North Carolina Society of Gastroenterology
2026 Annual Meeting

Gastroesophageal Reflux Disease (GERD) at a Glance: Diagnosis, Current Guidelines, & Emerging Therapies

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Joint Providership

Disclosures:

Phathom Pharmaceuticals (consultation)

Objectives:

As a result of this presentation, physicians/APPs will be able to:

- Use available diagnostic tools effectively for suspected GERD
- Apply updated management guidelines for GERD and extraesophageal reflux (EER)
- Understand the limitations of traditional medical treatment options and learn about a novel therapeutic agent for GERD

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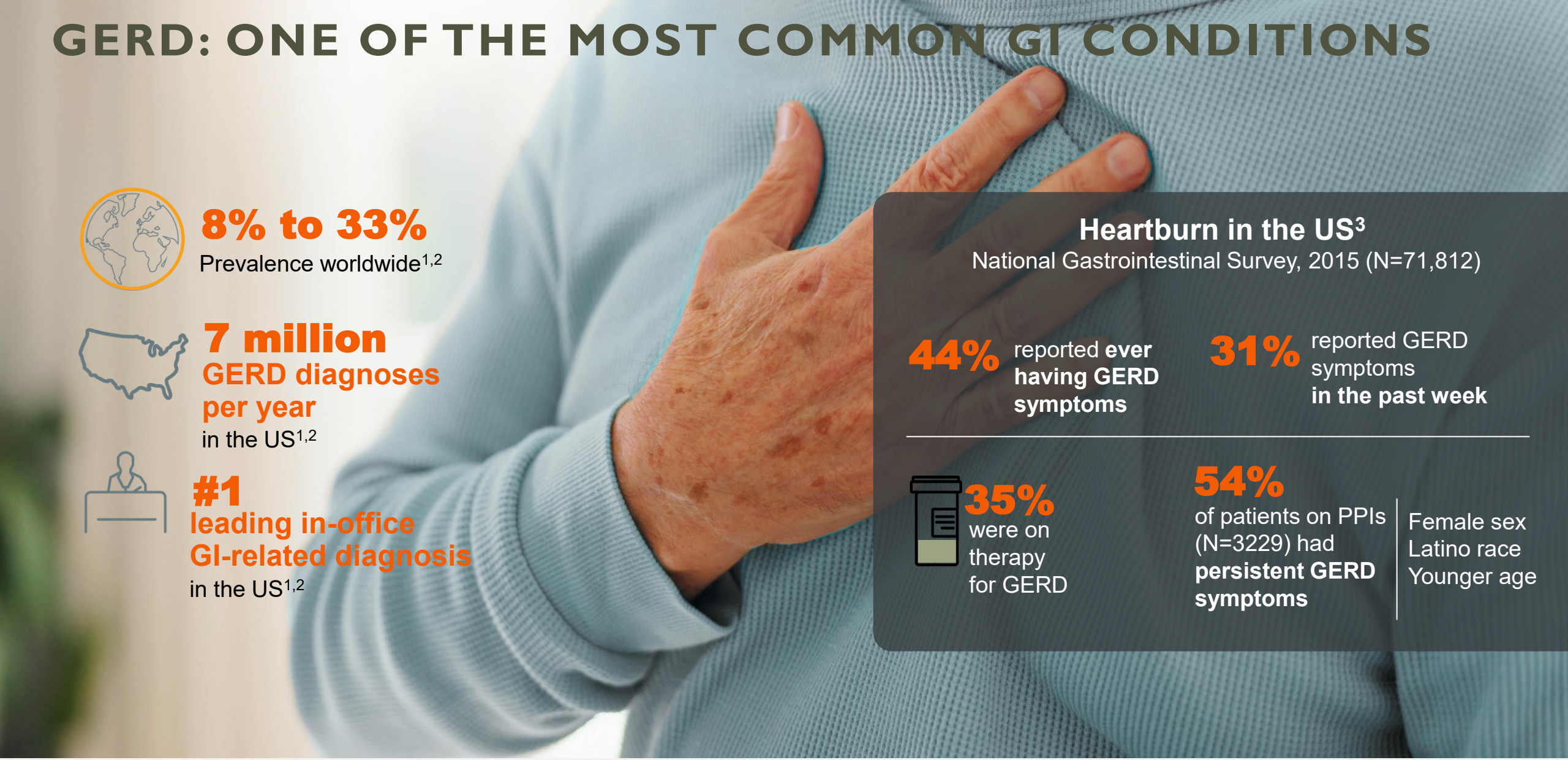
GERD: ONE OF THE MOST COMMON GI CONDITIONS



8% to 33%
Prevalence worldwide[1,2]

7 million
GERD diagnoses per year
in the US[1,2]

#1
leading in-office GI-related diagnosis
in the US[1,2]

Heartburn in the US[3]

National Gastrointestinal Survey, 2015 (N=71,812)

44% reported **ever having GERD symptoms**

31% reported GERD symptoms **in the past week**

35% were on therapy for GERD

54% of patients on PPIs (N=3229) had **persistent GERD symptoms**

Female sex
Latino race
Younger age

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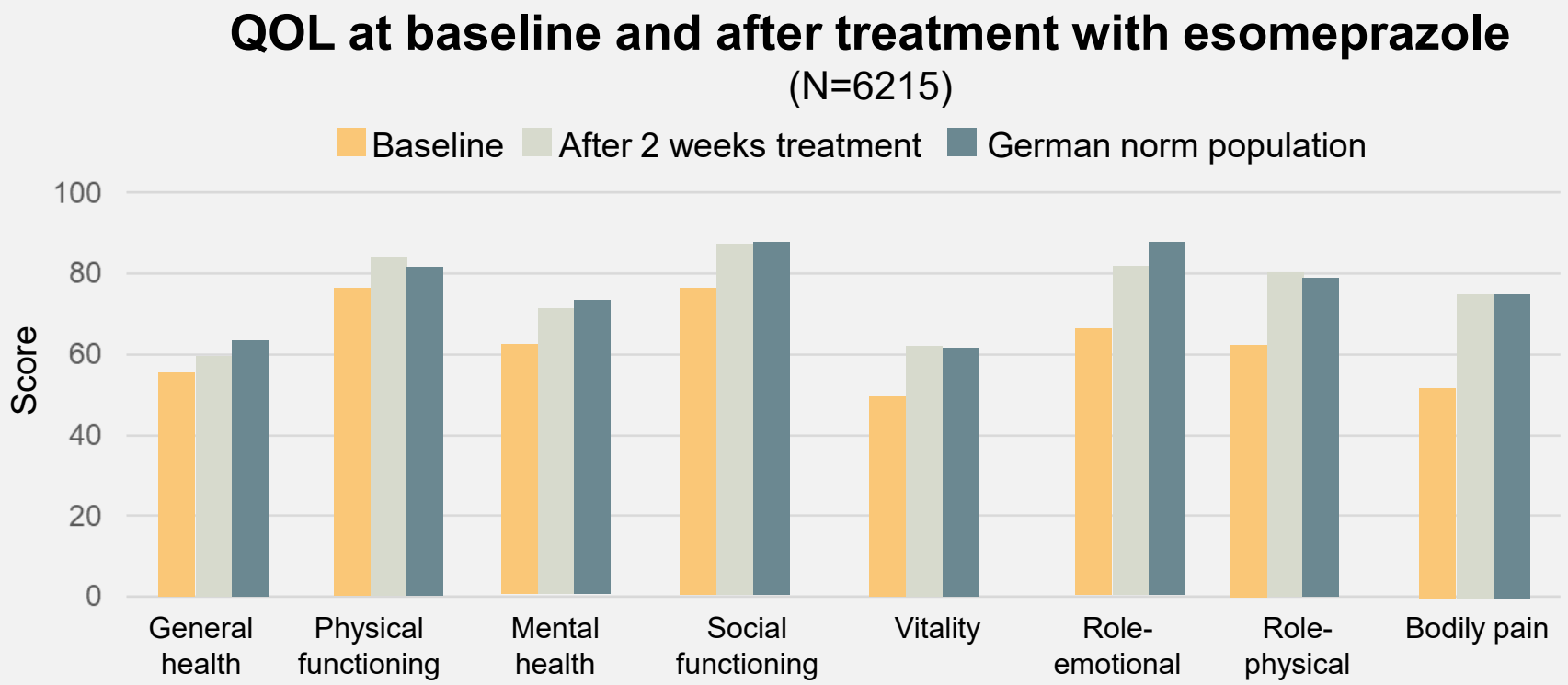
1. El-Serag HG et al. *Gut*. 2014;63(6):871-880. **2**. Peery AF et al. *Gastroenterology*. 2015;149(7):1731-1741. **3**. Delshad SD et al. *Gastroenterology*. 2020;158:1250-1261.

GERD HAS SUBSTAINTIAL IMPACT ON PATIENT QOL



Better

QoL in individuals with GERD is significantly lower than in the general population (similar to that in patients suffered from acute coronary events)

- 1. Kulig M et al. *Aliment Pharmacol Ther.* 2003;18:767-776.

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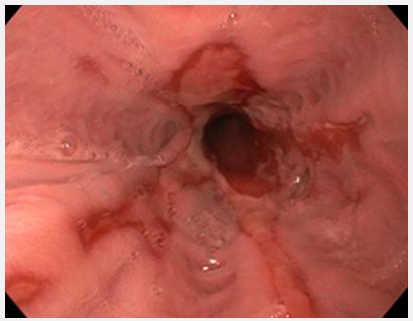
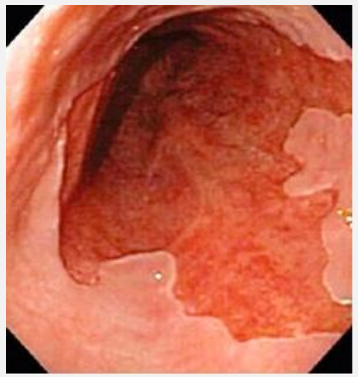
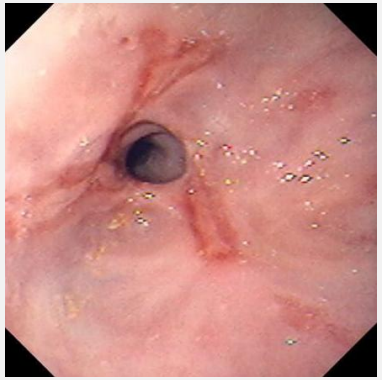
THE COMPLEXITY OF MANAGING GERD: DEFINITIONS OF GERD

Montreal Definition of GERD

A condition that develops when the reflux of stomach contents into the esophagus causes troublesome symptoms and/or complications[1]

Endoscopic Proof of GERD:
LA B, C, D Reflux Esophagitis
Barrett's esophagus
Peptic Stricture

- Based on ***symptoms***, reflux symptoms can be categorized into typical reflux symptoms (heartburn, regurgitation) and atypical/extraesophageal (chest pain, laryngitis, cough, etc.)
- Based on ***endoscopy***, GERD can be categorized into erosive and non-erosive reflux disease (NERD)
- Based on ***reflux testing***, heartburn patients can be further subcategorized into pathologic acid reflux, reflux hypersensitivity, functional heartburn

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- 1. Vakil N et al. *Am J Gastroenterol.* 2006;101(8):1900-1920

