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Clinical Pearls:

ACG 2025 Guideline for Diagnosis and Management of Eosinophilic Esophagitis

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Disclosures

General

- Ferring/Rebiotix Pharmaceutical: Consultant, Advisory Board, Speakers Bureau
- SERES Therapeutics: Advisory Board
- Takeda Pharmaceuticals: Advisory Board
- Probiotech: Advisory Board
- Sanofi Pharmaceuticals: Advisory Board, Speakers Bureau
- Regeneron Pharmaceuticals: Advisory Board, Speakers Bureau

Research Support

- Ferring Pharmaceuticals
- SERES Therapeutics
- Finch Therapeutics

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CME

ACG Clinical Guideline: Diagnosis and Management of Eosinophilic Esophagitis

Evan S. Dellon, MD, MPH, FACG[1], Amanda B. Muir, MD[2,3,4], David A. Katzka, MD, FACG[5], Shailja C. Shah, MD, MPH[6,7], Bryan G. Sauer, MD, MSc, FACG[8], Seema S. Aceves, MD, PhD[9,10], Glenn T. Furuta, MD[11,12], Nirmala Gonsalves, MD, FACG[13,*] and Ikuo Hirano, MD, FACG[13,*†]

Recommendation

Key Concept

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Case Presentation

- **35 year old man**
- **Chief complaint:**
  - Dysphagia
- **Past Medical History:**
  - Atopic dermatitis
  - Seasonal allergies
  - Trouble gaining weight
- **Past Surgical History:**
  - Cholecystectomy

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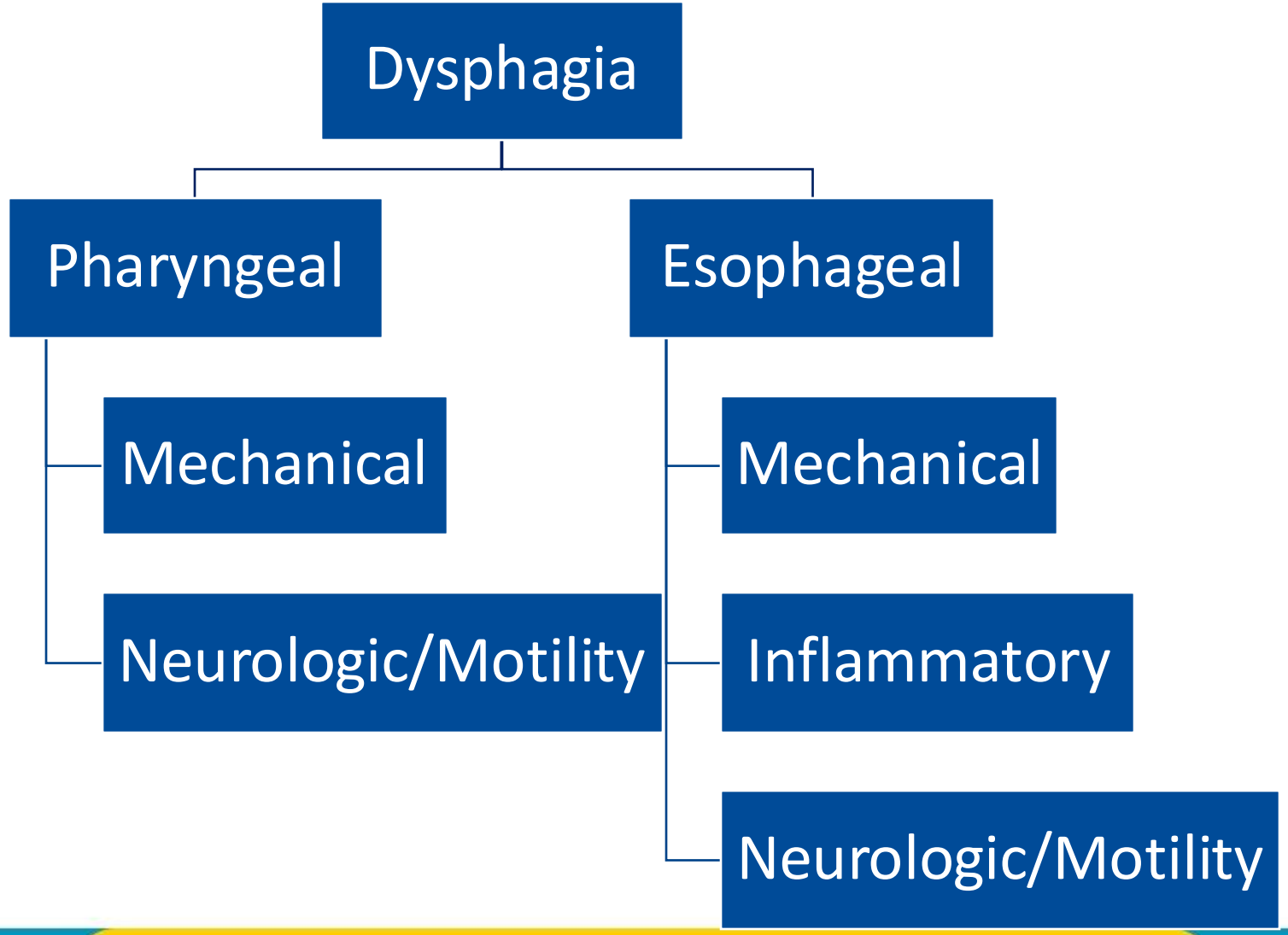

ACG 2025 EoE Guideline: Key Concept

Key Concept:

Providers should consider assessing for features that may increase risk of EoE including multiple atopic disease and family history

Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Case Presentation

What do you want to do next?

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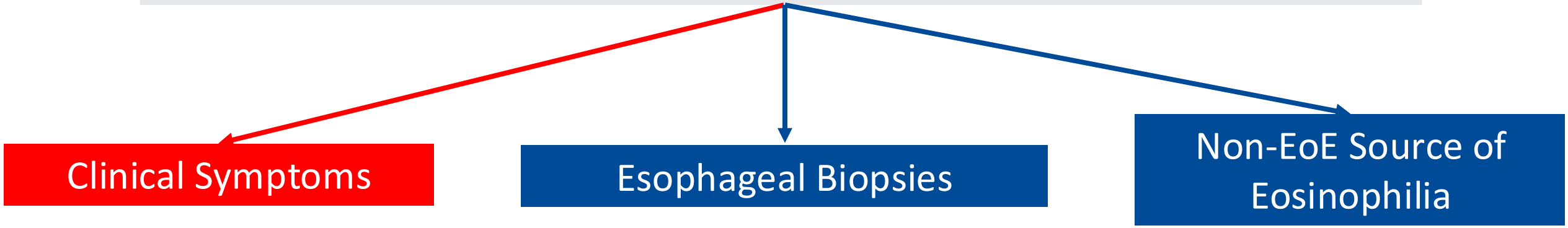
2025 ACG Clinical Guideline: Diagnosis

1. We recommend that EoE is diagnosed based on the presence of symptoms of esophageal dysfunction and at least 15 eosinophils per high-power field (eos/hpf) on esophageal biopsy, after evaluating for non-EoE disorders that cause or potentially contribute to esophageal eosinophilia (quality of evidence: low; strength of recommendation: strong).



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Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Clinical Presentation: Eosinophilic Esophagitis

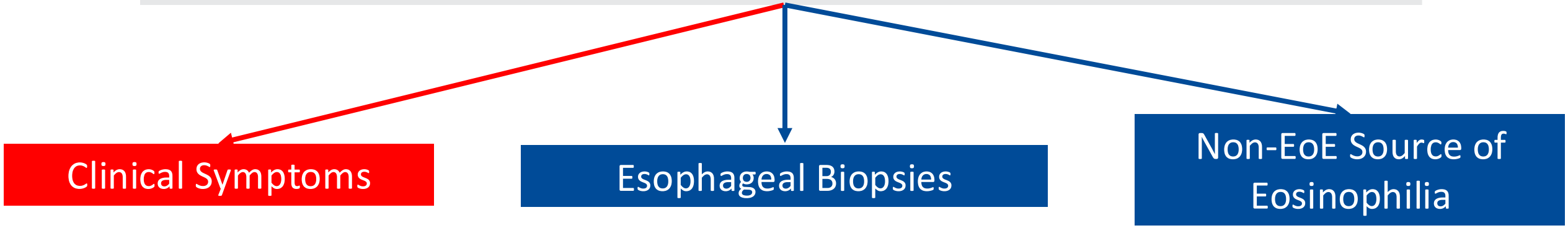
Adults
Dysphagia
Food impactions
Food avoidance
Heartburn
Regurgitation
Chest pain
Abdominal pain

Key Concept: History Taking is Essential

I	mbibe fluids with meals
M	odify foods (cut into small pieces)
P	rolong meal times
A	void hard texture foods
C	hew extensively
T	urn away tablets

2025 ACG Clinical Guideline: Diagnosis

1. We recommend that EoE is diagnosed based on the presence of symptoms of esophageal dysfunction and at least 15 eosinophils per high-power field (eos/hpf) on esophageal biopsy, after evaluating for non-EoE disorders that cause or potentially contribute to esophageal eosinophilia (quality of evidence: low; strength of recommendation: strong).



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Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

ACG 2025 EoE Guideline: Key Concept

Key Concept:

We advise performing endoscopy on no treatment (e.g., no dietary restriction and no PPI) when EoE is suspected to maximize diagnostic sensitivity

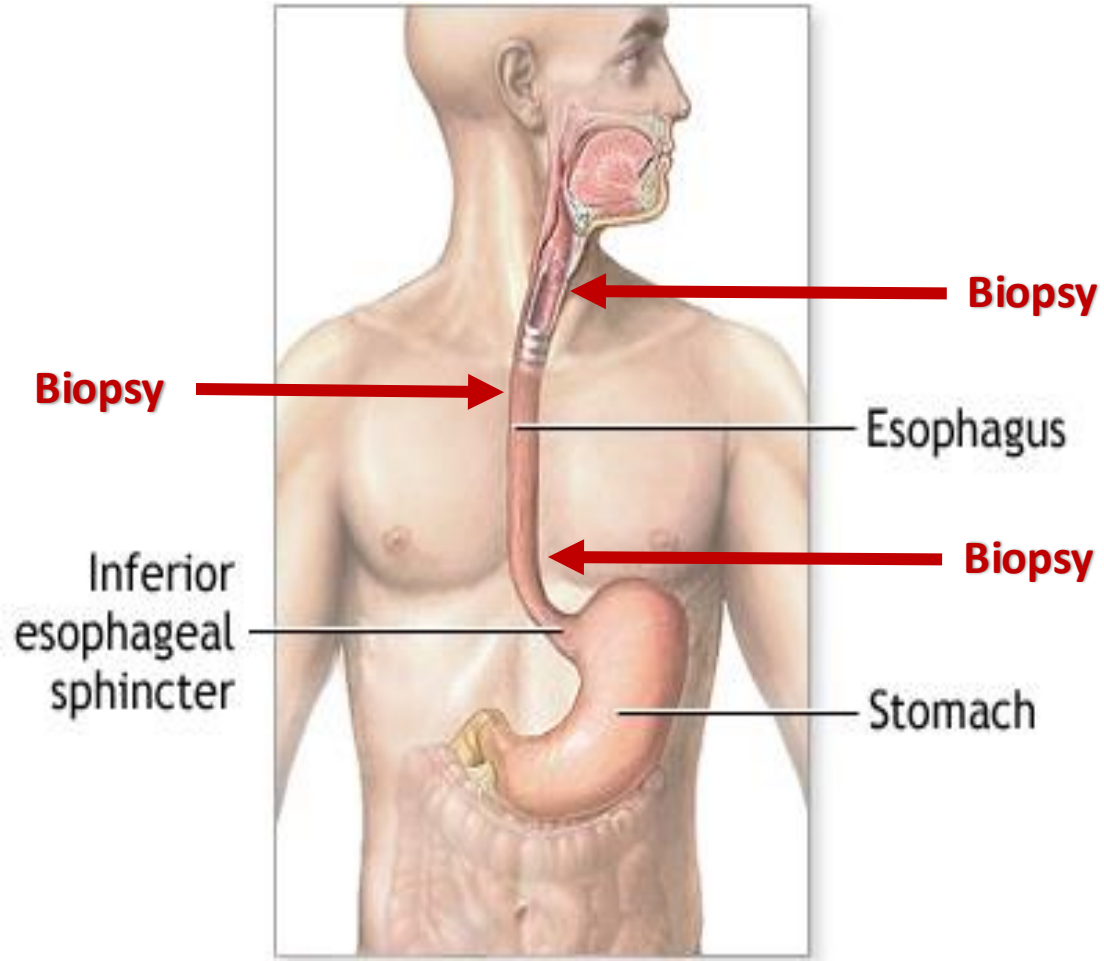
Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

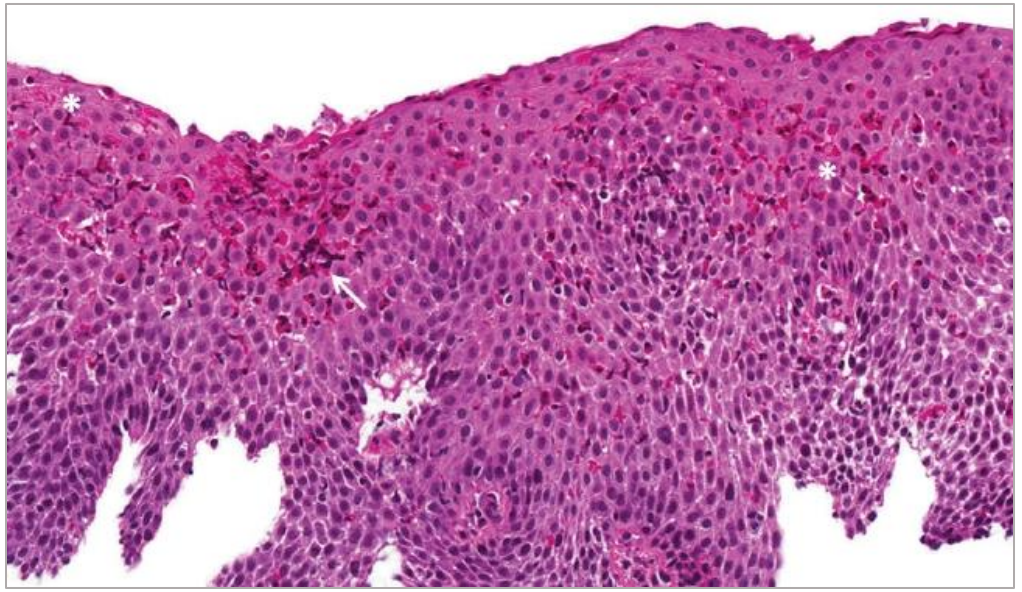
2025 ACG Clinical Guideline: Diagnosis

Recommendation:

3. We recommend obtaining at least 6 esophageal biopsies from at least 2 esophageal levels (e.g., proximal/mid and distal), targeting EoE endoscopic findings, if possible, to assess for histologic features consistent with EoE (quality of evidence: low; strength of recommendation: strong).

