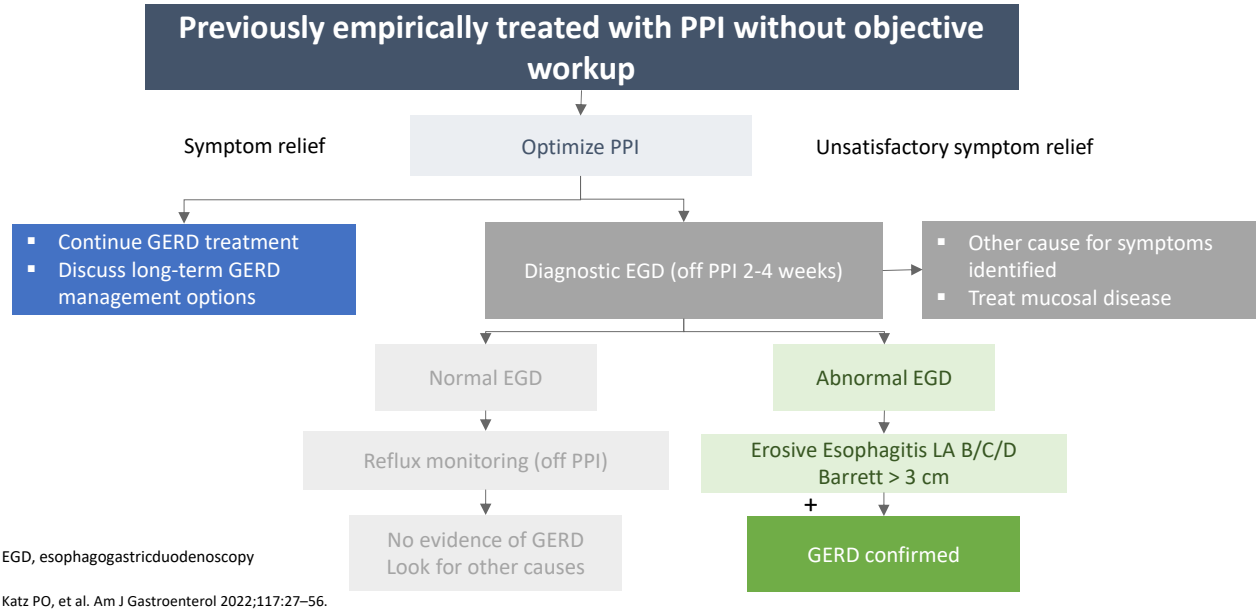
ACG Guidelines: Management of Refractory GERD



- EGD, esophagogastricduodenoscopy
- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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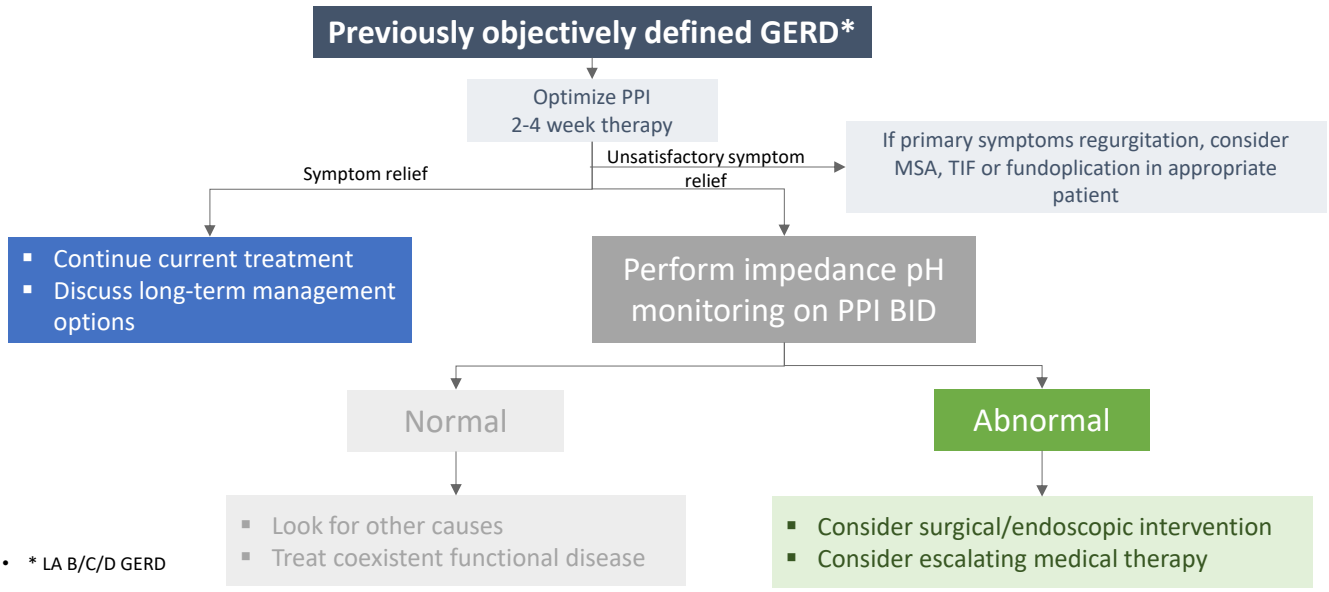
ACG Guidelines 2022: Management of Refractory GERD



- * LA B/C/D GERD
- Katz PO, et al. Am J Gastroenterol 2022;117:27–56.

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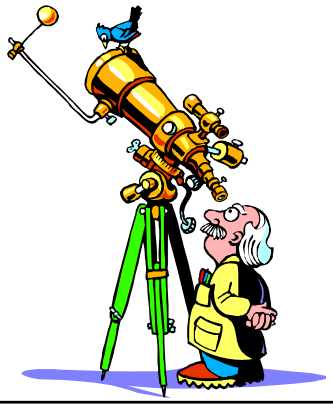
Truth

It is more important for a philosophy to be interesting, than true.

A.N. Whitehead



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Truth

I didn't say everything that I said.

Yogi Berra

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Questions and Answers

Philip O. Katz, MD, MACG, AGAF

Rena Yadlapati, MD, MSHS, FACG

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