DIAGNOSTIC TESTING

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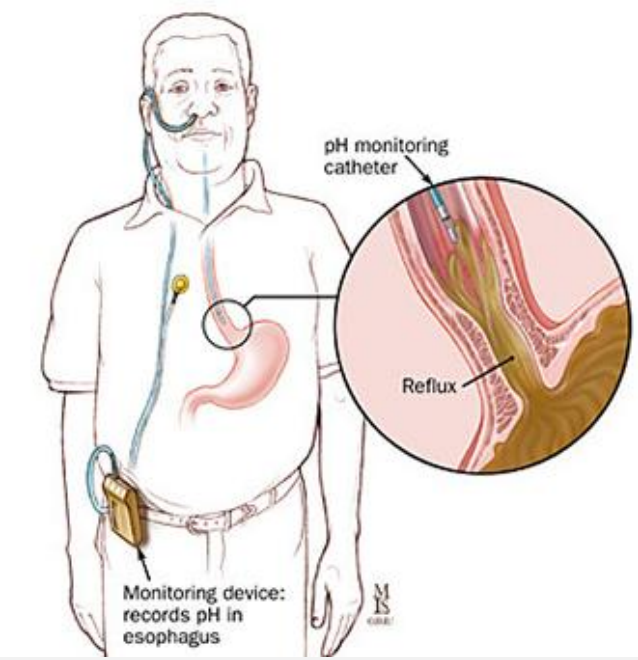
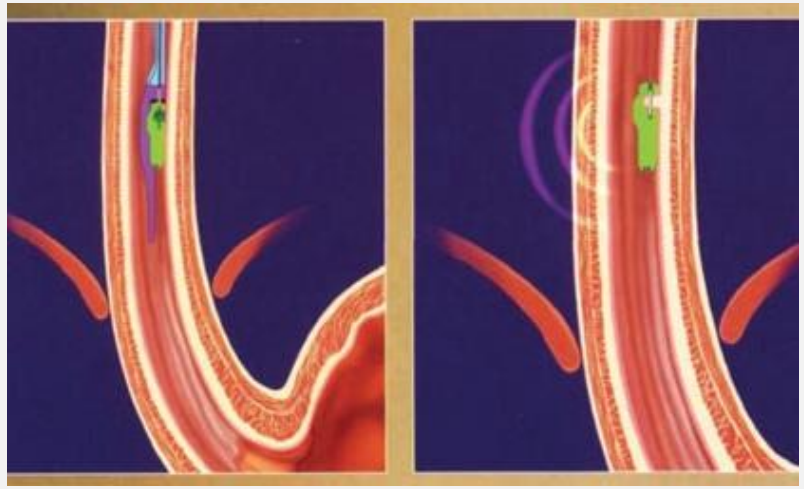
AMBULATORY REFLUX MONITORING

pH-only Testing:

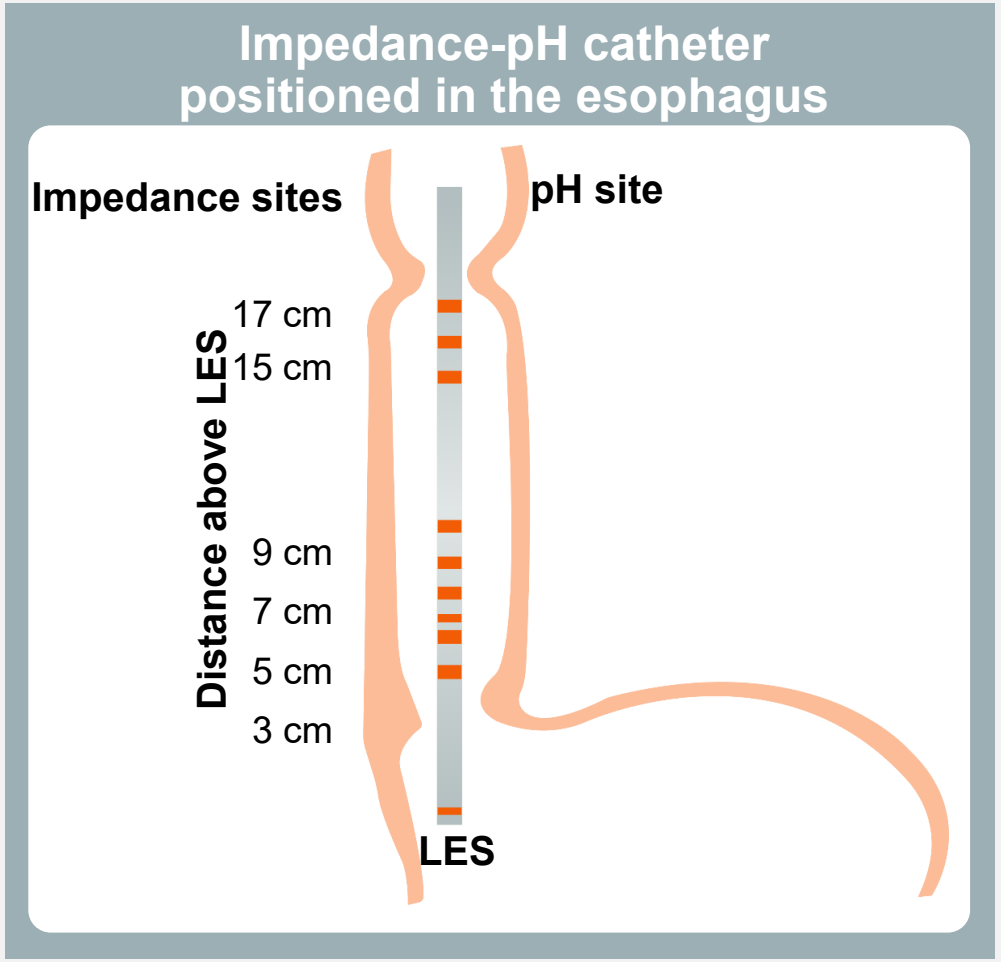
Wired:



Wireless:



Impedance-pH Testing:



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AMBULATORY REFLUX MONITORING

	pH-catheter	Wireless pH capsule	pH-impedance catheter	
Standard distal pH sensor positioning	5-cm proximal to LES (manometrically identified)	6-cm proximal to SCJ (endoscopically identified)	5-cm proximal to LES (manometrically identified)	
Test duration	24 hours	48-96 hours	24 hours	
Test setting	Placed in awake patient	Typically placed during sedated endoscopy	Placed in awake patient	
Reflux composition detected	Acidic	Acidic	Acidic, weak-acidic, non-acidic	
Proximal reflux detected?	Possible	No	Yes	
Primary/ secondary parameters assessed	AET SRA	AET SRA	AET SRA (acid/nonacid) # Reflux episodes based on impedance	# Nonacid Reflux Proximal Reflux % Bolus exposure

AET, acid exposure time; LES, lower esophageal sphincter; SRA, symptom-reflux association

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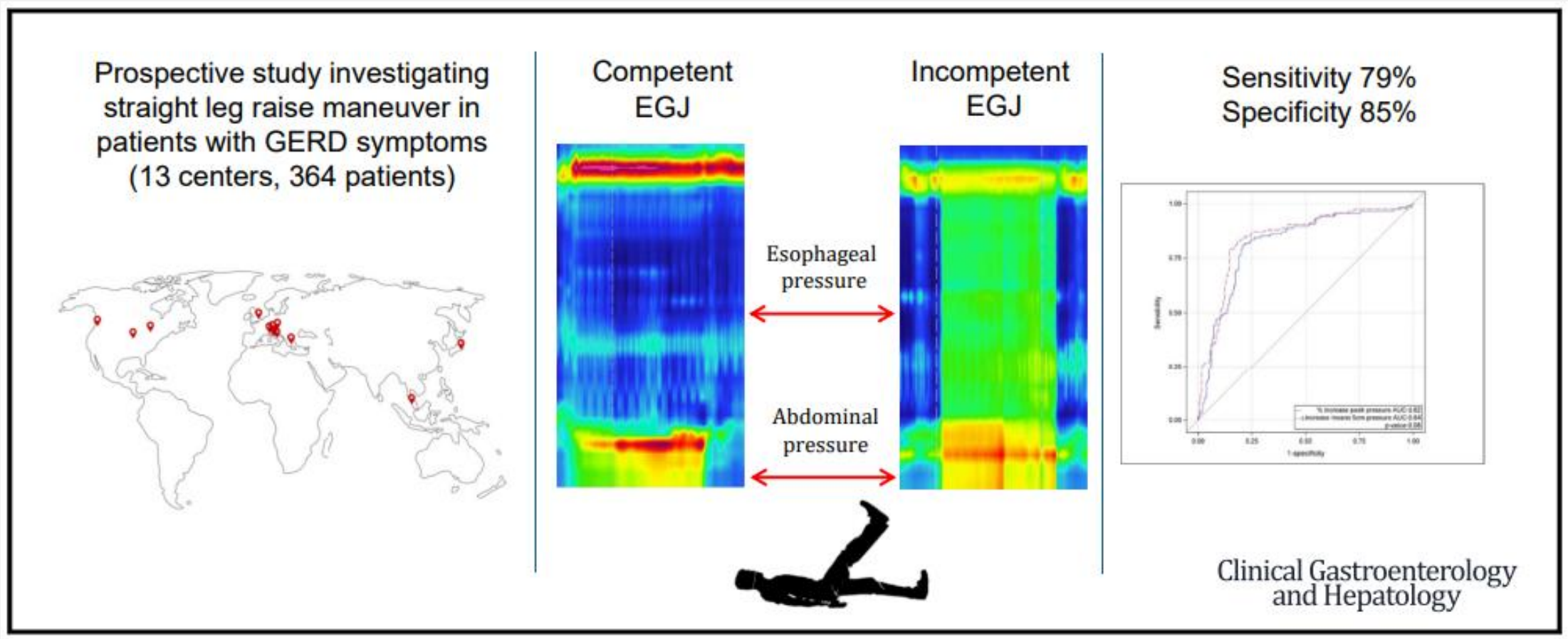
- Chen J et al. *Clin Gastroenterol Hepatol*. 2023;21(6):1414-1421.

ROLE OF HIGH-RESOLUTION MANOMETRY IN GERD: STRIGHT LEG RAISE (SLR)



Increase in IEP of 11mmHg provided ~80% sensitivity and ~85% specificity in identifying GERD patients.

- Siboni S, et al., *Clin Gastroenterol Hepatol*. 2023;2197):1761-70

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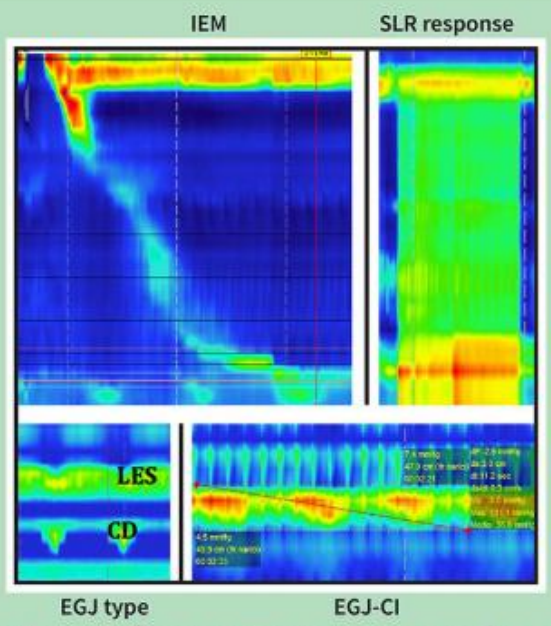
The Milan Score: a novel manometric tool for a more efficient diagnosis of gastro-esophageal reflux disease

Method

295 patients with GERD symptoms prospectively collected from 13 centers

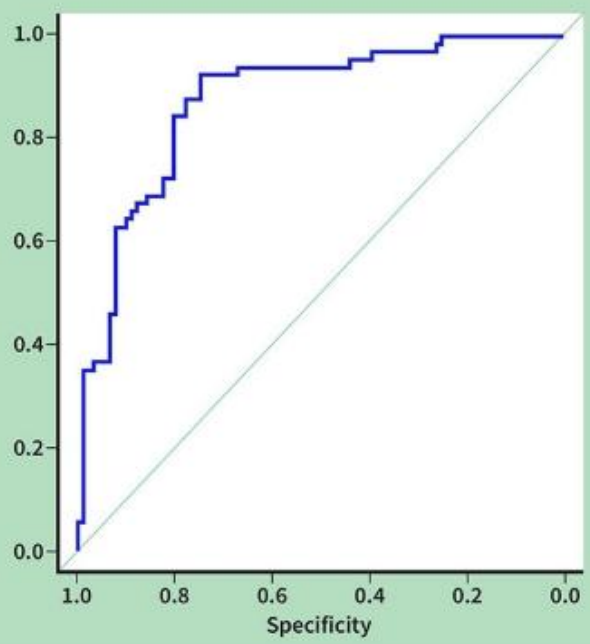


Creation of a nomogram and a score with HRM variables

Results

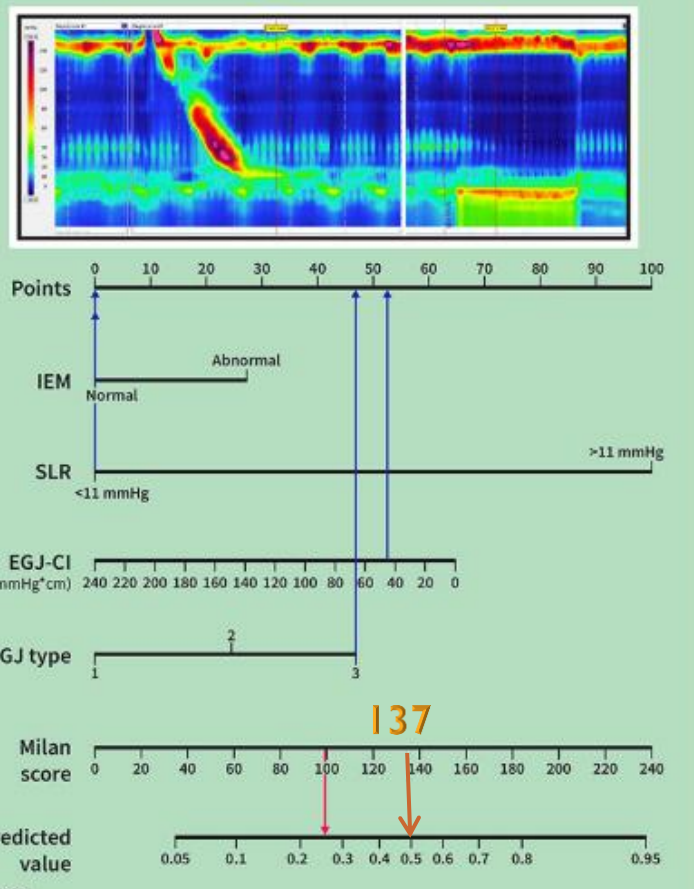
A supplemental cohort of 233 patients validated the model