Esophageal Biopsies





- ≥ 15 eosinophils per high power field on esophageal biopsy
- Eosinophilic infiltration isolated to the esophagus

Image: MedlinePlus. Upper gastrointestinal system. Available at: https://medlineplus.gov/ency/imagepages/9305.htm.

Dellon ES. *Curr Opin Gastroenterol*. 2012;28(4):382-388; Dellon ES, et al. *Gastroenterology*. 2018;155(4):1022-1033.e10.

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2025 ACG Clinical Guideline: Diagnosis

Recommendation:

4. We recommend that eosinophil counts be quantified on esophageal biopsies from every endoscopy performed for EoE (quality of evidence: low; strength of recommendation: strong).

Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

2025 ACG Clinical Guideline: Diagnosis

CLINICAL: Eosinophilic esophagitis.

SPECIMEN:

1. GASTRIC ANTRUM/BODY
2. DISTAL ESOPHAGUS
3. PROXIMAL ESOPHAGUS

DIAGNOSIS:

1 - GASTRIC ANTRUM/BODY, BIOPSY:

GASTRIC ANTRAL AND OXYNTIC MUCOSA WITH PATCHY MILD CHRONIC GASTRITIS.
REACTIVE LYMPHOID AGGREGATES NOTED.
NEGATIVE FOR HELICOBACTER, INTESTINAL METAPLASIA, ATROPHY, DYSPLASIA, OR MALIGNANCY.

2 - DISTAL ESOPHAGUS, BIOPSY:

ESOPHAGEAL SQUAMOUS MUCOSA WITH MILD TO MODERATE CHRONIC ESOPHAGITIS AND INCREASED EOSINOPHILS (UP TO 20 TO 25 PER HIGH POWER FIELD).
NEGATIVE FOR BARRETT'S ESOPHAGUS, FUNGAL ORGANISMS, DYSPLASIA, OR MALIGNANCY.

3 - PROXIMAL ESOPHAGUS, BIOPSY:

ESOPHAGEAL SQUAMOUS MUCOSA WITH MILD TO MODERATE CHRONIC ESOPHAGITIS AND INCREASED EOSINOPHILS (UP TO 30 TO 40 PER HIGH POWER FIELD).
NEGATIVE FOR BARRETT'S ESOPHAGUS, FUNGAL ORGANISMS, DYSPLASIA, OR MALIGNANCY.

COMMENT: A mild chronic gastritis is present which may be within normal limits or represent mild chemical gastropathy, a treated / resolving infectious gastritis, or drug injury.
A history of eosinophilic esophagitis is noted. The histology of the esophageal biopsies is consistent with that diagnosis, in the appropriate clinical context.

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2025 ACG Clinical Guideline: Diagnosis

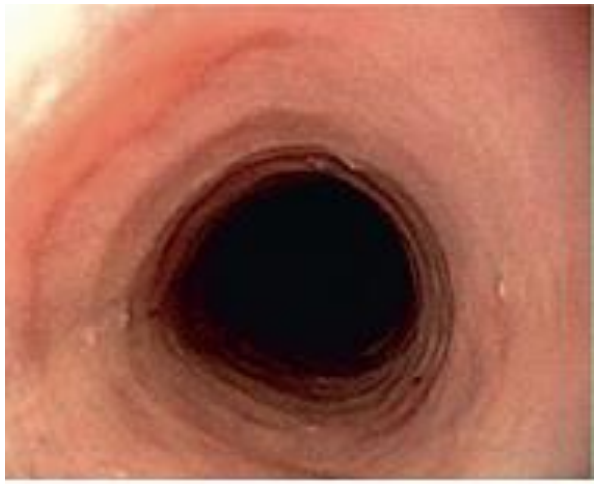
Recommendation:

2. We recommend using a systematic endoscopic scoring system (e.g., the EoE Endoscopic Reference Score [EREFS]) to characterize endoscopic findings of EoE at every endoscopy (quality of evidence: low; strength of recommendation: strong).

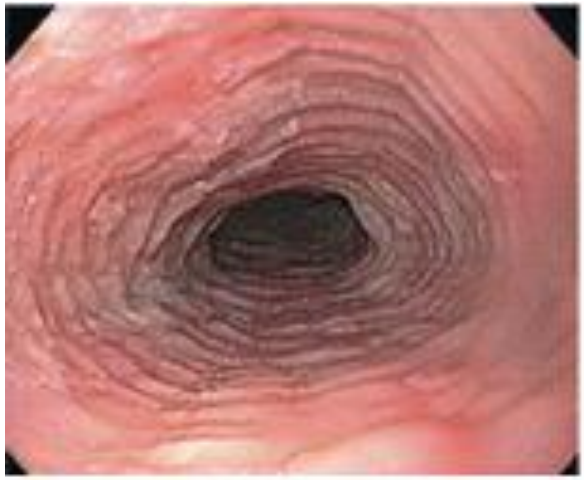
Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

EREFS Scoring System

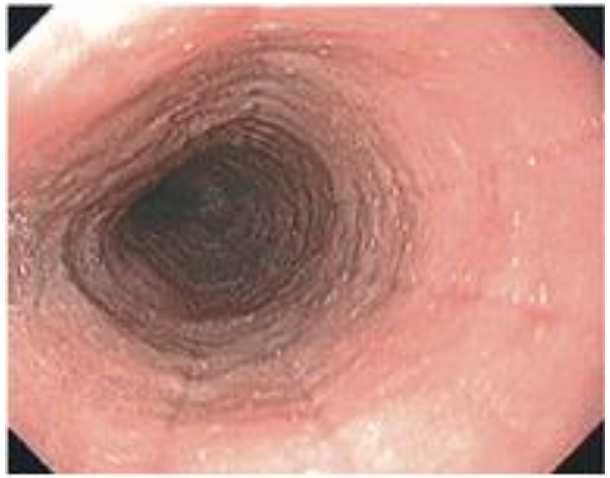
Edema



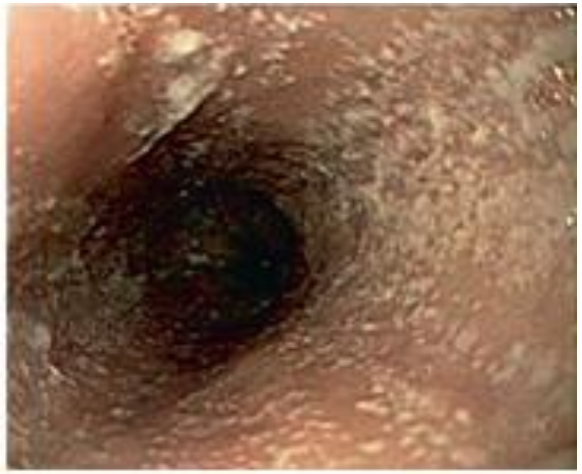
Rings



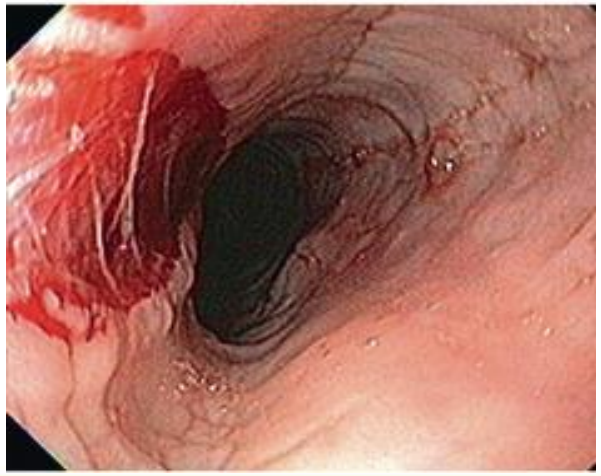
Furrows



Exudates



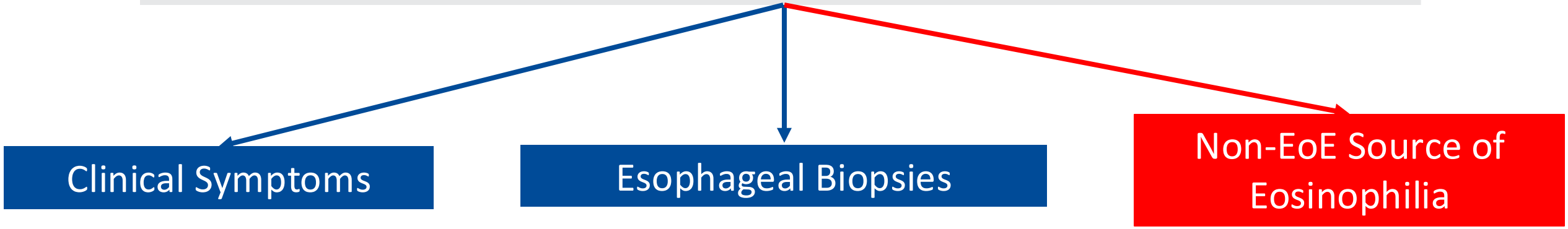
Strictures



Hirano I, et al. *Gut*. 2013;62(4):489-495.

2025 ACG Clinical Guideline: Diagnosis

1. We recommend that EoE is diagnosed based on the presence of symptoms of esophageal dysfunction and at least 15 eosinophils per high-power field (eos/hpf) on esophageal biopsy, after evaluating for non-EoE disorders that cause or potentially contribute to esophageal eosinophilia (quality of evidence: low; strength of recommendation: strong).



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Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Differential Diagnosis For Eosinophils on Esophageal Biopsy

- GERD
- Crohn's Disease
- Achalasia
- Drug Induced
- Malignancy
- Fungal Infection
- Allergy
- Adrenohypocortisolism
- Autoimmune diseases
- Idiopathic

Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Case Presentation

Should we continue the patient on their current treatment?

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Things to Address at Follow Up

- Endoscopy Results
- Histology Results
- Current symptomatic status
- Disease pathophysiology and importance of control
- Treatment options
- Plan for future endoscopies

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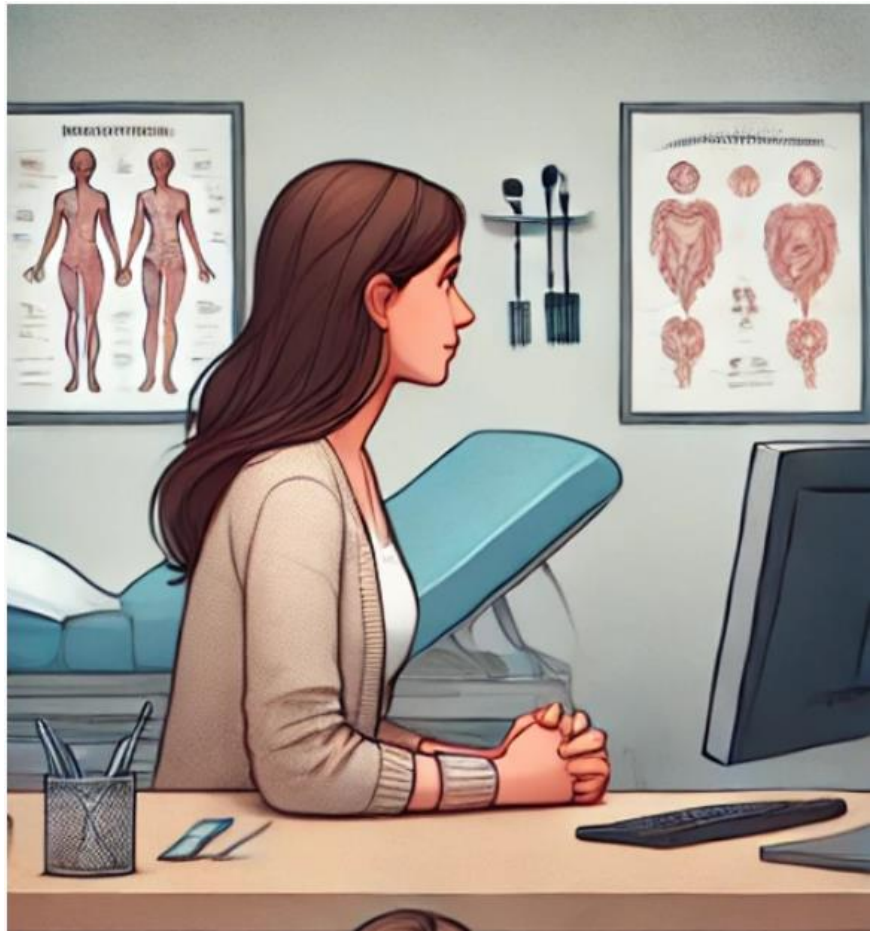
Case Presentation