AUC = 0.88 (CI 95%: 0.82 – 0.93)



Practical use

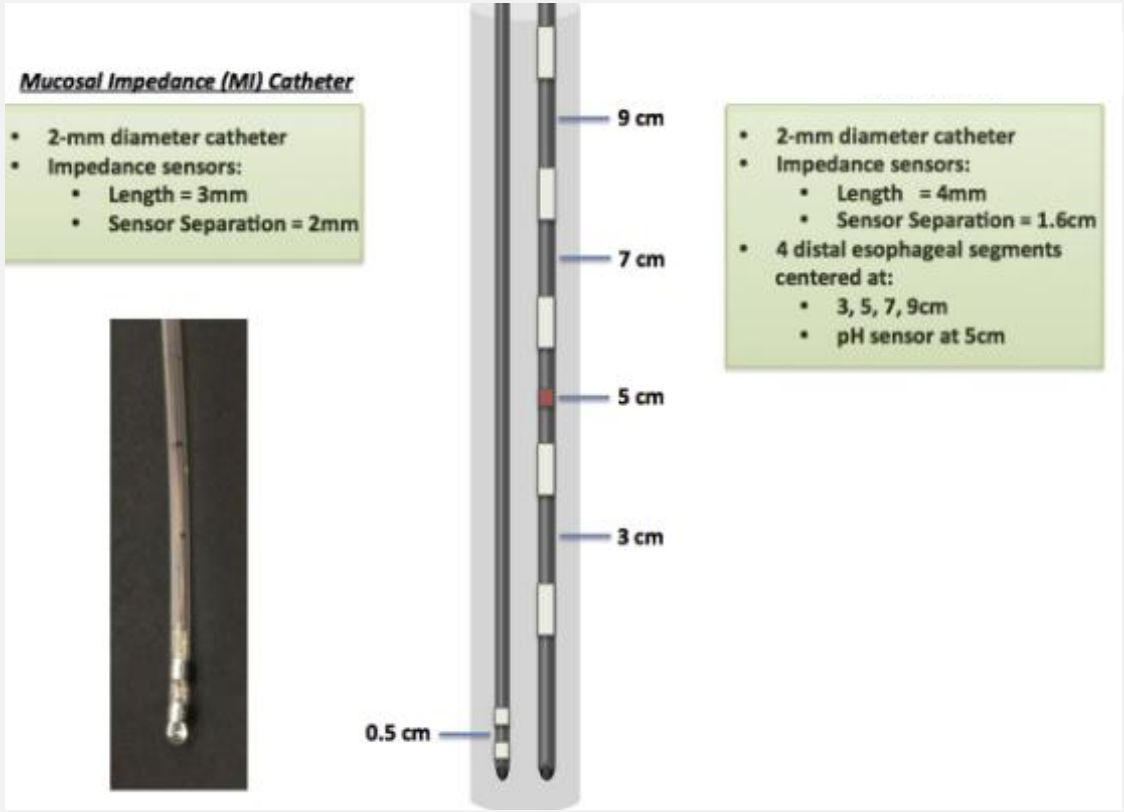
Low probability of GERD (23% - Milan score 98) – AET: 2.1%



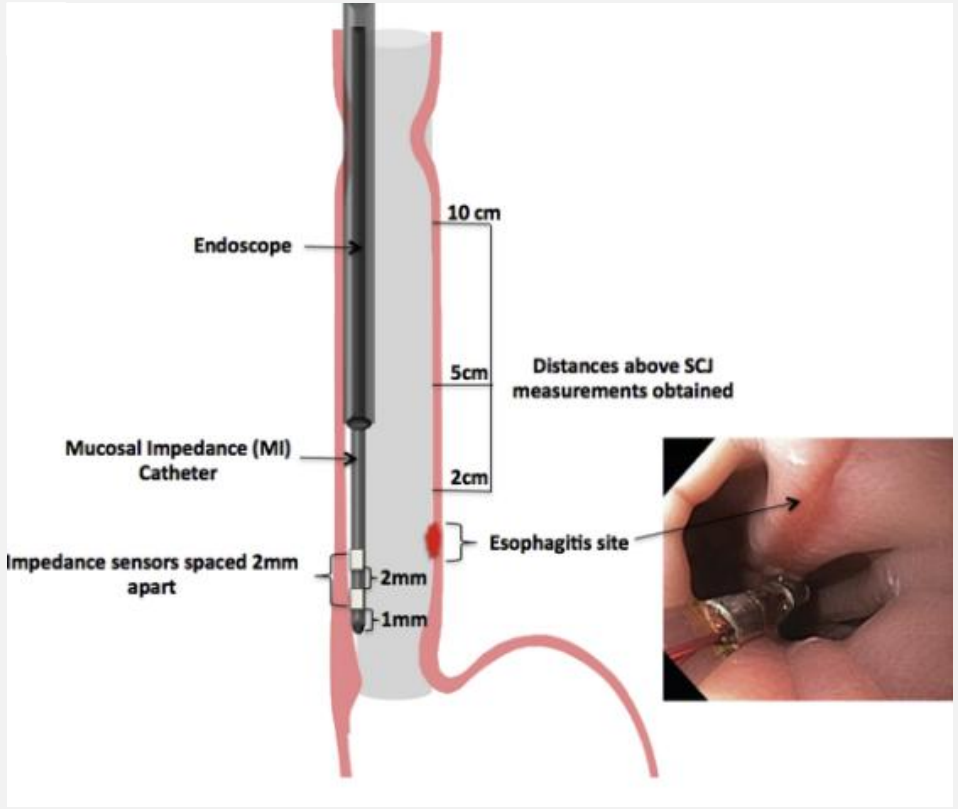
ueg journal
Siboni, S et al. United European Gastroenterology J. 2024
Visual abstract created by Susan Tyler

NOVEL DIAGNOSTIC TOOLS: MUCOSAL IMPEDANCE

- Esophageal MI measurement via either multichannel intraluminal impedance catheters or endoscopic impedance catheters, measures esophageal epithelial *integrity*



Traditional multichannel impedance-pH catheter
24-hour recording



Mucosal impedance (MI) catheter
Real time data during endoscopy

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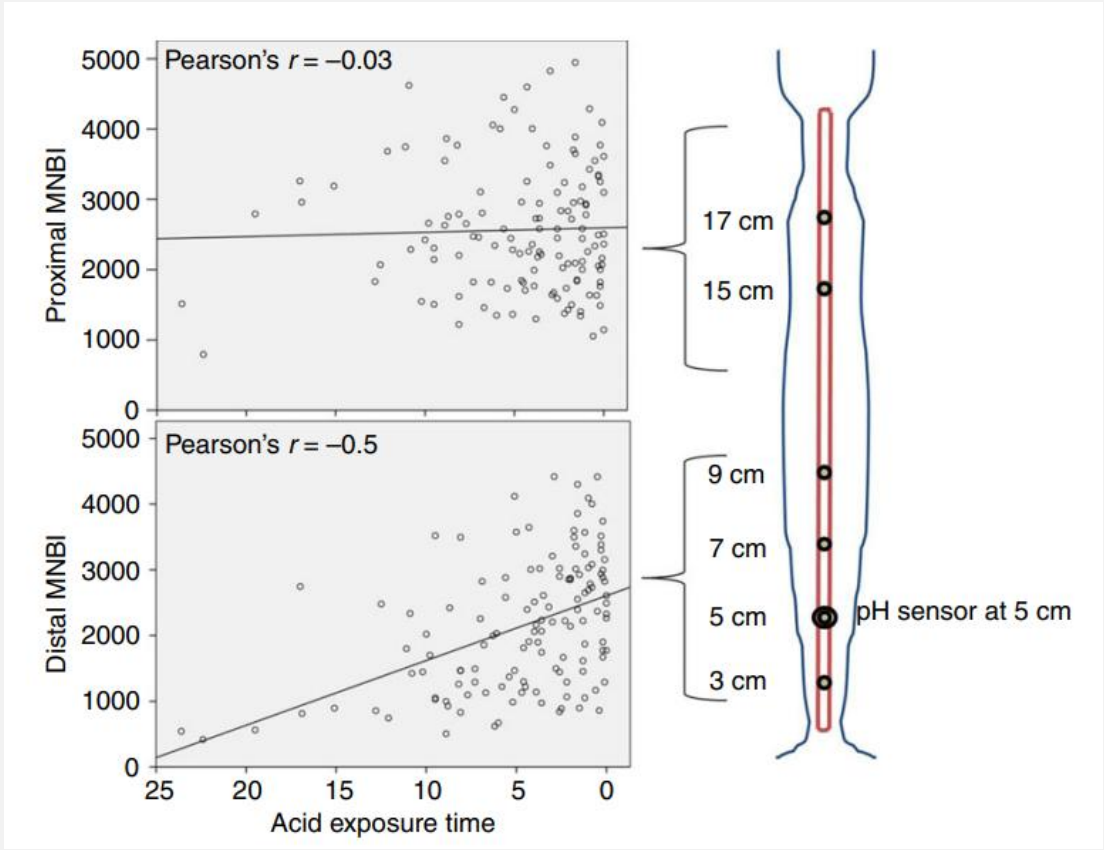
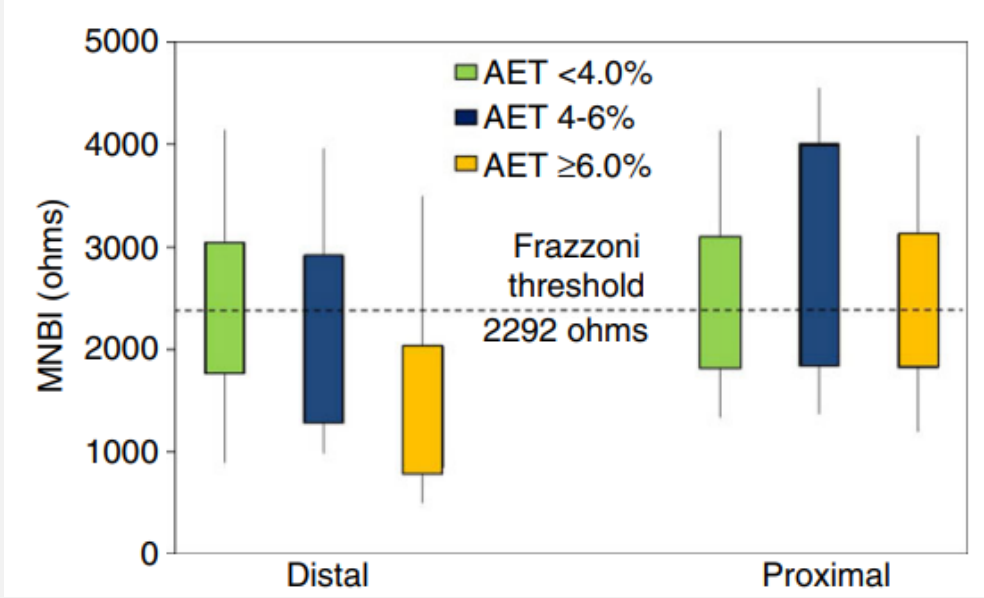
1. Patel A et al. AP&T 2016 2. Frazzoni L et al. Gut 2022

MUCOSAL IMPEDANCE FOR DIAGNOSIS OF GERD

MEAN NOCTURNAL BASELINE IMPEDANCE (MNBI)

Distal MNBI correlated modestly with AET but not proximal MNBI





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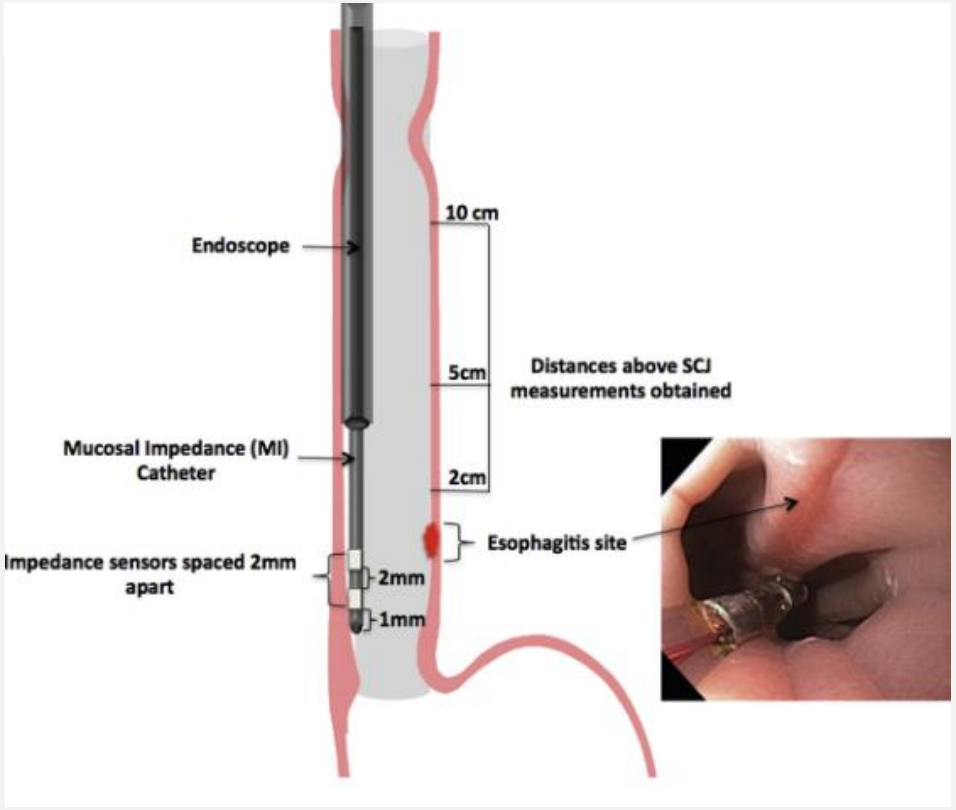
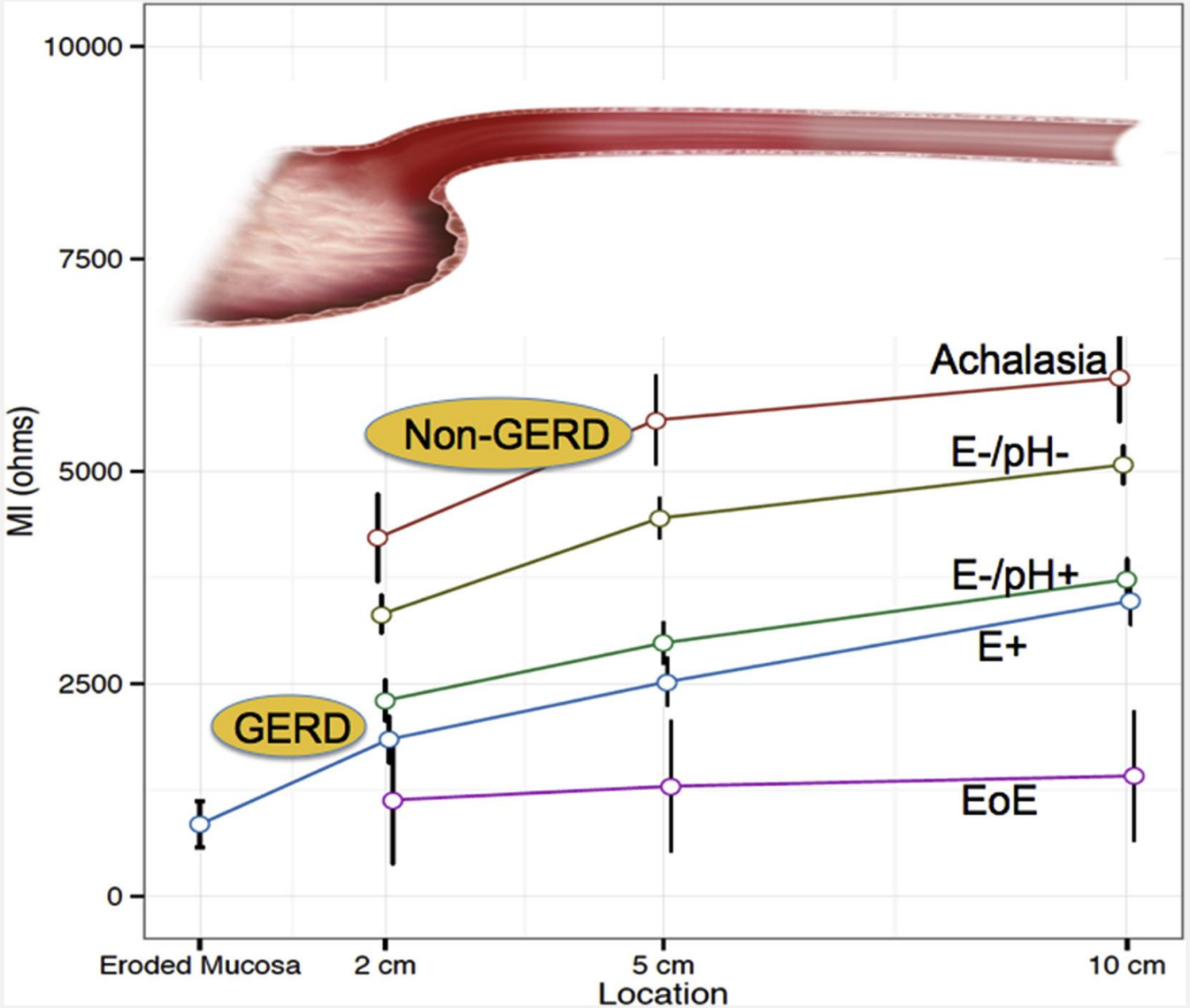
I. Patel A et al. AP&T 2016 2. Frazzoni L et al. Gut 2022

MUCOSAL IMPEDANCE FOR DIAGNOSIS OF GERD



Mucosal impedance (MI) catheter



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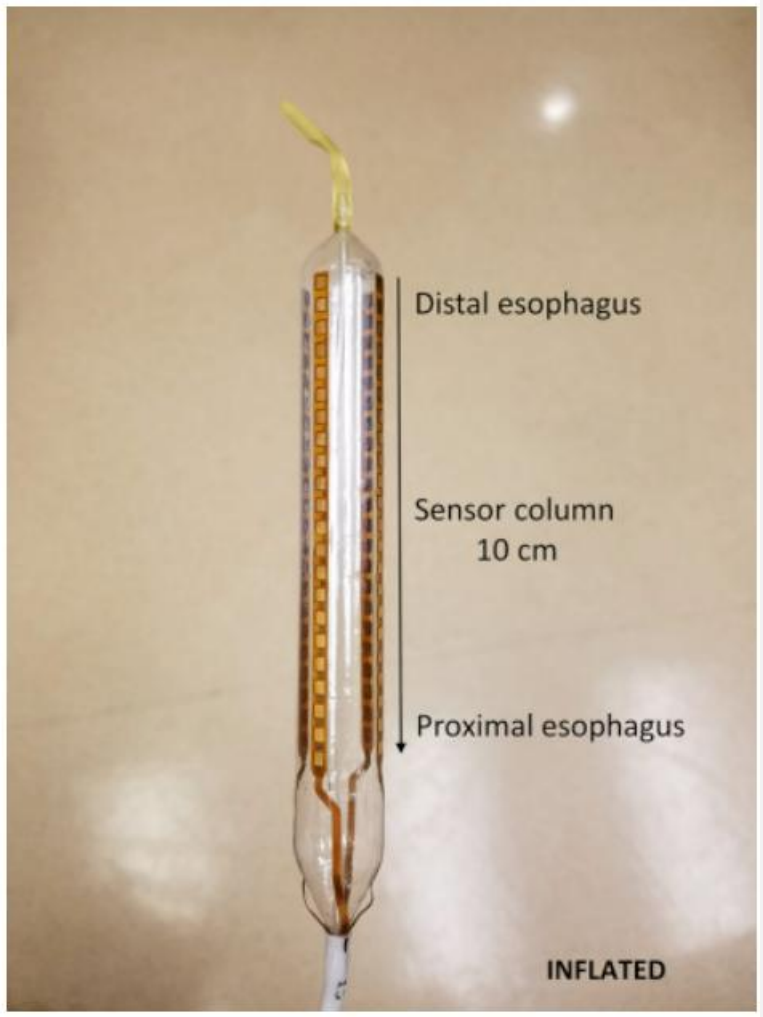
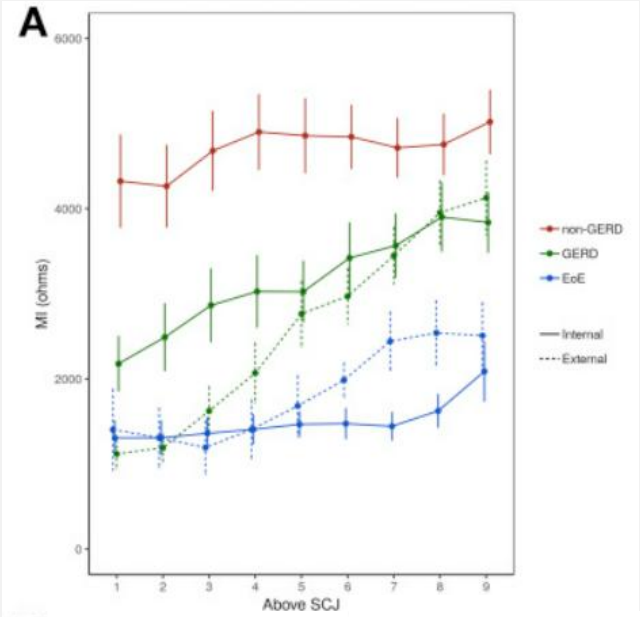
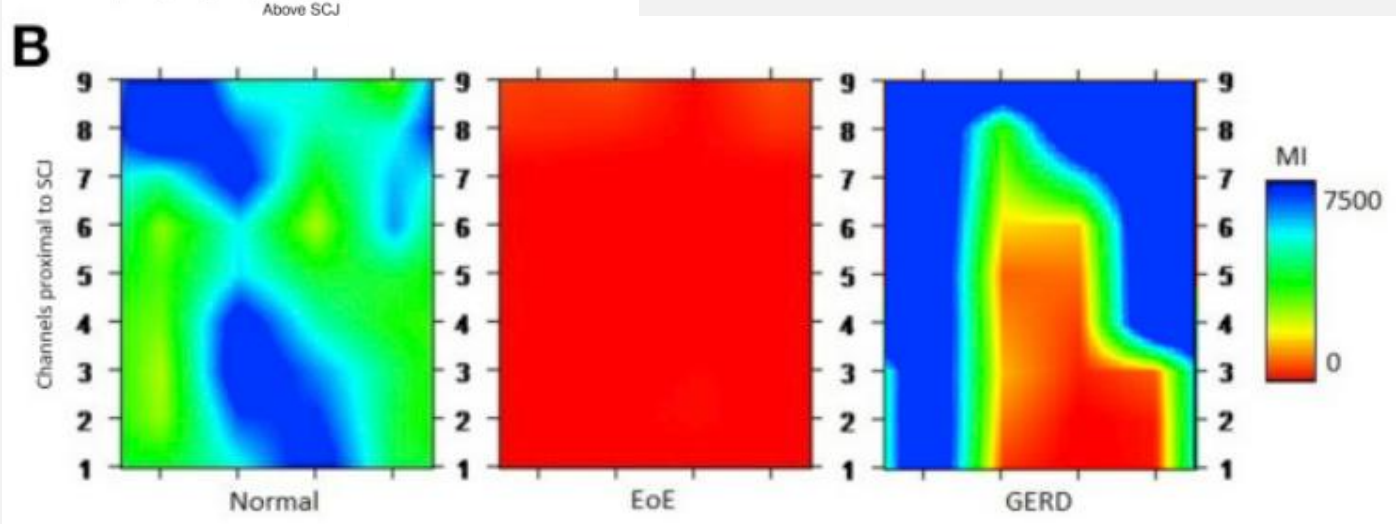
1. Lei W, et al. J Formos Med Assoc. 2020;119(11):1575-80. 2. Ates F, et al. Gastroenterology, 148:334-43

MUCOSAL IMPEDANCE FOR DIAGNOSIS OF GERD





Current guidelines acknowledge that catheter-based MI devices show promise for differentiating GERD from non-GERD and may be particularly valuable when conventional investigations yield equivocal results.