- **23 year old woman**
- **Chief complaint:**
  - Dysphagia
- **Past Medical History:**
  - Anxiety
  - Eosinophilic esophagitis
- **Past Surgical History:**
  - Appendectomy

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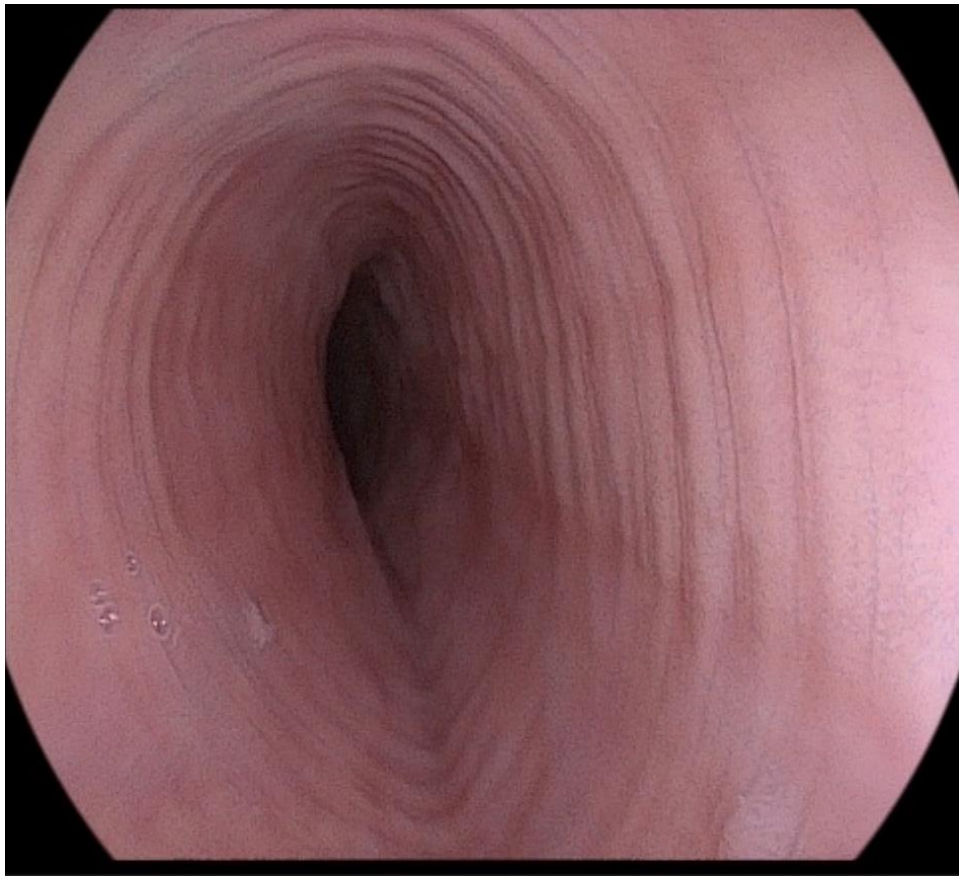
Treatment History

- **PPI**
  - Pantoprazole 40 mg once daily
  - Pantoprazole 40 mg twice daily
  - Esomeprazole 40 mg once daily

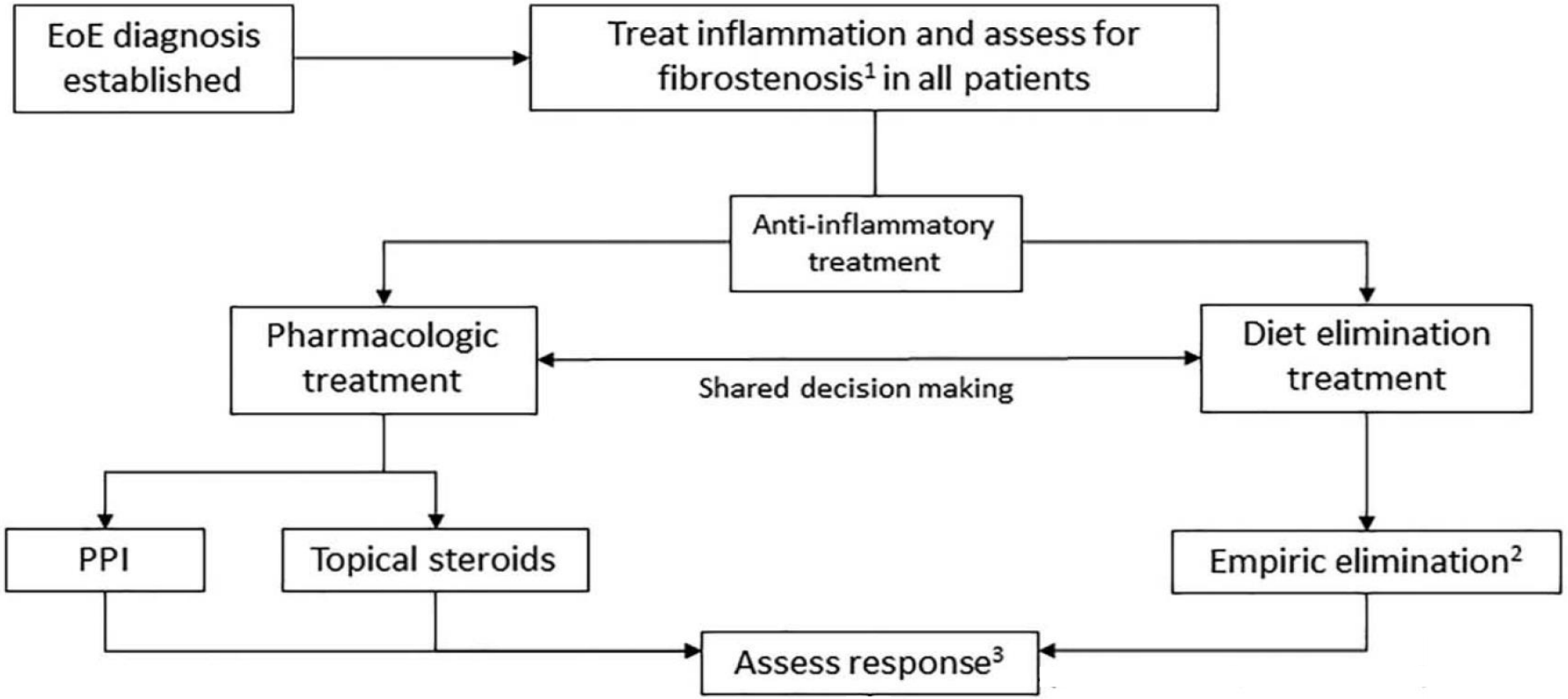
- **Elimination diet**
  - Lactose elimination

Endoscopy



- **EREFS:**
  - Edema: 1
  - Rings: 1
  - Exudates: 0
  - Furrows: 1
  - Stricture: 1
- **Histology:**
  - 50 eos/hpf

2025 ACG Clinical Guideline: Management



Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

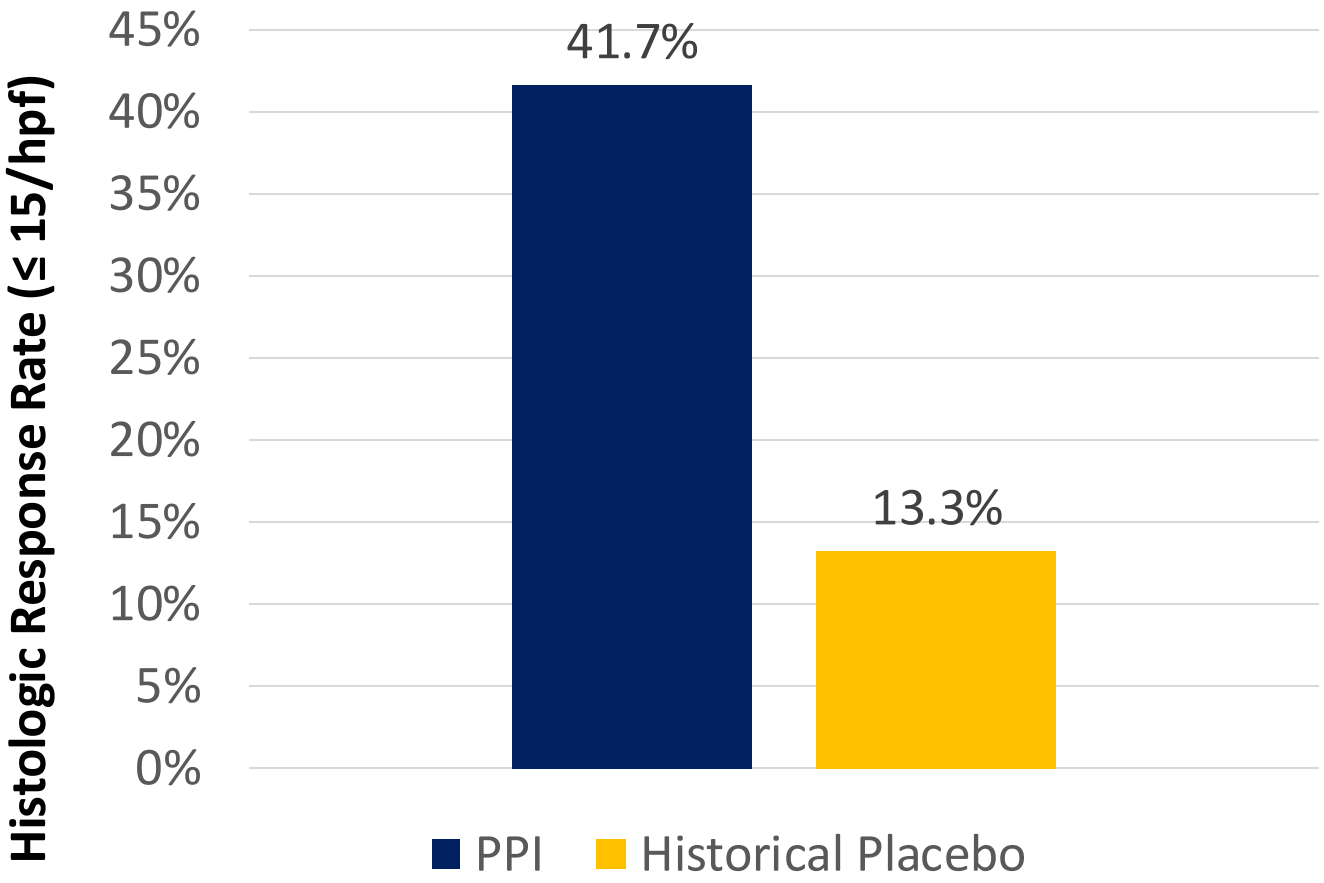
2025 ACG Clinical Guideline: PPI Management

Recommendation:

5. We suggest PPIs as a treatment for EoE (quality of evidence: low; strength of recommendation: conditional).

Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

PPI Therapy



- Part of the AGA-JTF guideline recommendations
- 23 observational studies
- 1,051 patients with EoE

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Rank MA, et al. *Gastroenterology*. 2020;158(6):1789-1810.e15.

2025 ACG Clinical Guideline: PPI Management

Recommendation:

5. We suggest PPIs as a treatment for EoE (quality of evidence: low; strength of recommendation: conditional).

Key Concept:

We advise "high-dose" PPI use for EoE treatment	
We advise providers to counsel patients as to the rationale for PPI use in EoE	Patients without heartburn or reflux symptoms could be confused as to why a PPI is prescribed without this explanation

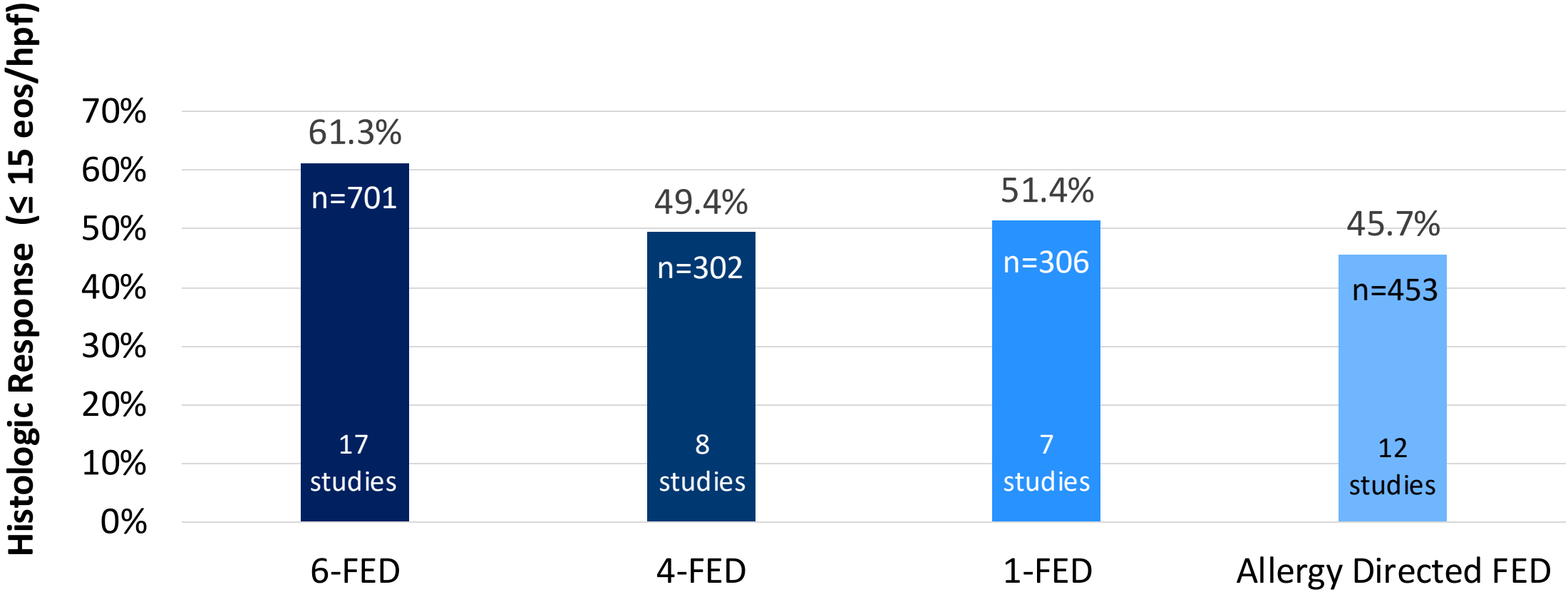
Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

2025 ACG Clinical Guideline: Elimination Diet

Recommendation:

8. We suggest an empiric food elimination diet as a treatment for EoE	Low	Conditional
9. We do not suggest currently available allergy testing to direct food elimination diets for treatment of EoE	Very low	Conditional

Meta-Analysis of Elimination Diets in EoE



Mayerhofer C, et al. *Clin Gastroenterol Hepatol*. 2023;21(9):2197-2210.e3.