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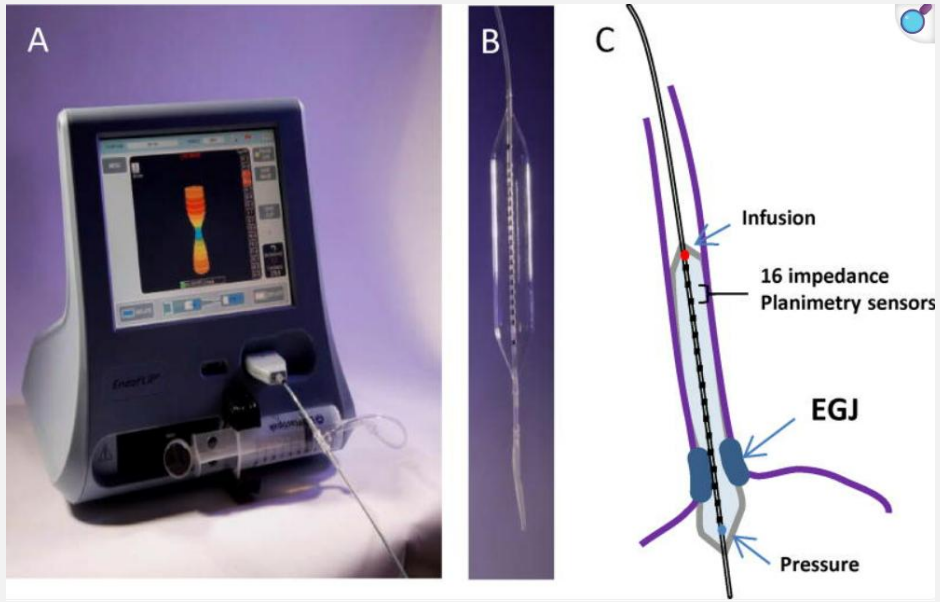
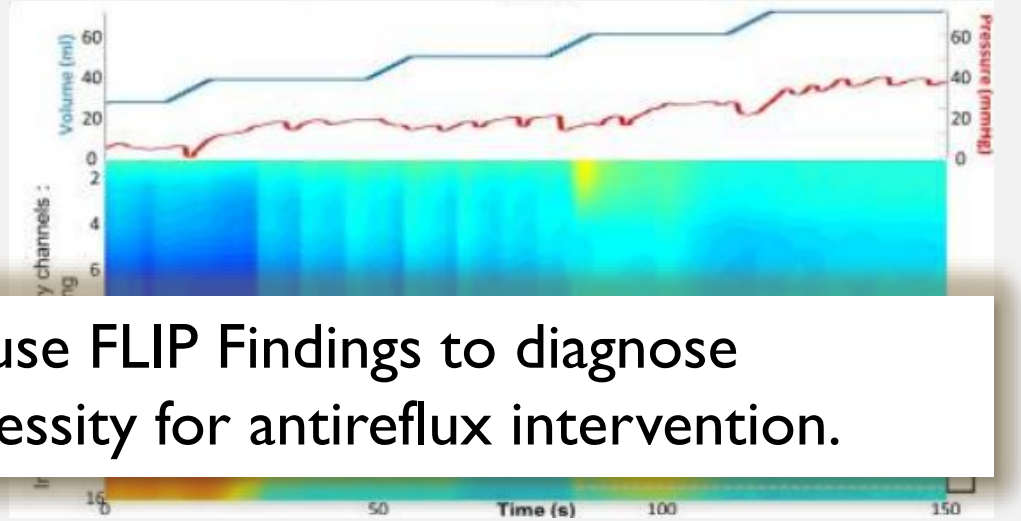
1. Patel DA, et al. Gastroenterology 2019 156(6):1617-26

ENDOFLIP IN GERD ASSESSMENT

endoFLIP: endoluminal Functional Lumen Imaging Probe (FLIP)

- Assessment of EGJ competence may help understand GERD pathophysiology.
- FLIP evaluation of EGJ barrier function in GERD have not demonstrated a discriminative distensibility threshold for segregating symptomatic GERD from controls.
- Abnormal esophageal acid exposure was associated with impaired contractile response (i.e. AET was higher in patients without repetitive antegrade contractions). This supports that acid exposure is dependent on acid clearance mechanisms





AGA CPU Best Practice Advice 8: Clinicians should not use FLIP Findings to diagnose gastroesophageal reflux disease or to determine the necessity for antireflux intervention.

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- 1. Carlson DA, et al. *Neurogastroenterol Motil*. 2018;30(3):10.1111/nmo.13240 2. Nguyen, Anh D. et al. Gastroenterology 2025;169(4):726-736

GERD GUIDELINES

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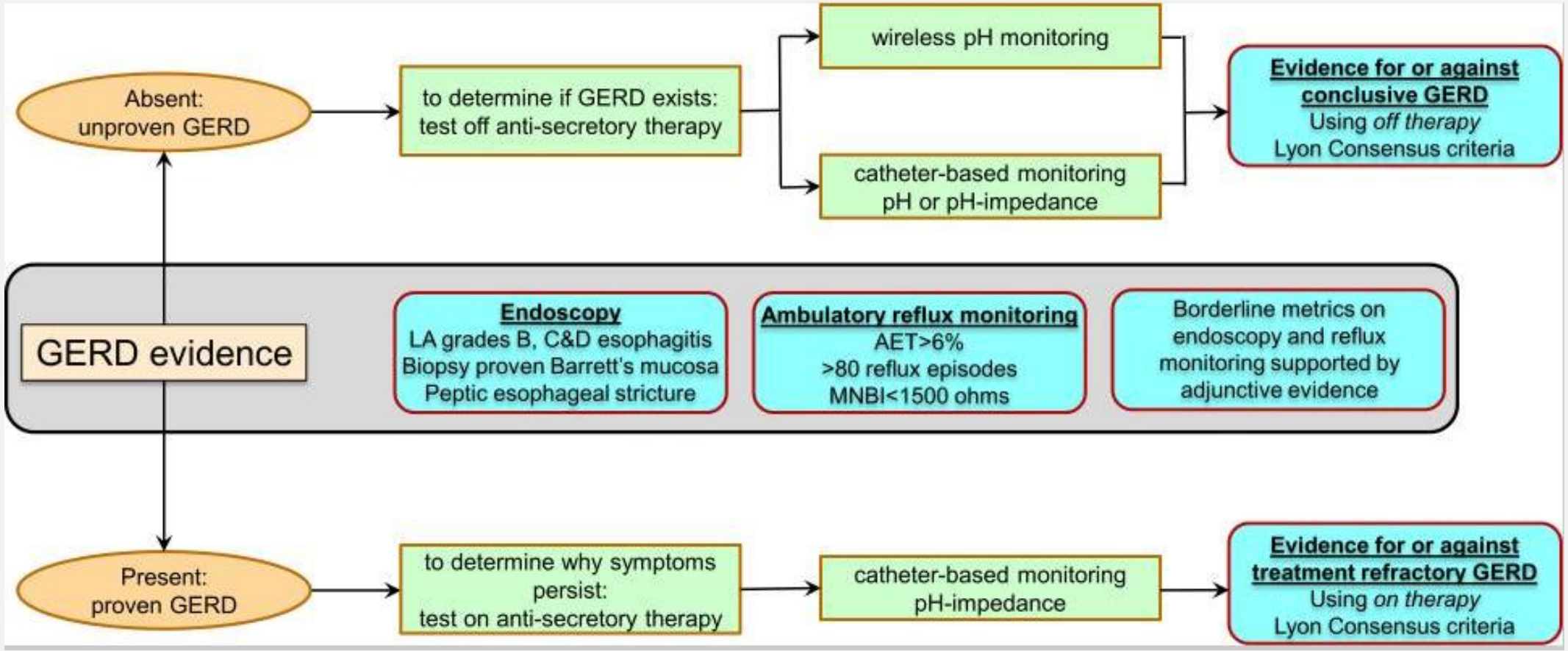
LYON CONSENSUS 2.0



- Gyawali CP, et al. *Gut*. 2024;73(2):361-371

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LYON CONSENSUS 2.0

	UNPROVEN GERD Endoscopy ,wireless pH study, 24- hour pH, or pH impedance, HRM OFF THERAPY			PROVEN GERD 24-hour pH impedance ON THERAPY
	ENDOSCOPY	pH or pH-IMPEDANCE	HRM	ENDOSCOPY pH-IMPEDANCE
Conclusive evidence for pathologic reflux	LA grades B, C, and D esophagitis Biopsy-proven Barrett's mucosa Peptic esophageal stricture	AET>6% on 24-hour studies AET>6% on ≥2 days on wireless studies		LA grades B, C, and D esophagitis Peptic esophageal stricture AET>4%, reflux episodes>80
Borderline or inconclusive evidence	LA grade A esophagitis	AET 4-6% on 24-hour studies AET4-6% on ≥2 days on wireless studies Total reflux episodes 40-80/day		LA grade A esophagitis AET 1-4% Total reflux episodes 40-80/day MNBI1500-2500 Ω
Adjunctive or supportive evidence[a]	Hiatus hernia Histopathologic scoring systems Electron microscopy of biopsies	Reflux-symptom association Total reflux episodes>80/day MNBI<1500 Ω	Hypotensive EGJ Hiatus hernia IEM/absent contractility	Hiatus hernia MNBI <1500 Ω Reflux symptom association
Evidence against pathologic reflux		AET≤4% each day of study[b] Total reflux episodes<40/day MNBI>2500 Ω		AET<1% Total reflux episodes <40/day MNBI>2500 Ω

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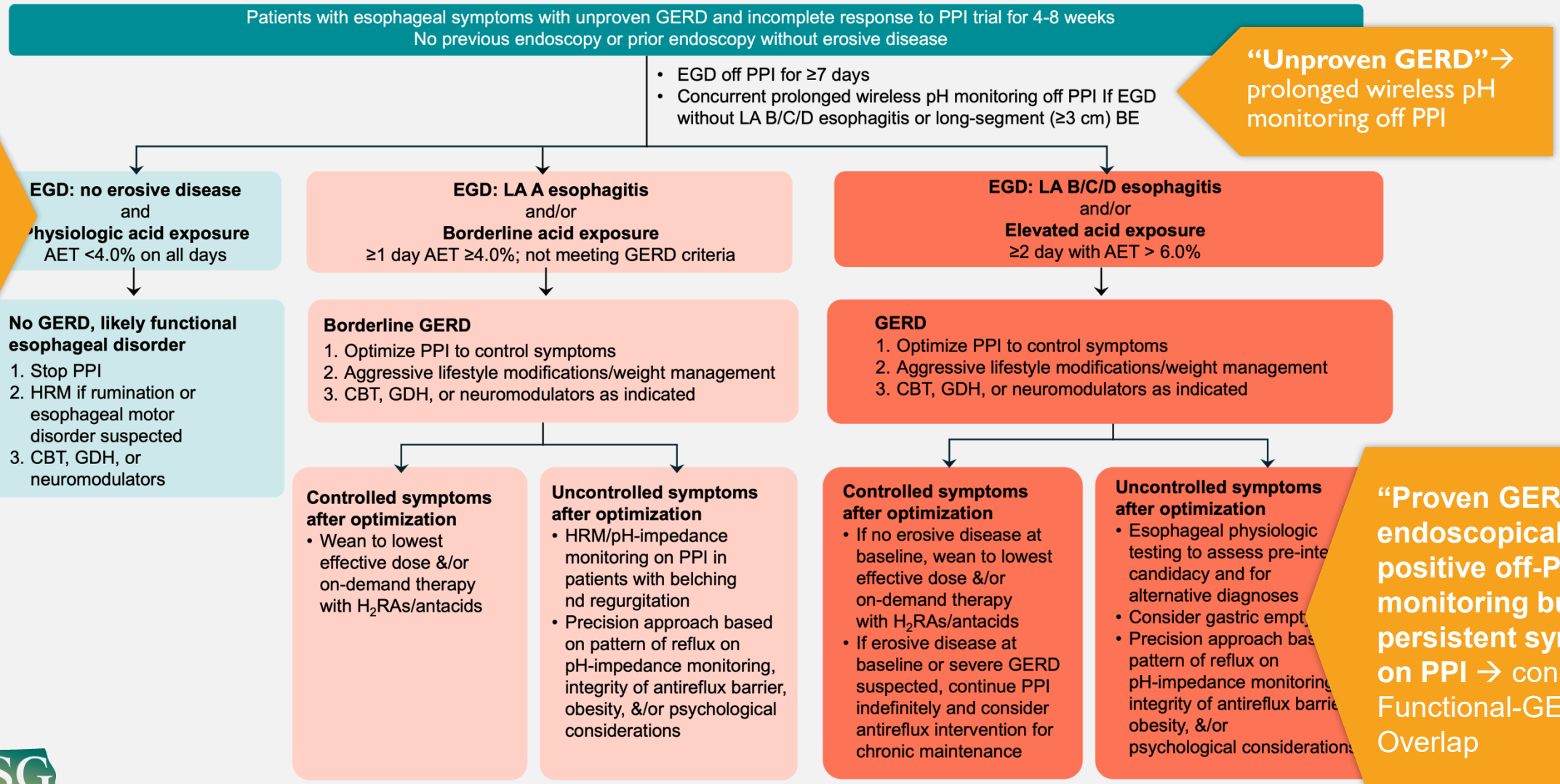
- Gyawali CP, et al. *Gut*. 2024;73(2):361-371

AGA GERD CLINICAL PRACTICE UPDATE



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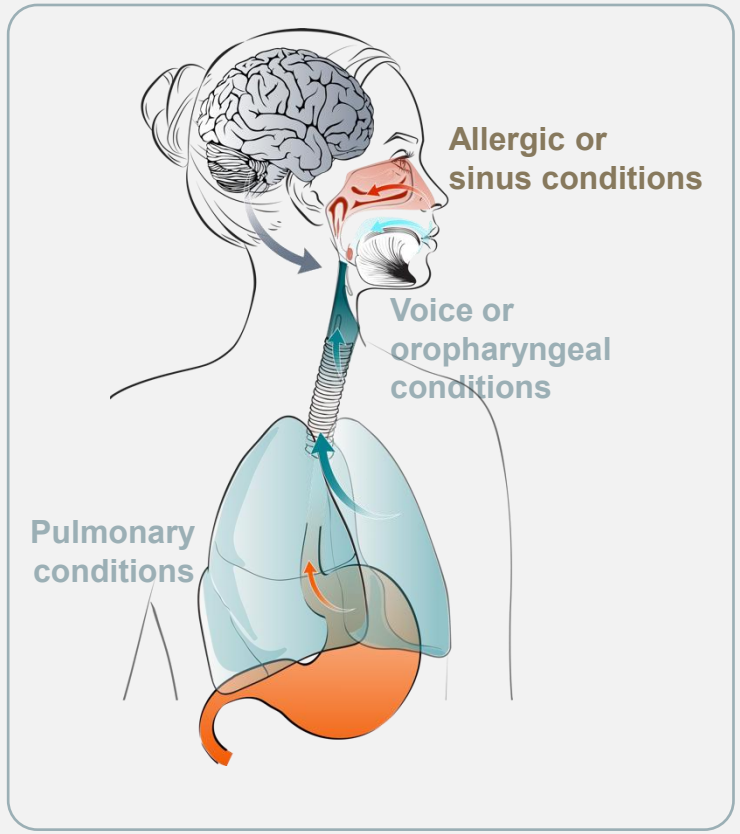
- Yadlapati R et al. *Clin Gastroenterol Hepatol*. 2022;20:984-994.

EXTRAESOPHAGEAL REFLUX SYMPTOMS & DIFFERENTIAL DIAGNOSIS



Extraesophageal symptoms and manifestations	Differential diagnosis	Multidisciplinary team
Laryngeal/ENT	Postnasal drip	Otolaryngology
Laryngitis/hoarseness	Laryngeal allergy	Gastroenterology
Globus	Functional dysphonia	Allergy/Immunology
Mucus in throat	Laryngeal papilloma	Speech pathology
Throat clearing	Muscle tension dysphonia	Behavioral psychology
Throat pain	Vocal cord paralysis	
Sinus inflammation	Vocal cord polyps	
Post-nasal drip	Sinusitis (occult)	
	Gastric inlet patch	
Pulmonary	Post-nasal drip	Pulmonology
Asthma	Asthma	Otolaryngology
Chronic cough	Vocal cord dysfunction	Allergy/Immunology
Pulmonary fibrosis	Medication reaction (ie, angiotensin converting enzyme inhibitors)	Gastroenterology
Allograft failure	Lung transplant rejection	Primary care
Dentition	Poor dietary habits (ie, acidic soft drinks, fruit juices)	Dentistry
Dental erosions	Eating disorders with regurgitation (bulimia)	Gastroenterology
Dental caries	Xerostomia (Sjogren's)	Nutrition
	Environmental (ie, around acidic fumes)	Primary care
		Psychology

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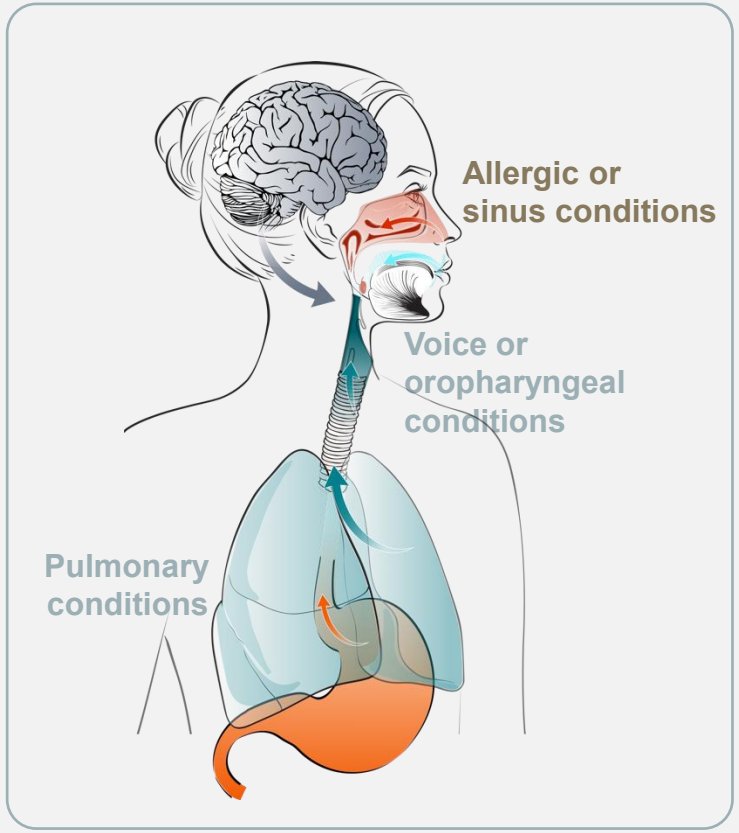
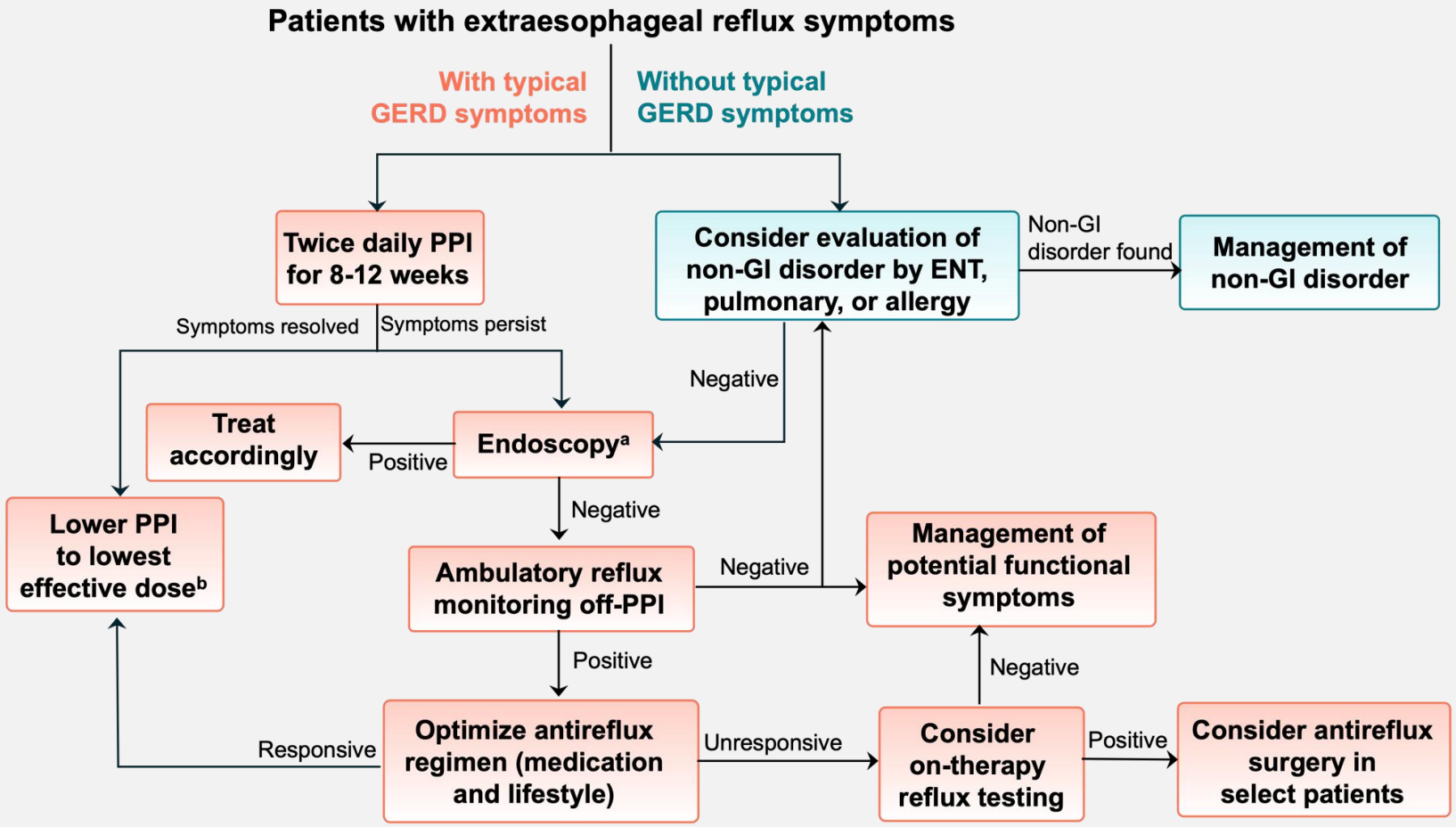
AGA CLINICAL PRACTICE UPDATE ON EXTRAESOPHAGEAL REFLUX (EER) SYMPTOMS





[a]Look for evidence of GERD-related injury or complications and rule out alternative esophageal diseases.
[b]Consider endoscopy and reflux monitoring to support long-term use of PPI.

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- Chen JW et al. *Clin Gastroenterol Hepatol*. 2023;21:1414-1421.