2025 ACG Clinical Guideline: Elimination Diet

Recommendation:

8. We suggest an empiric food elimination diet as a treatment for EoE	Low	Conditional
9. We do not suggest currently available allergy testing to direct food elimination diets for treatment of EoE	Very low	Conditional

Key Concept:

Providers may consider starting with a less-restrictive empiric elimination (i.e., 1FED or 2FED) as the initial diet therapy choice	Patient preference for diet selection should be incorporated in a shared decision-making process
We advise providers to collaborate with a dietician or nutritionist for patients undergoing dietary elimination	Dieticians can help with education, label reading and contaminant avoidance, food substitutions, meal planning, and other activities to help maximize success and adherence
After an initial response to dietary elimination, we advise a structured food reintroduction process	A food reintroduction process is needed to identify food triggers
Symptoms should not be used in isolation to determine food triggers	Endoscopy with biopsy is required after each food is reintroduced to assess whether eosinophilia has recured

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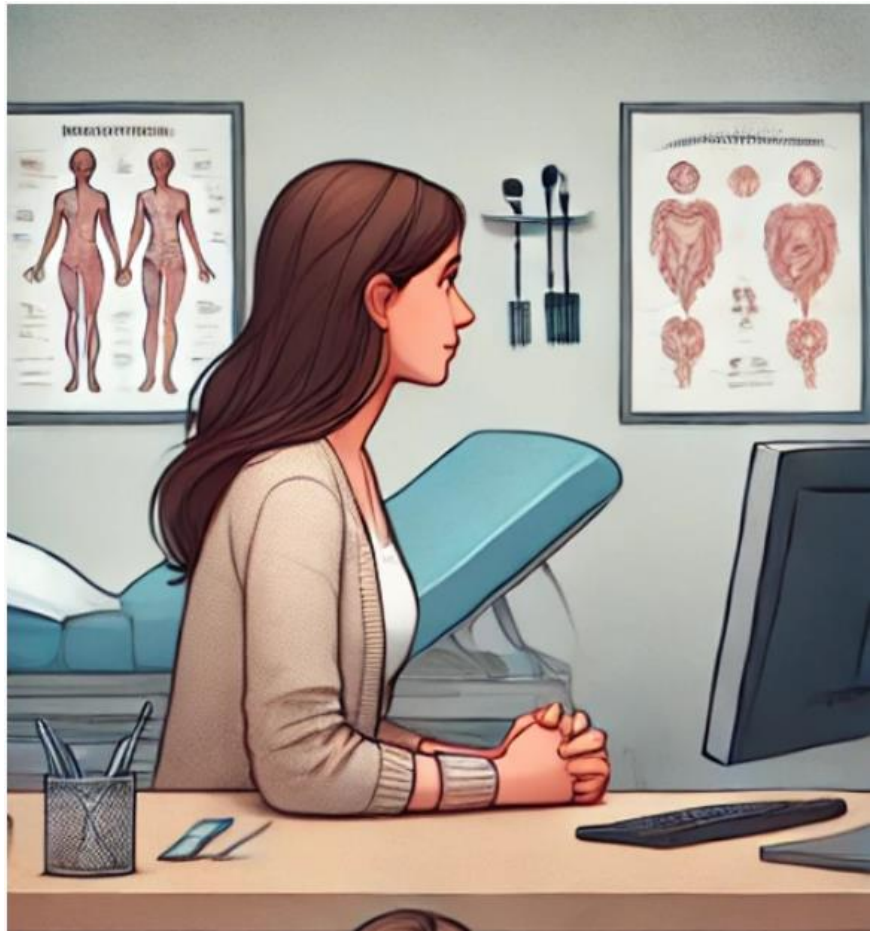
Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Case Presentation



- Dysphagia episodes 4-5 times a week after eating hard textured foods and most solids
- Food impaction about 4 weeks ago
- Expresses frustration that she is not able to eat socially without concern for an episode

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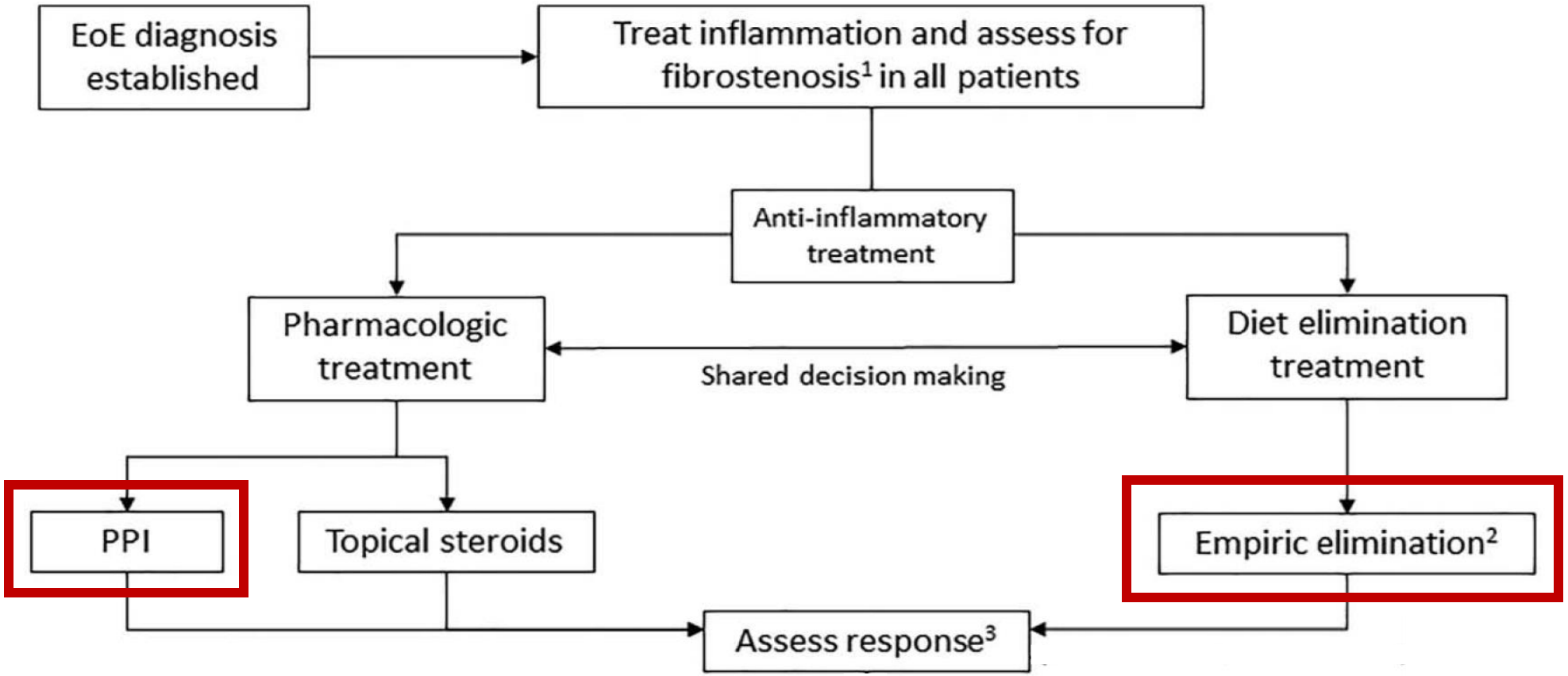
2025 ACG Clinical Guideline: Management



Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Case Presentation

- What can we use now that I have not responded to these other things?

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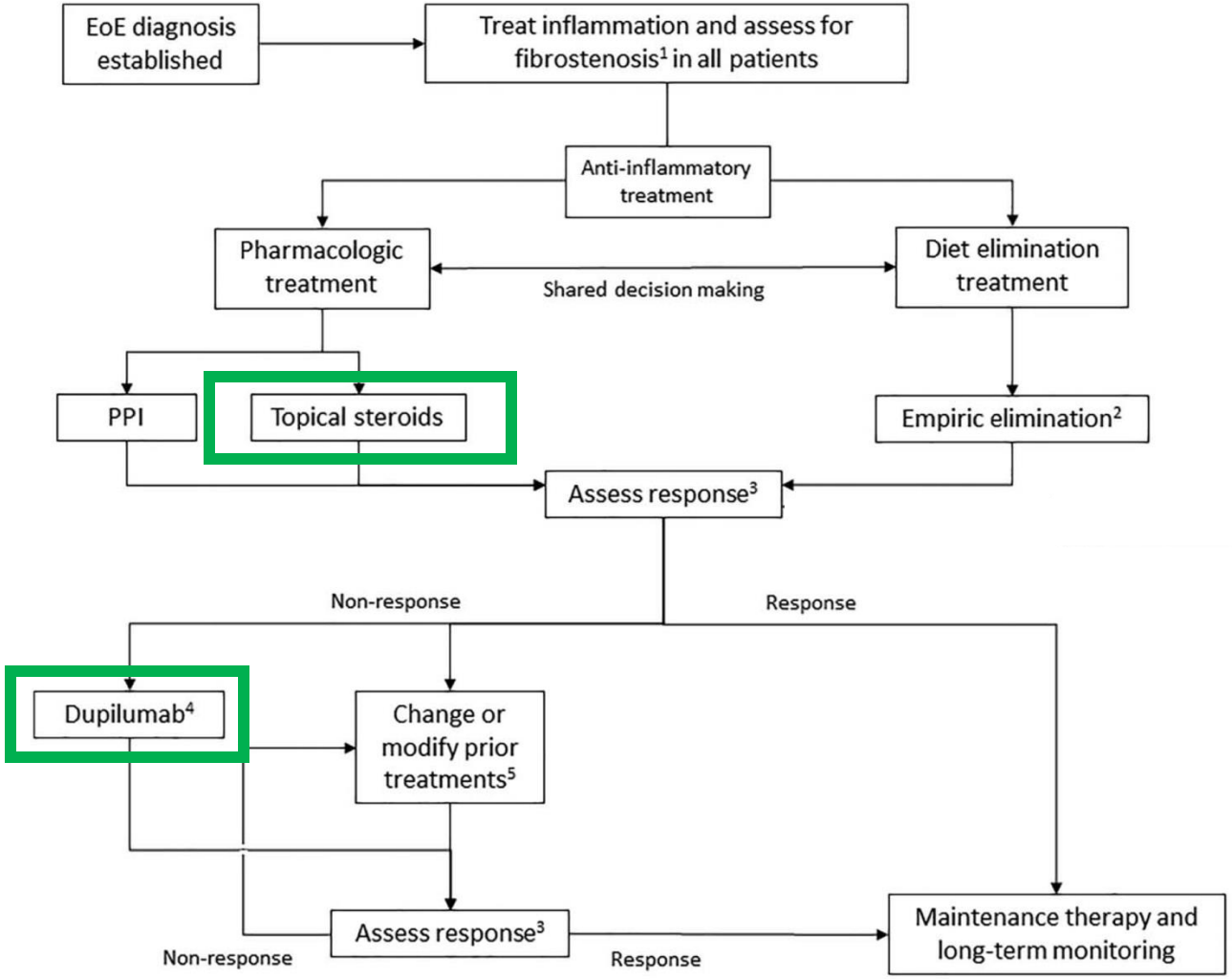
2025 ACG Clinical Guideline: Specialist Management



Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

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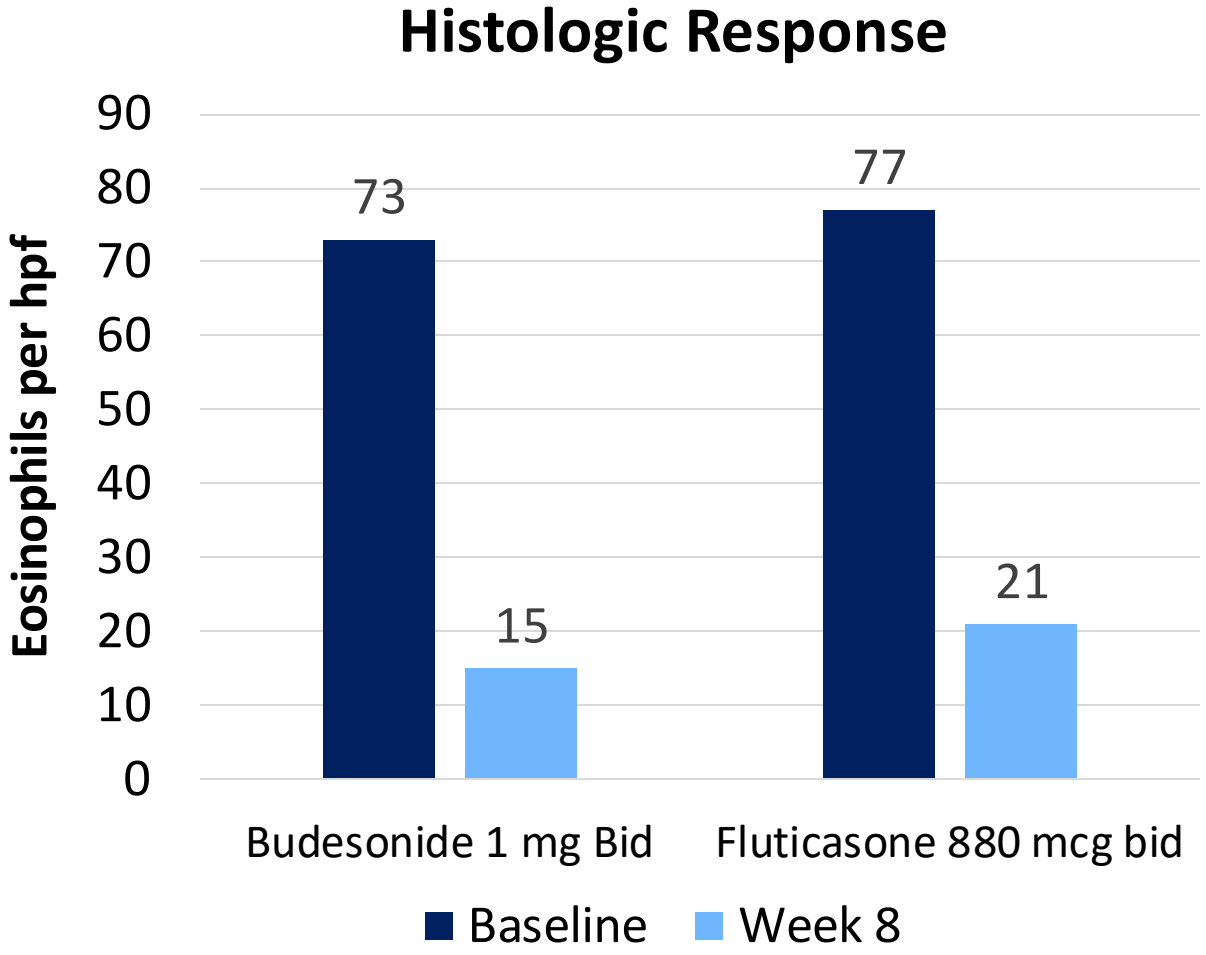
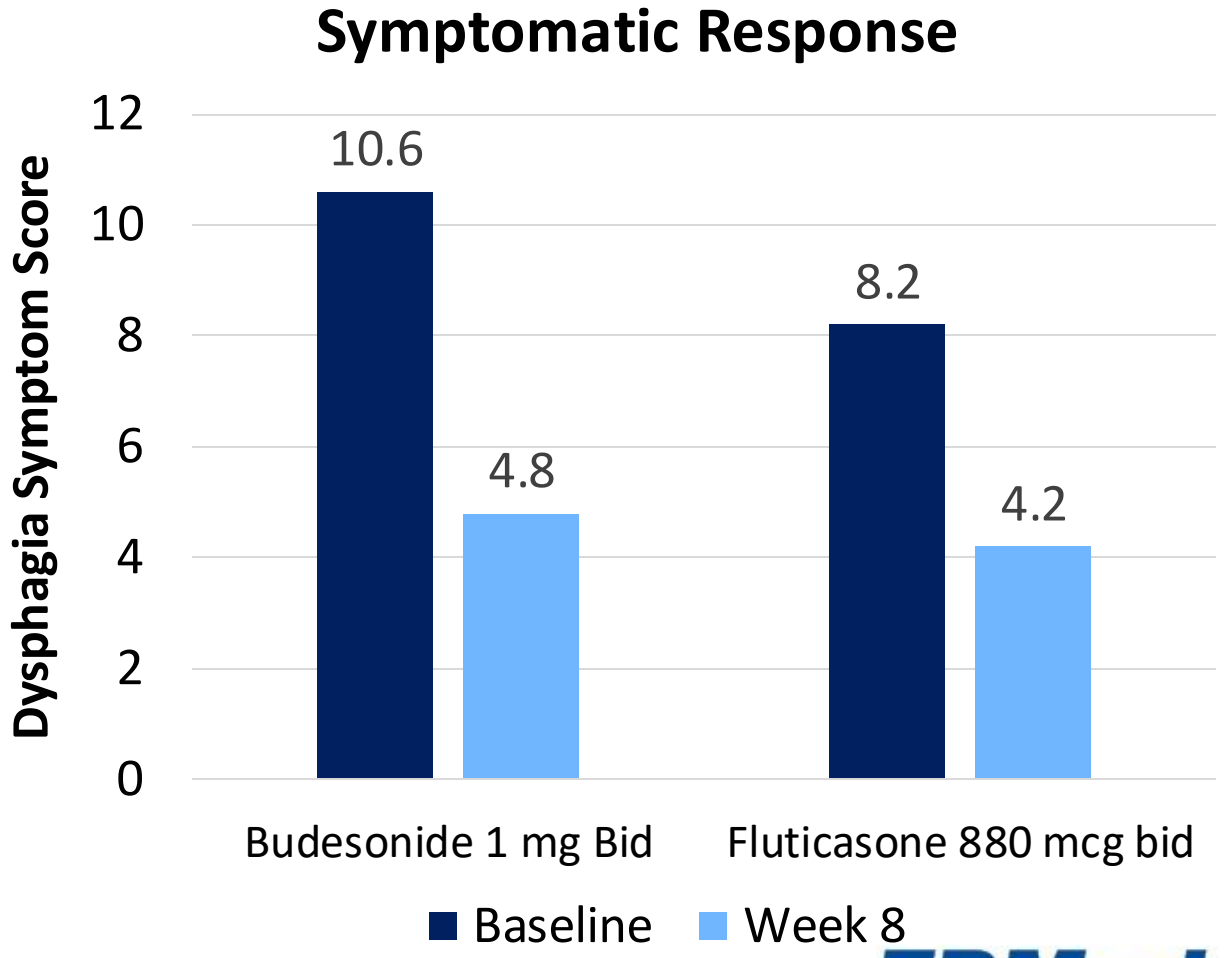
2025 ACG Clinical Guideline: Topical Corticosteroids

Recommendation:

6. We recommend the use of swallowed topical steroids as a treatment for EoE	Moderate	Strong
7. We suggest the use of either fluticasone propionate or budesonide in patients with EoE being treated with topical steroids	Low	Conditional

Fluticasone vs. Budesonide RCT





Dellon ES, et al. *Gastroenterology*. 2019;157(1):65-73.e5.

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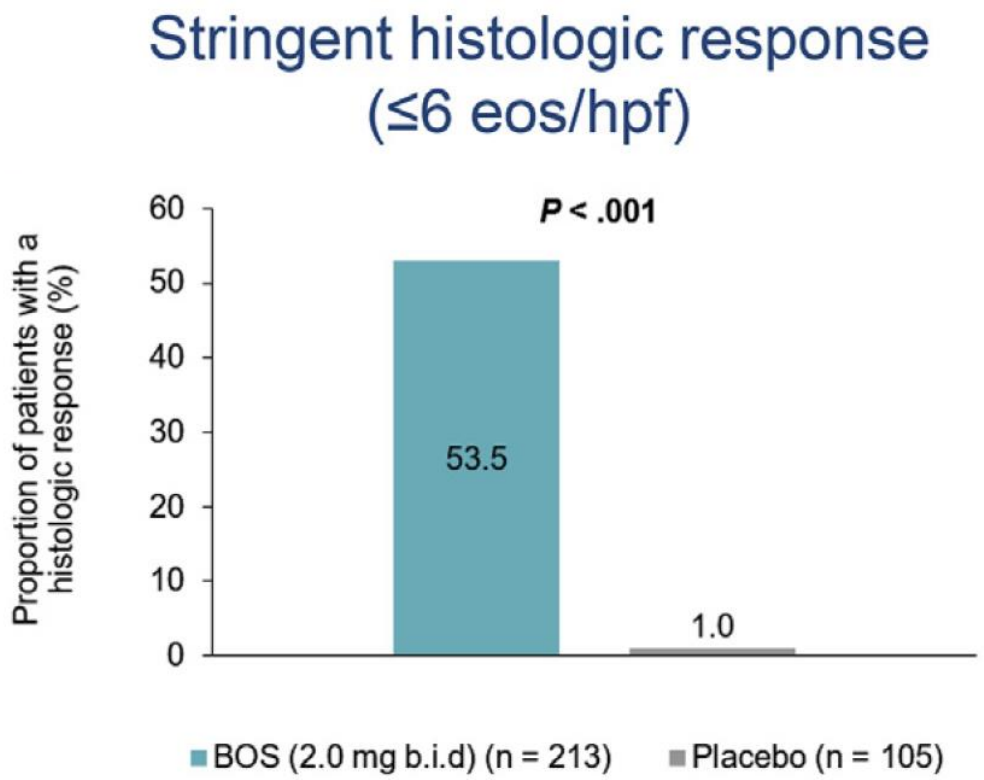
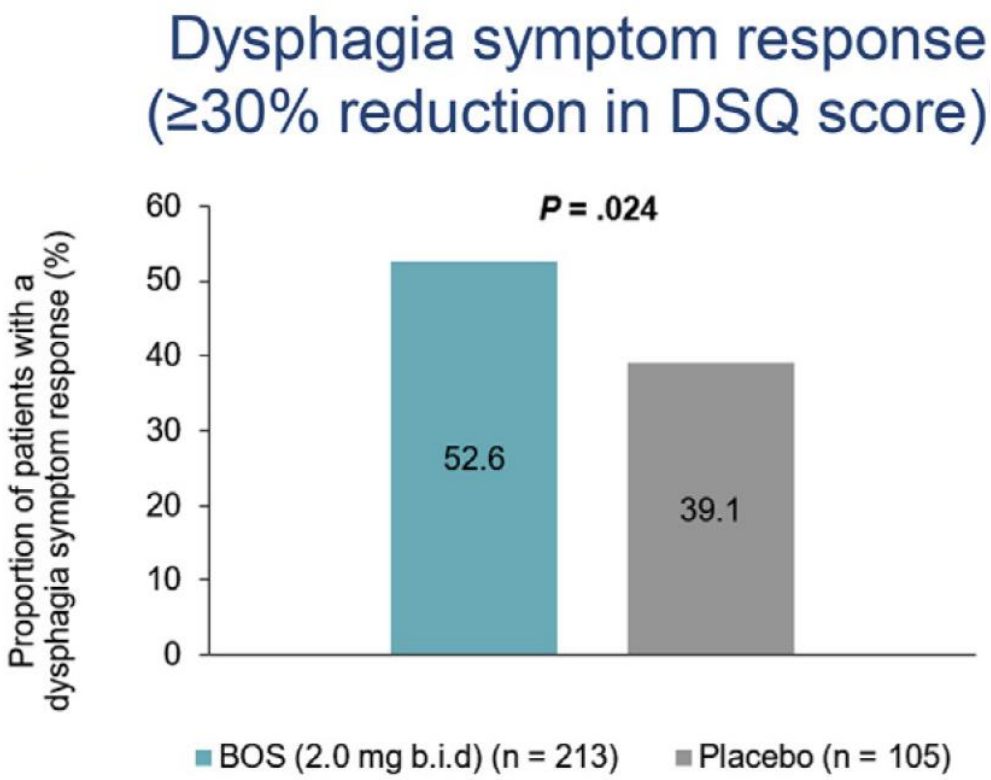
Budesonide Oral Suspension Phase 3 RCT





Hirano I, et al. *Clin Gastroenterol Hepatol*. 2022;20(3):525-534.e10.