GERD TREATMENT

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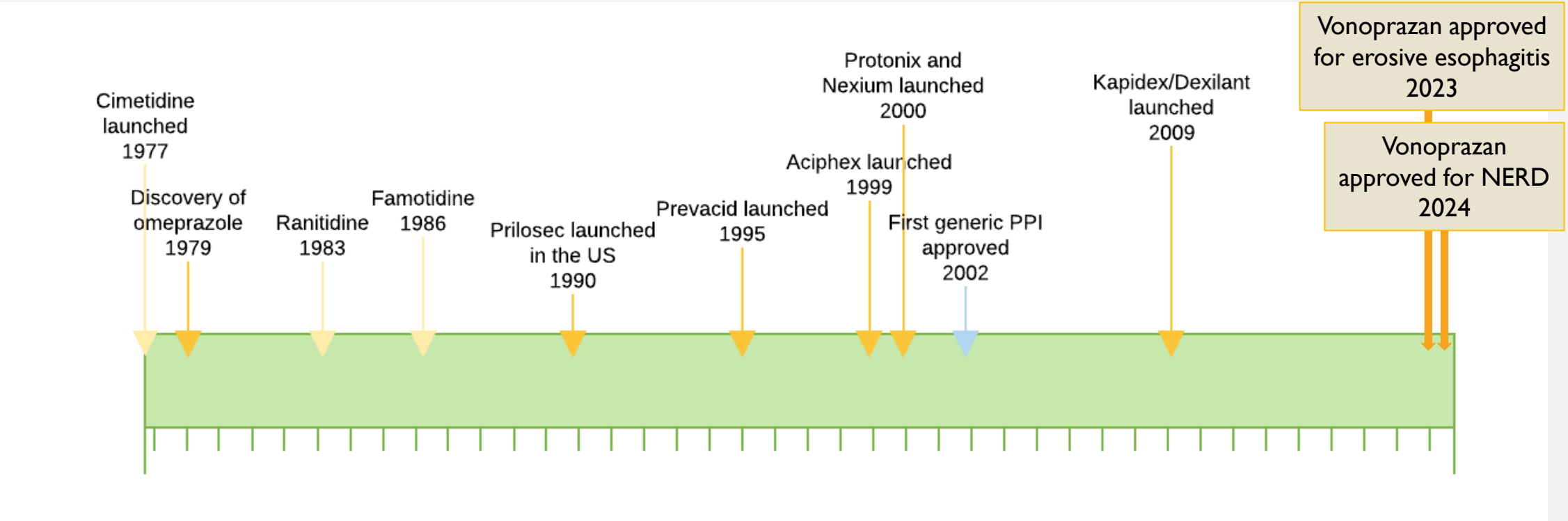
HISTORY OF MEDICAL THERAPY FOR GERD



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UNMET NEEDS WITH STANDARD PPI THERAPY

- Activation of PPI from prodrug requires an acidic environment
- Binds to activated proton pumps (meal dependent)
- Slow onset, full effect requires repeated dosing
- Short half-life
- Pharmacokinetics affected by genetic polymorphism

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MECHANISTIC DIFFERENCES BETWEEN PCAB* & PPI

Characteristics	PCABs	PPIs
Mechanism of action	Prevents proton pump activation by blocking passage of K+ ions	Prodrug needs to be converted to active form (sulfenamide)
Concentration in parietal cell acid space	100,000-fold more elevated than in plasma	1000-fold more elevated than in plasma
H+/K+ ATPase binding	Reversible, ionic	Irreversible, covalent
Acid stability	Yes	No
Half-life	6-9 h	1-2 h
Maximum pharmacodynamic effect	Soon after first dose	After 3-5 days of repeated daily dose
Antisecretory activity	Acts on active and inactive pumps	Only acts on active pumps
CYP2C19 Polymorphism effect	No	Yes

**PCABs: potassium-competitive acid blockers*

- Kothadia JP, Howden CW. *Foregut*. 2023.

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**PCABs: potassium-competitive acid blockers*

- Kothadia JP, Howden CW. *Foregut*. 2023.

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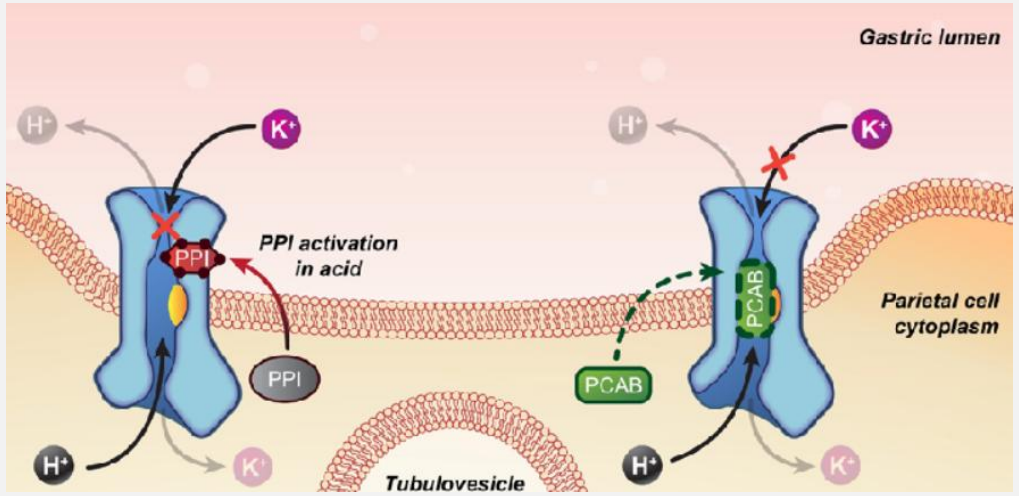
CLINICAL DIFFERENCES BETWEEN PCAB & PPI



PPI

- Best taken 30-60 min before meals
- Enteric coating needed
- Repeated dosing needed for effect
- Short duration of effect
- Less effective in CYP2C19 rapid metabolizers

P-CAB

- No need to time with meals
- No need for enteric coating
- Effect seen after first dose
- Longer duration of effect
- Not affected by CYP2C19 polymorphism

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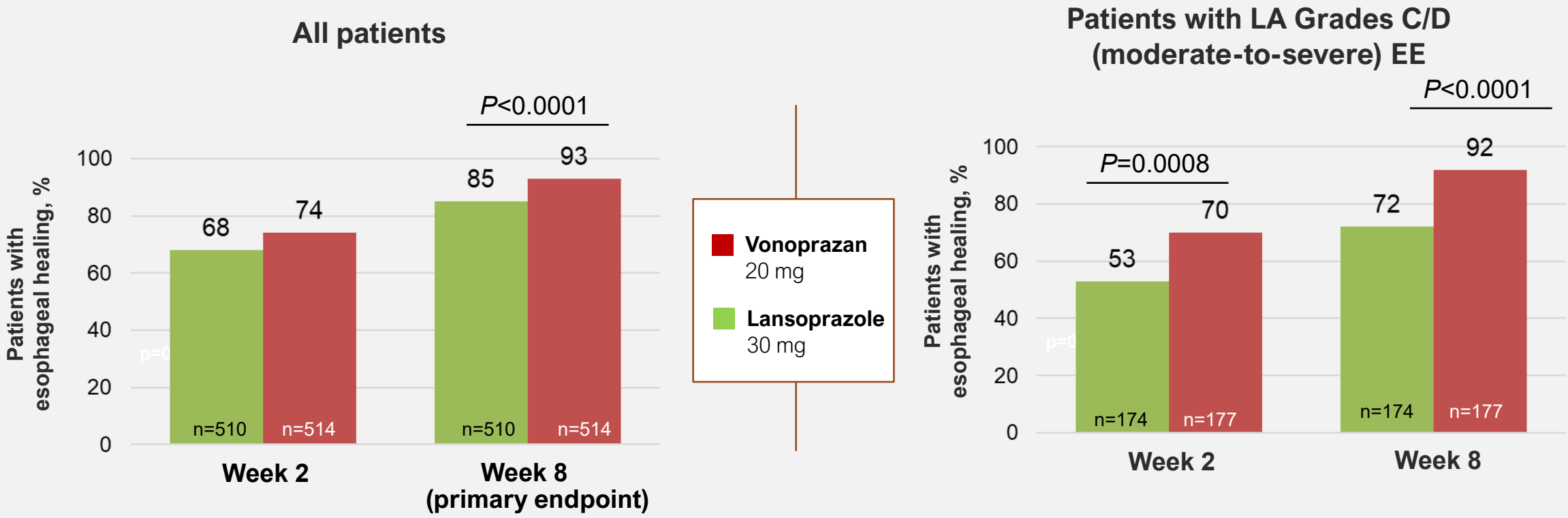
- Shibli F et al. *Current Gastroenterol Reports* 2020

VONOPRAZAN EFFICACY IN EE: ESOPHAGEAL HEALING AT WEEK 8

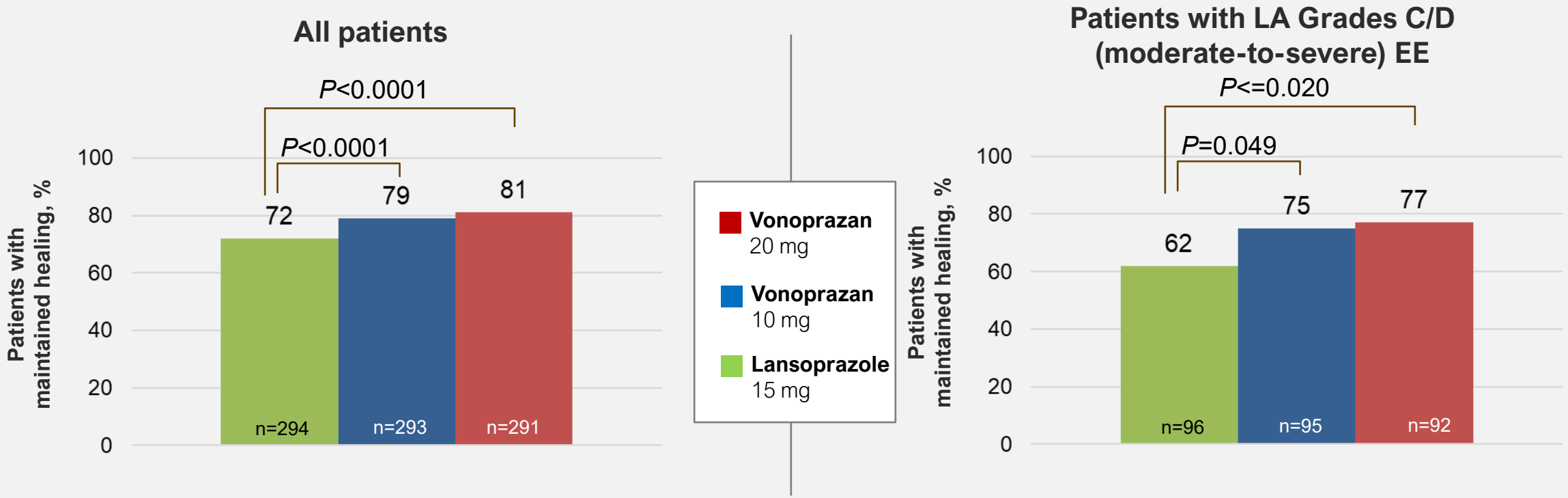
Proportion of patients with complete healing of EE in Phalcon phase 3 study



- Laine L et al. *Gastroenterology*. 2023;164:61-71

VONOPRAZAN EFFICACY IN EE: MAINTENANCE OF HEALING

Proportion of patients with healing maintained (at 24 weeks) in Phalcon phase 3 study



- Laine L et al. *Gastroenterology*. 2023;164:61-71

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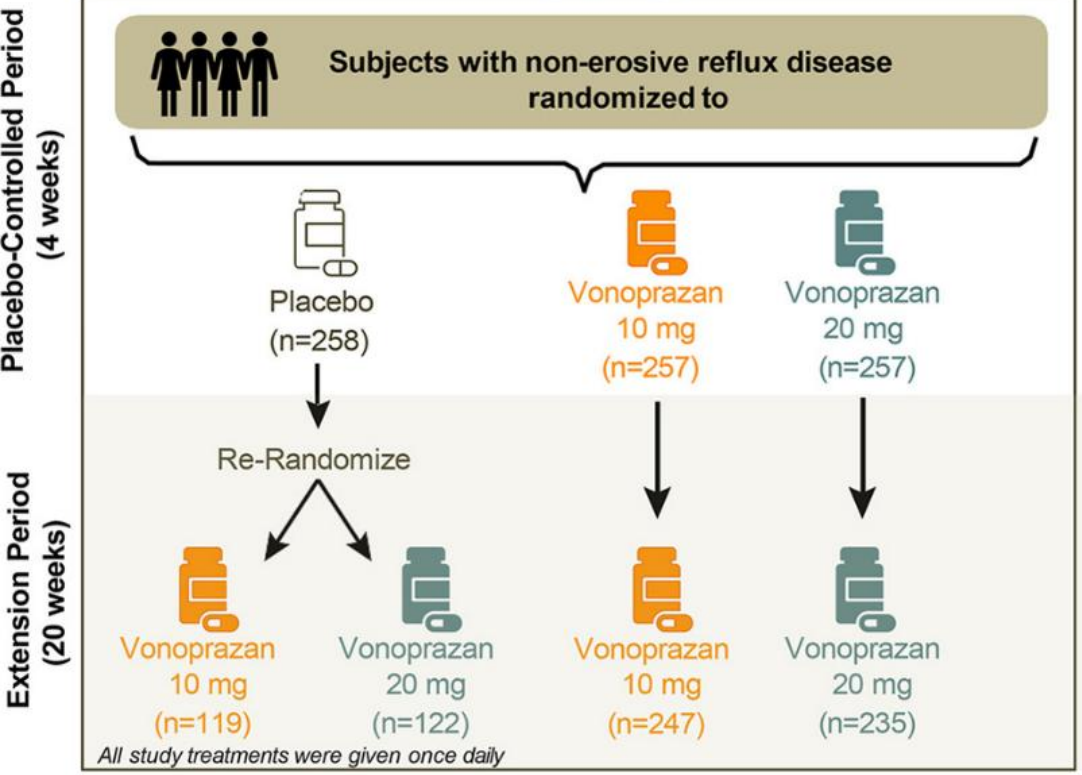
VONOPRAZAN IN NON-EROSIVE REFLUX DISEASE