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2025 ACG Clinical Guideline: Topical Corticosteroids

Recommendation:

6. We recommend the use of swallowed topical steroids as a treatment for EoE	Moderate	Strong
7. We suggest the use of either fluticasone propionate or budesonide in patients with EoE being treated with topical steroids	Low	Conditional

Key Concept:

We advise that induction with swallowed topical steroids with budesonide and fluticasone improve symptoms, histology, and endoscopic disease activity in adolescents and adults with EoE	Options for swallowed topical steroids include the EMA-approved budesonide orodispersible tablet and FDA-approved budesonide oral suspension as well as off-label use of asthma preparations adapted for esophageal delivery
We advise administration of topical steroids after meals or before bedtime with nothing to eat or drink after 30–60 minutes to help maximize medication dwell time in the esophagus	If patients drink or eat right after medication administration, the medication will be cleared from the esophagus and will be less effective

Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

2025 ACG Clinical Guideline: Dupilumab

Recommendation:

10. We suggest dupilumab as a treatment for EoE in individuals 12 years of age or older who are nonresponsive to PPI therapy	Moderate	Conditional

Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

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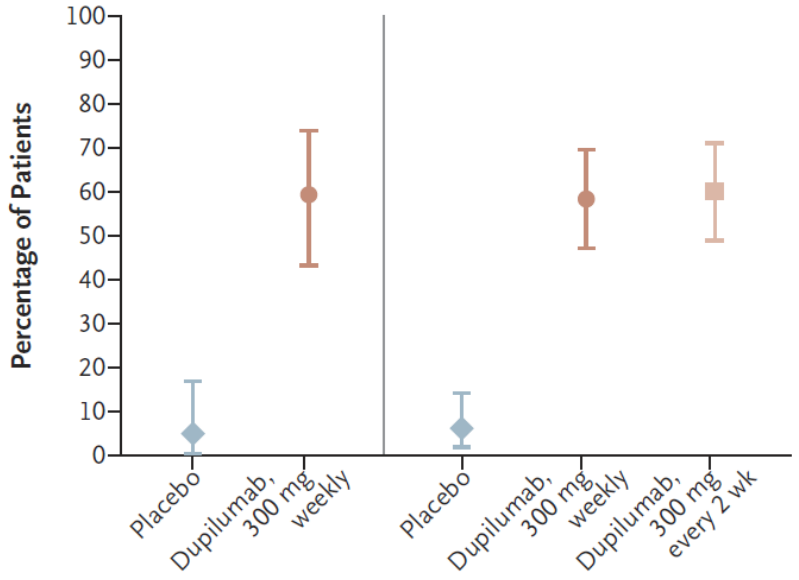
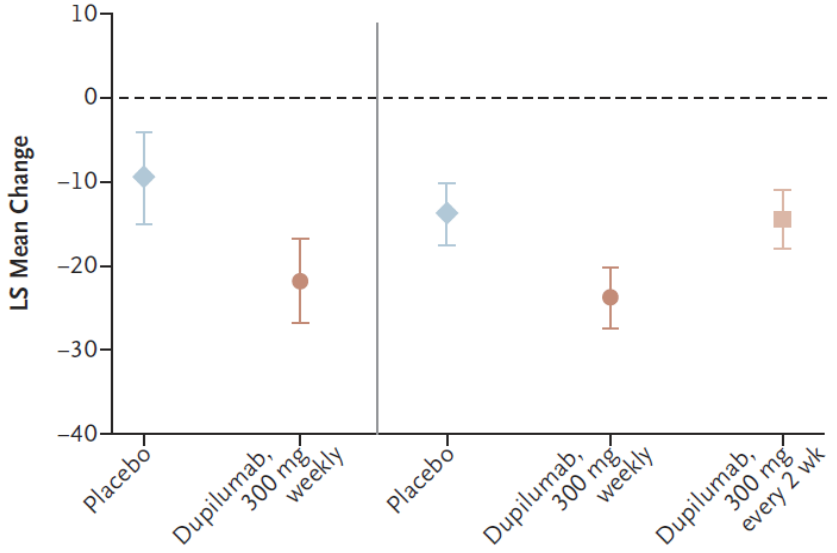
Dupilumab Phase 3 Randomized Controlled Trial

Histologic Response



	Part A, Wk 24		Part B, Wk 24		
No. of Patients	39	42	79	80	81
No. of Patients with Response (%)	2 (5)	25 (60)	5 (6)	47 (59)	49 (60)

Symptomatic Response



	Part A, Wk 24		Part B, Wk 24		
No. of Patients/No. with Imputed Values	28/11	38/4	59/19	63/17	62/19
LS Mean Change (95% CI)	−9.6 (−15.06 to −4.12)	−21.9 (−26.87 to −16.97)	−13.9 (−17.61 to −10.12)	−23.8 (−27.43 to −20.13)	−14.4 (−18.02 to −10.72)

Dellon ES, et al. *N Engl J Med*. 2022;387(25):2317-2330.

2025 ACG Clinical Guideline: Dupilumab

Recommendation:

10. We suggest dupilumab as a treatment for EoE in individuals 12 years of age or older who are nonresponsive to PPI therapy	Moderate	Conditional

Key Concept:

We advise providers to use dupilumab as step-up therapy in difficult-to-treat patients, and providers should consider using it in patients with EoE with multiple atopic conditions that would also meet requirements for dupilumab use	The position of dupilumab in the EoE treatment algorithm is being determined

Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Case Presentation

- But doc, you said I have a narrowing in my esophagus, how can we treat that?

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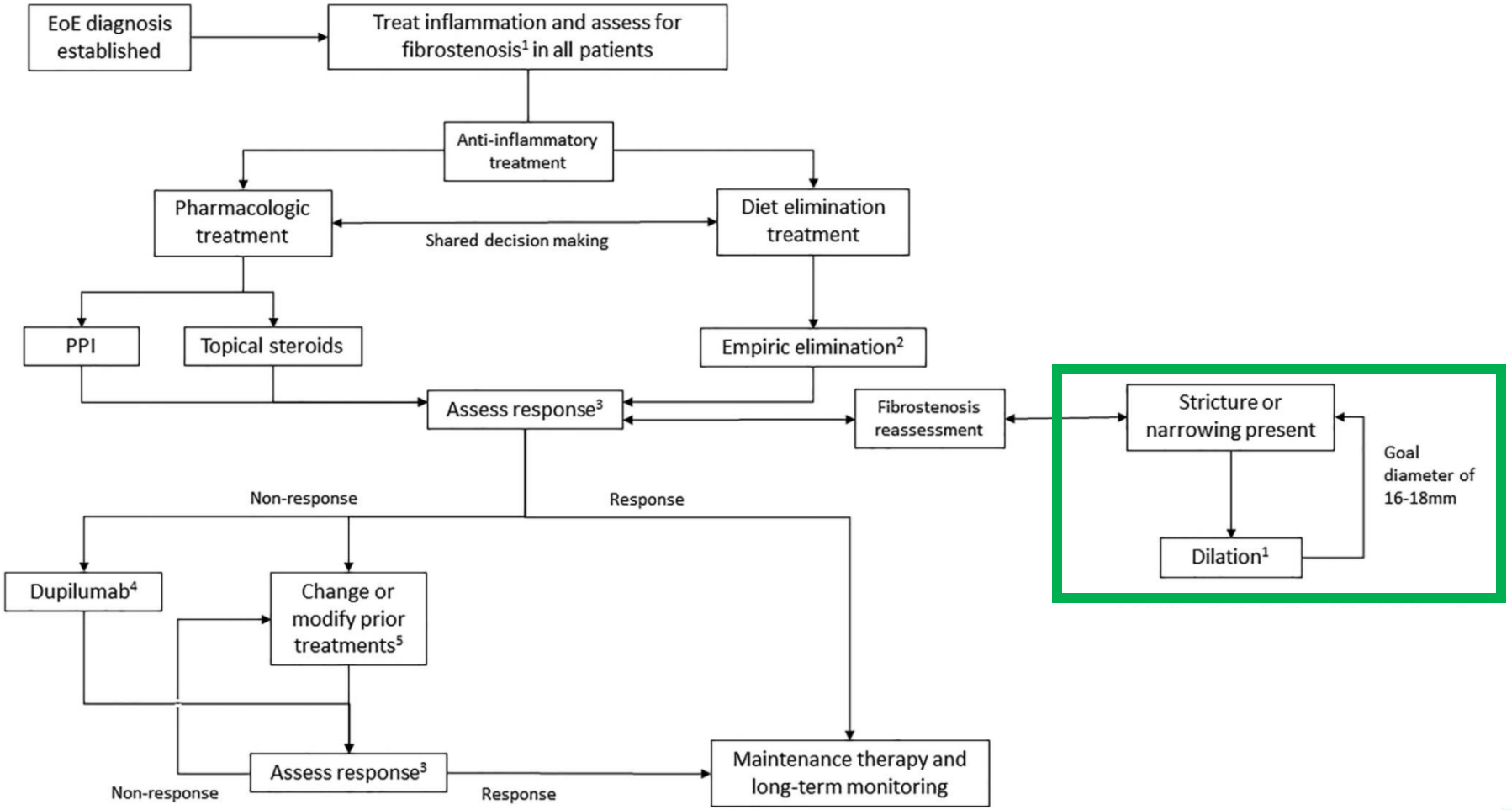
2025 ACG Clinical Guideline: Specialist Management



Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

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2025 ACG Clinical Guideline: Dilation

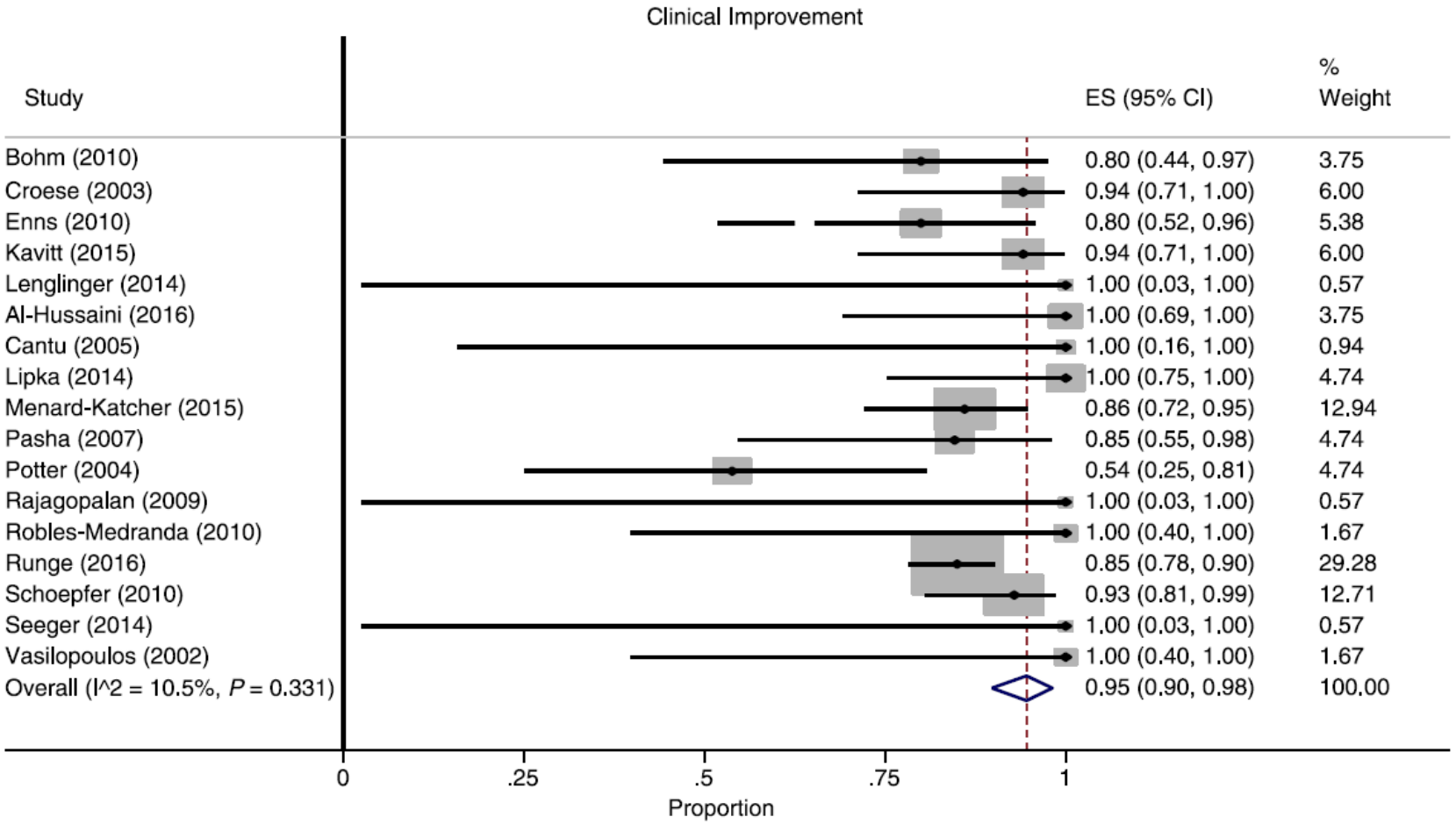
Recommendation:

15. We suggest the use of endoscopic dilation as an adjunct to medical therapy as a treatment for esophageal strictures causing dysphagia in patients with EoE	Low	Conditional

Key Concept:

We advise endoscopists to have a high level of suspicion for strictures and esophageal narrowing in EoE, especially in patients with dysphagia or dietary avoidance/modification behaviors	Strictures and luminal narrowing can be difficult to detect on endoscopy
We advise a "start low and go slow" approach for esophageal dilation	Table 7 outlines a general approach for performing dilation
We advise that dilation be combined with an anti-inflammatory treatment	Dilation does not impact the underlying inflammatory disease activity in EoE

Esophageal Dilation



Moawad FJ, et al. *Aliment Pharmacol Ther*. 2017;46(2):96-105.

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Case Presentation

- How do we keep an eye on this and make sure I remain controlled?

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2025 ACG Clinical Guideline: Maintenance/Monitoring

Recommendation:

Maintenance:

16. We suggest continuation of effective dietary or pharmacologic therapy for EoE to prevent recurrence of symptoms, histologic inflammation, and endoscopic abnormalities	Low	Strong

Monitor:

17. We recommend evaluating response to treatment of EoE with assessment of symptomatic and endoscopic and histologic outcomes	Low	Strong

Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Conclusions

- Diagnosis
  - Clinical presentation
  - Histology
  - Endoscopic appearance
- Management
  - Collaborative decision making
  - Anti-inflammatory treatments
    - 1-2 Food elimination is favored
    - PPI, Elimination diet and TCS first line
    - Dupilumab second line for most, first line for those with concomitant atopic conditions
- Dilations should be low and slow

Debate: Test or Treat for PPI-resistant Non-erosive GERD

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Assess Don’t Guess!

Perform Diagnostic Testing (FIRST) in PPI-Resistant GERD Patients

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Professor of Clinical Medicine

Director, Jay Monahan Center

Associate Chief Medicine, Network & Outreach/NYPBMH

Weill Cornell Medicine

Former President and Incoming Chair AFS

Disclosures: Medtronic (consulting); Diversatek (consulting); Braintree (consulting)

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“All that glisters is not gold”

William Shakespeare, The Merchant of Venice

“All the burns is not GERD”

Anonymous GI Attending

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Why Should W… g in PPI Refractory Sym…

- It is cost effective…
- It is patient centr…
- Because it gets t…
- Because John Pa… career developing these…

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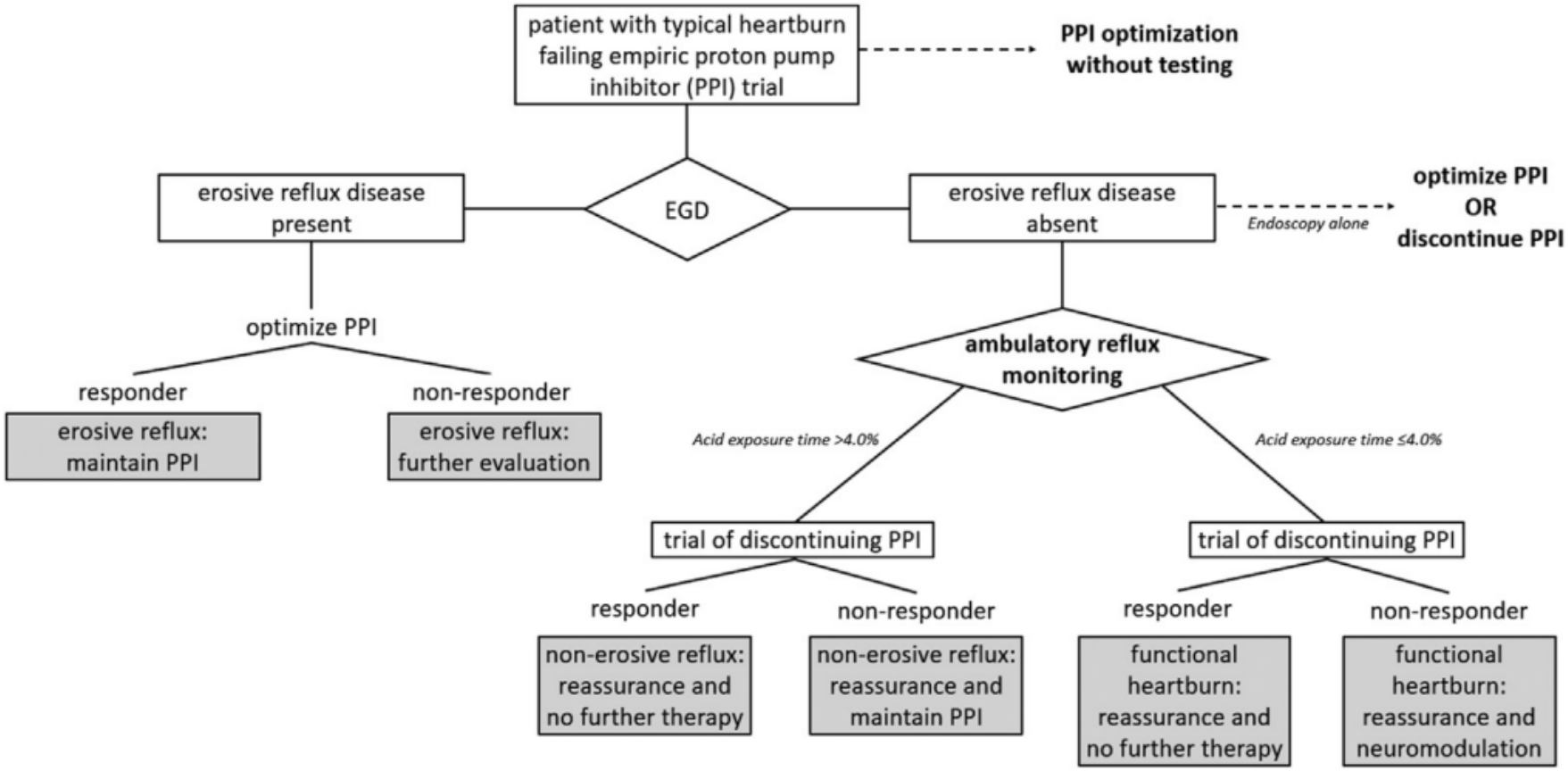
What are the Potential Diagnostic Avenues?



Shah ED, et al. *Clin Gastroenterol Hepatol*. 2024;22(10):2011-2022.e5.

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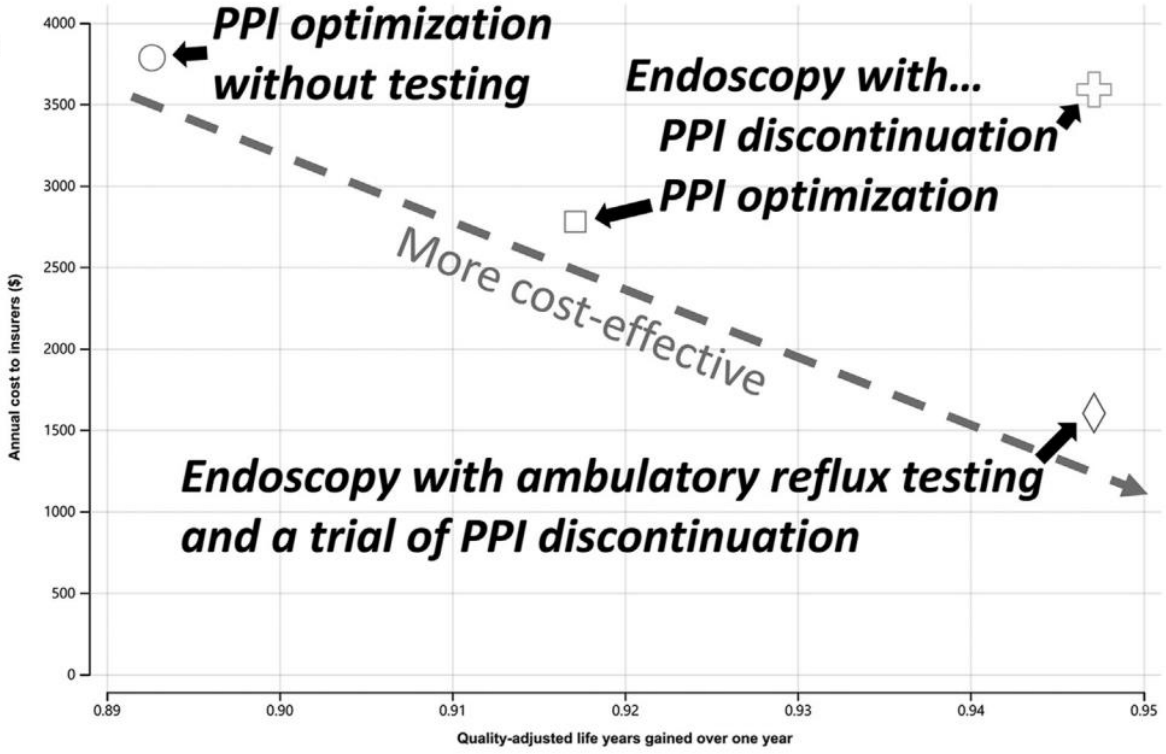
What is the Response to PPIs?
(Data from randomized controlled studies)

	Response to treatment (%)	Response to placebo (%)	Risk ratio for response (95% confidence intervals)	Number needed to treat
Uninvestigated heartburn[1]	70.3	25.1	2.80 (2.25-3.50)	2.2
Heartburn without esophagitis[1]	39.7	12.6	3.15 (2.71-3.67)	3.7

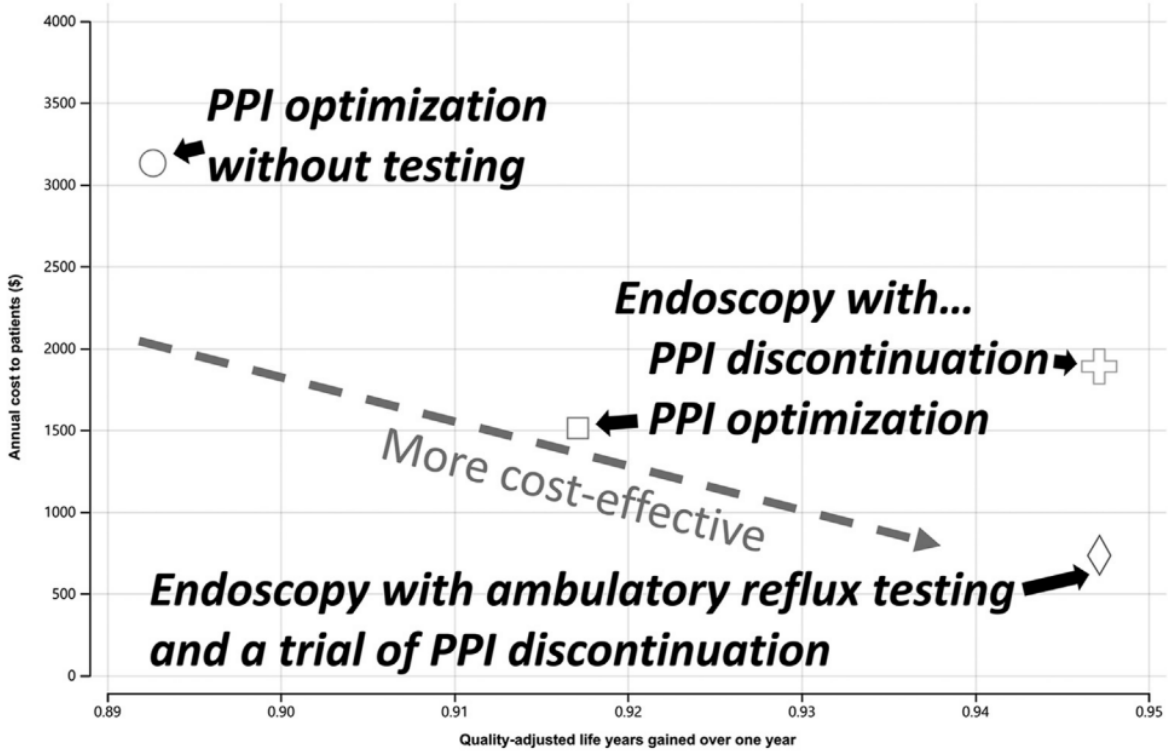
1. Sigterman KE, et al. *Cochrane Database Syst Rev*. 2013;2013:CD002095; 2. Dean BB, et al. *Clin Gastroenterol Hepatol*. 2004;2:656-664; 3. Khan M, et al. *Cochrane Database Syst Rev.* 2007;(2):CD003244; 4. Kahrilas PJ, et al. *Am J Gastroenterol*. 2011;106:1419-1426; 5. Kahrilas PJ, et al. *Gut*. 2011;60:1473-1478; 6. Chang AB, et al. *Cochrane Database Syst Rev*. 2011;2011:CD004823; 7. Vaezi MF, et al. *Laryngoscope*. 2006;116:254-260; 8. Gyawali CP, Fass R. *Gastroenterology*. 2018;154:302-318.

Is Diagnostic Testing Cost Effective?

Insurer's Perspective



Patient Perspective



Shah ED, et al. *Clin Gastroenterol Hepatol*. 2024;22(10):2011-2022.e5.

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Why Should We Never Offer pCABs Empirically?

- Because pCABs are ridiculously expensive
- Because the AGA tells us not to even use them for GERD
- …..and certainly not for unproven GERD
- Acid suppression is so great that side effects are potentially likely
- Most people with PPI-refractory heartburn do not have GERD