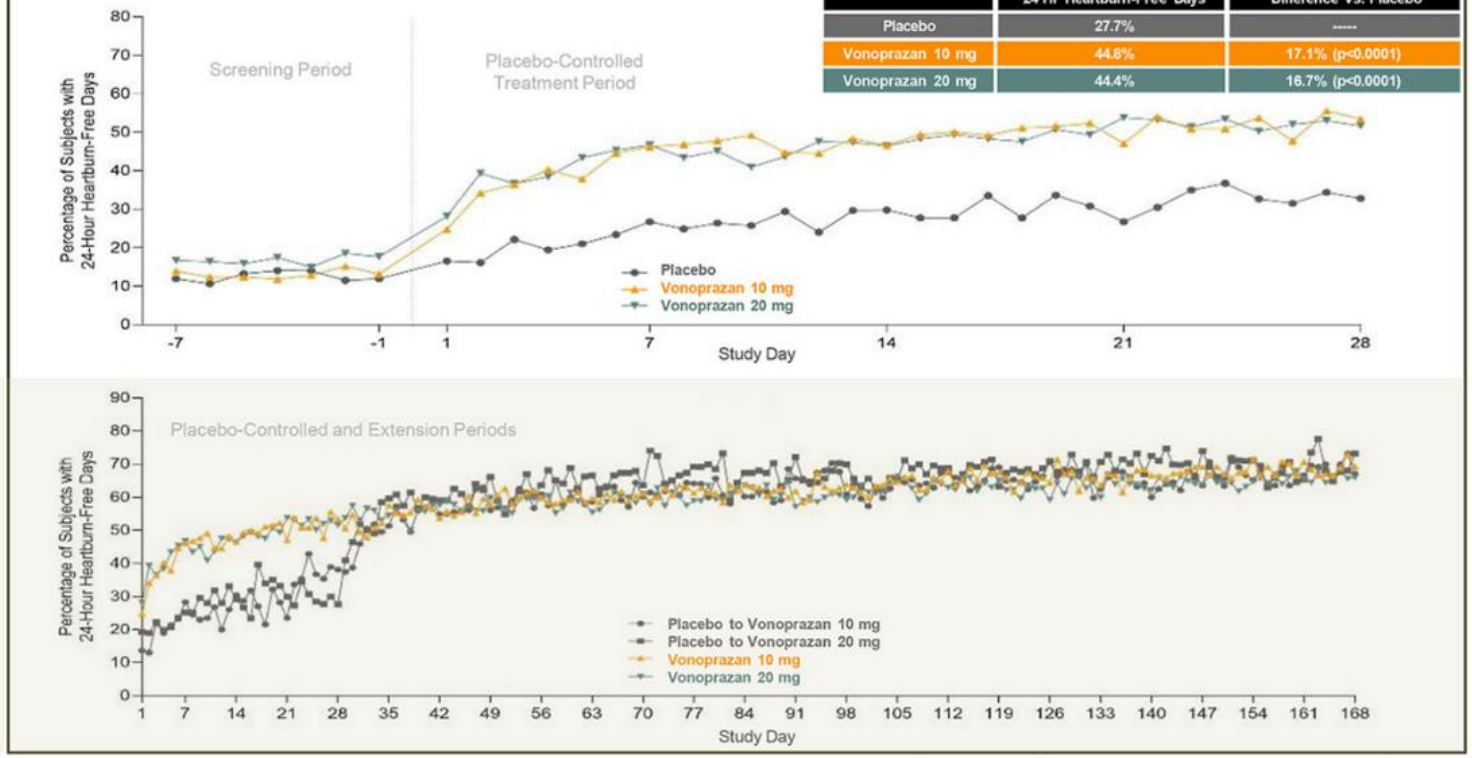
Vonoprazan for Treatment of Heartburn in Non-Erosive Reflux Disease: A Randomized Trial

Study Design



Results

	24 Hr Heartburn-Free Days	Difference vs. Placebo
Placebo	27.7%	------
Vonoprazan 10 mg	44.8%	17.1% (p<0.0001)
Vonoprazan 20 mg	44.4%	16.7% (p<0.0001)



Clinical Gastroenterology and Hepatology

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- Laine et al, Clinical Gastroenterology and Hepatology, 2024, 22(11):2211-2220.e10

Integrated Analysis of Vonoprazan Safety for Symptomatic Gastro-Oesophageal Reflux Disease or Erosive Oesophagitis

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- 14 Clinical trials of vonoprazan conducted in multiple countries between 2014 and 2023 were included (mean duration of exposure to vonoprazan: 2068 person-years).

Objective

To evaluate the safety of vonoprazan, a P-CAB, in an integrated analysis of 8108 adult patients.

Integrated Analysis

- Subjects with erosive oesophagitis or sGERD from 14 clinical trials of vonoprazan
- Adverse Events of Special Interest were assessed

Conclusions

Vonoprazan has been well tolerated with a similar safety profile to PPI comparators with respect to adverse events and adverse events of special interest in adults with erosive oesophagitis and sGERD.

Post-marketing Outcomes

- No new safety concerns were identified
- Safety profile is consistent with what was established in clinical trials

Incidence rate per 100 patient year

	C. Difficile Infection	Bone Fracture	Gastric Malignancy	Severe Cutaneous Adverse Reactions	Tubulointerstitial Nephritis	B12 Deficiency	Hypomagnesaemia
Vonoprazan (N=5318; PY=2068) IR/100 PY	0	2.27	0.05	0.05	0.05	0	0
Lansoprazole/ Esomeprazole (N=2011; PY=751) IR/100 PY	0	2.00	0.13	0	0	0.13	0

→ Vonoprazan is well-tolerated, with a safety profile comparable to PPIs.

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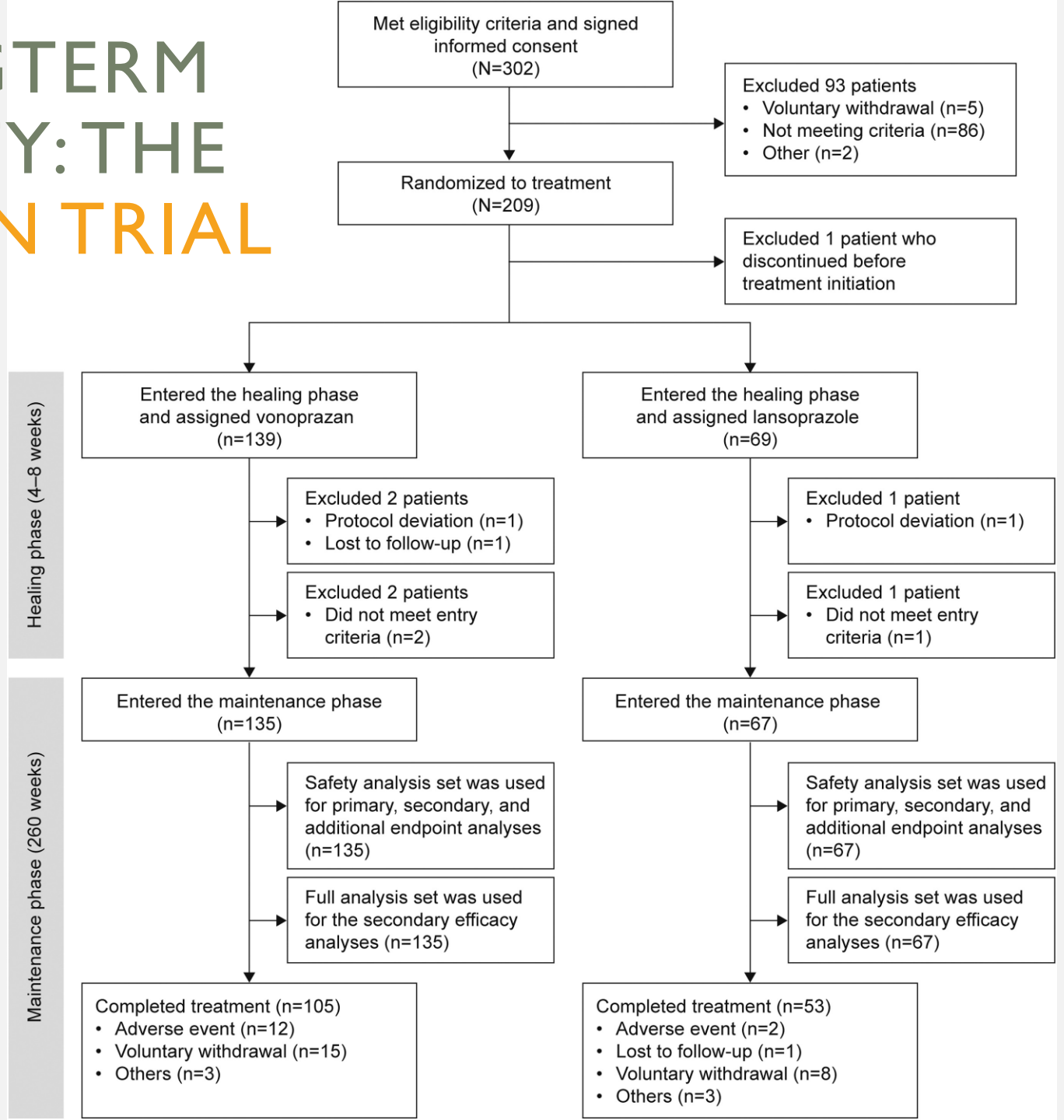
- Howden CW, et al. *Aliment Pharmacol Ther.* 2024;62(5):835-851

LONGTERM SAFETY: THE VISION TRIAL



- Phase IV, randomized trial involving patients with erosive esophagitis in Japan
- 5-year histopathological follow-up data in patients on maintenance vonoparazan 10-20 mg vs lansoprazole 15-30 mg
  - Parietal cell and foveolar hyperplasia were more frequently detected in the vonoprazan group
  - Median serum gastrin levels were consistently higher in the vonoprazan group
  - No increased risk of malignant epithelial cell alterations or gastric neuroendocrine tumors in either group
- Uemura N, et al. *Clin Gastroenterol Hepatol* 2025. 23(5):748-757

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TAILORED USE OF P-CAB IN GERD PATIENTS

Patients with EE
especially high grade
(LA C/D reflux esophagitis)

Patients with severe symptoms
who need more
rapid response

Patients with persistent acid reflux on PPI on ambulatory reflux testing
(including possible PPI rapid metabolizer due to polymorphism)

Patients with NERD
possible on-demand dosing

EE, erosive esophagitis; NERD, nonerosive reflux disease; PPI, proton pump inhibitor.

SUMMARY

- GERD is a prevalent condition worldwide that negatively impacts quality of life.
- In patients with reflux symptoms and without endoscopically proven GERD, reflux testing off therapy (preferably prolonged wireless pH testing) should be considered.
- Lyon 2.0 offers diagnostic criteria for GERD and for potential exclusion of GERD.
- High-resolution manometry, mucosal impedance, and potentially FLIP are tools that may serve as adjunctive roles in GERD diagnosis.
- PCABs have demonstrated superiority in healing and maintenance of healing in patients with erosive esophagitis (especially moderate to severe) and improvement in heartburn in NERD patients.

CME/MOC Question:
(multiple choice – list 4 answers to choose from)

Which of the following is NOT a property of potassium competitive acid blockers (PCABs) or proton pump inhibitors (PPIs)?

a. PCABs prevents proton pump activation by competitively blocking passage of K^+ ions
b. PPIs are prodrugs that requires conversion to active form
c. The antisecretory effect of PCABs are meal-dependent
d. PCABs are not susceptible to the CYP2C19 polymophism effect

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CME/MOC Answer

Answer: c. The antisecretory effect of PCABs are meal-dependent

PCABs act on active and inactive proton pumps and thus their antisecretory effects are not meal dependent, while PPIs can only act on proton pumps that are activated by meals and thus are meal-dependent.

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