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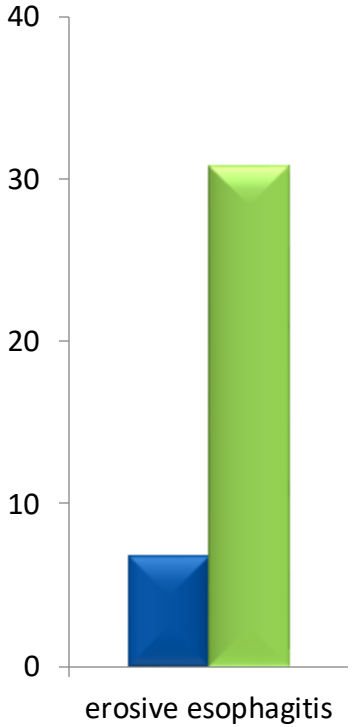
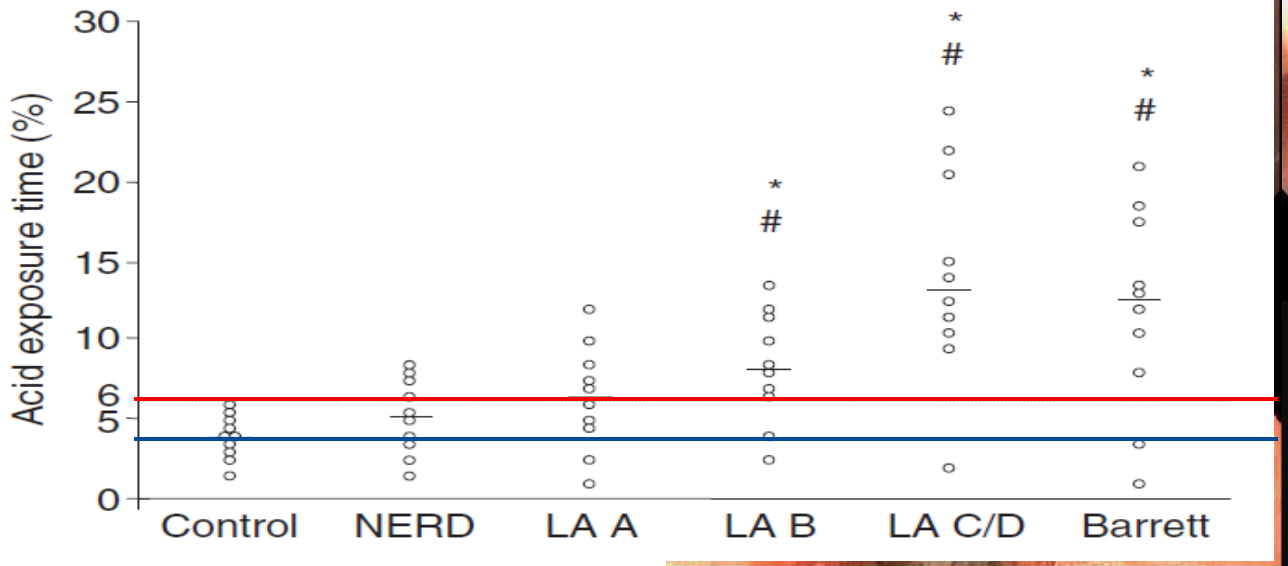
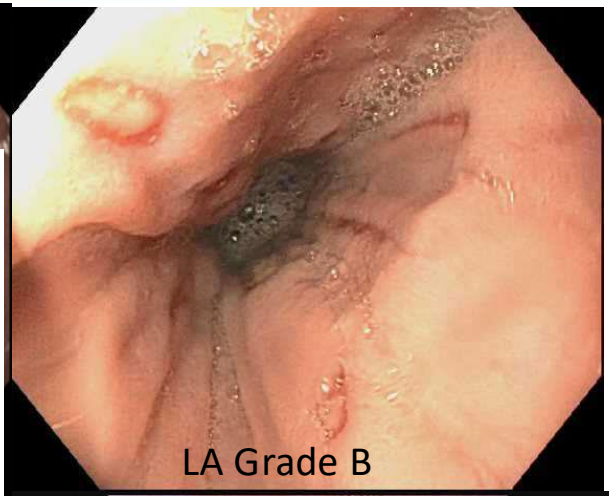
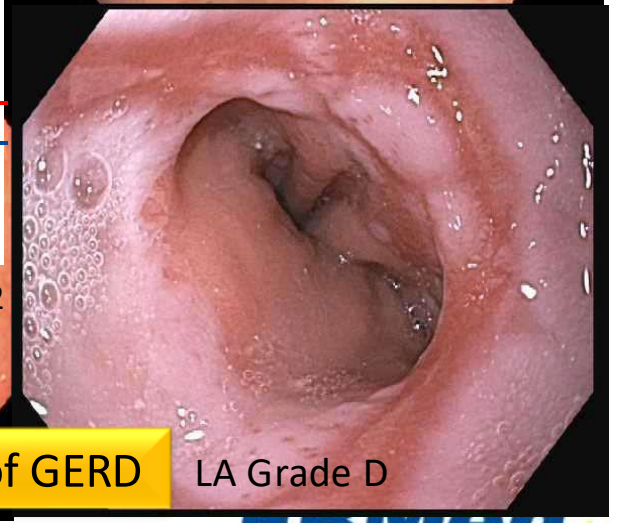
What is the Value of Endoscopy?





Bredenoord AJ, et al. *Neurogastroenterol Motil.* 2009;21:807-812



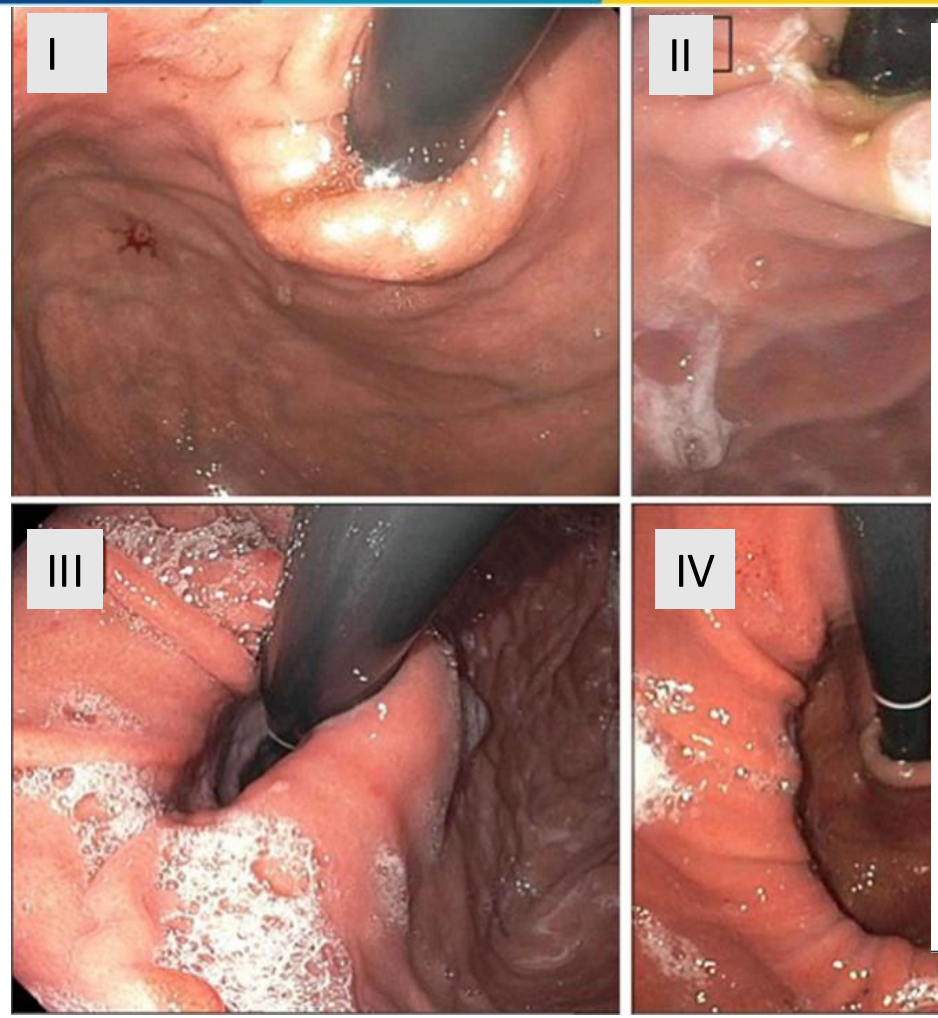


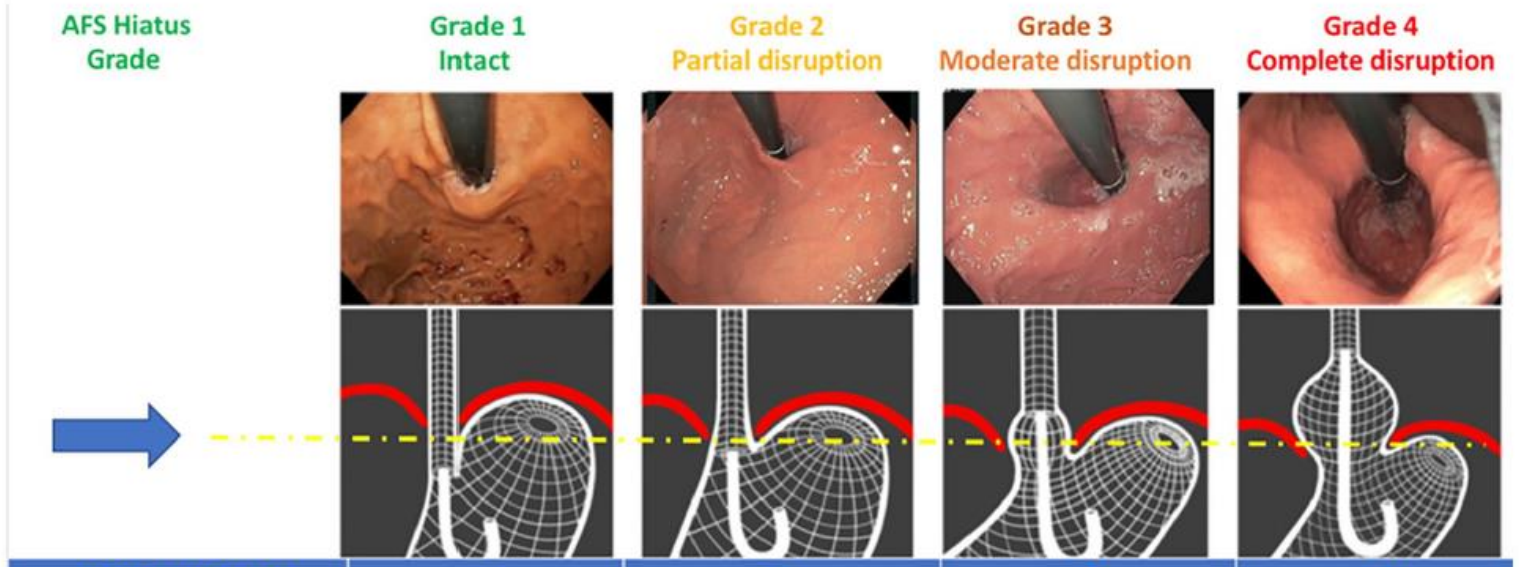
105 with PPI failure, EGD on PPI
91 with no treatment
≥3 heartburn episodes

Endoscopy has high specificity but low sensitivity for the presence of GERD

Akdamar K, et al. *Gastrointest Endosc*. 1986;32:78-80; Takashima T, et al. *Digestion*. 2012;86:55-58; Zagari RM, et al. *Gut*. 2008;57:1354-1359; Poh CH, et al. *Gastrointest Endosc*. 2010;71:28-34.

Value of Endoscopy



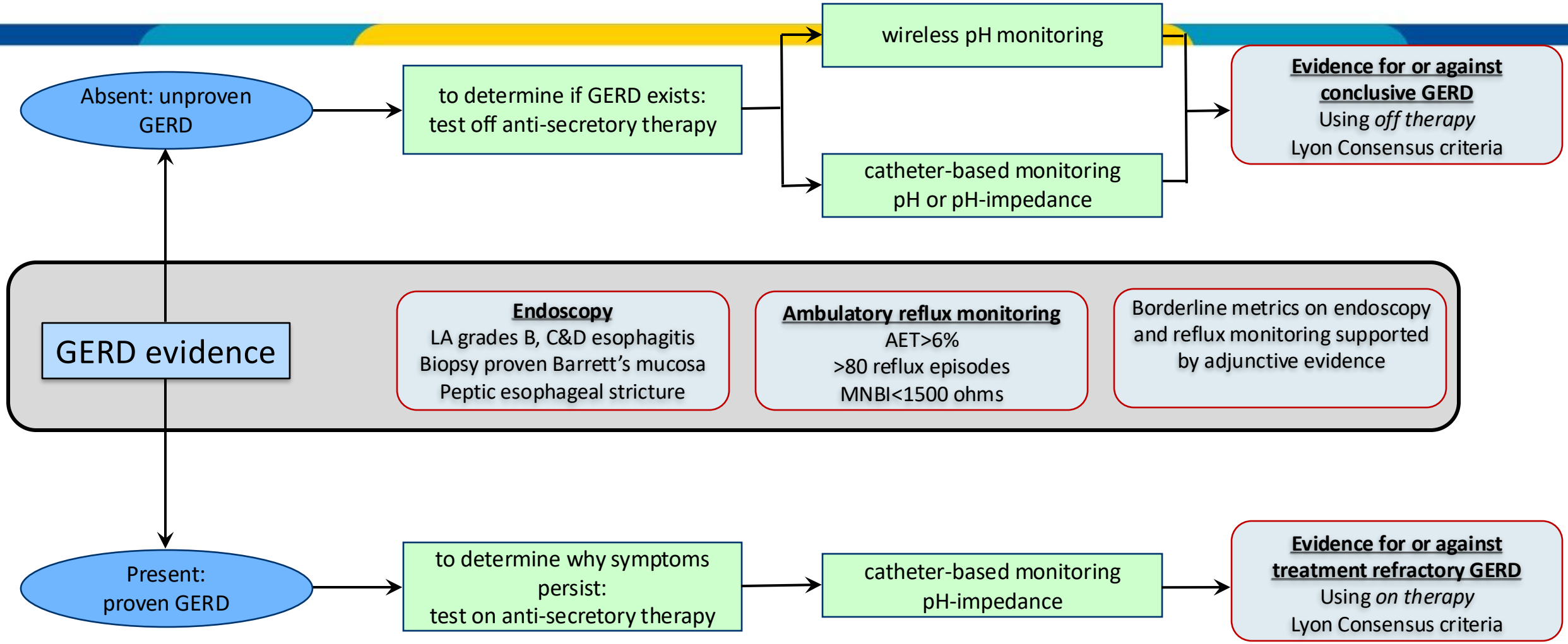


AFS Hiatus Grade	1	2	3	4
Hiatal axial Length, cm (L)	None (0 cm)	None (0 cm)	0-2 cm	>2 cm
Hiatal aperture, cm (D)	Snug to scope 1 cm	Loose 1-2 cm	Open 2-3 cm	Wide open >3 cm
Flap valve (F)	Present, full lip with Omega shape (F+)	Absent, thinning & flattening valve lip (F-)	Absent (F-)	Absent (F-)
LDF components	L0, D1, F+	L0, D1-2, F-	L0-2, D2-3, F-	L>2, D>3, F-

Hill grade of EGJ on retroflexion

Hill LD, et al. *Gastrointest Endosc*. 1996;44:541-547; ASGE Standards of Practice Committee, Desai M, et al. *Gastrointest Endosc*. 2025;101:267-284; Nguyen NT, et al. *Foregut*. 2022;2:339-348.

Value of Ambulatory Reflux Monitoring



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

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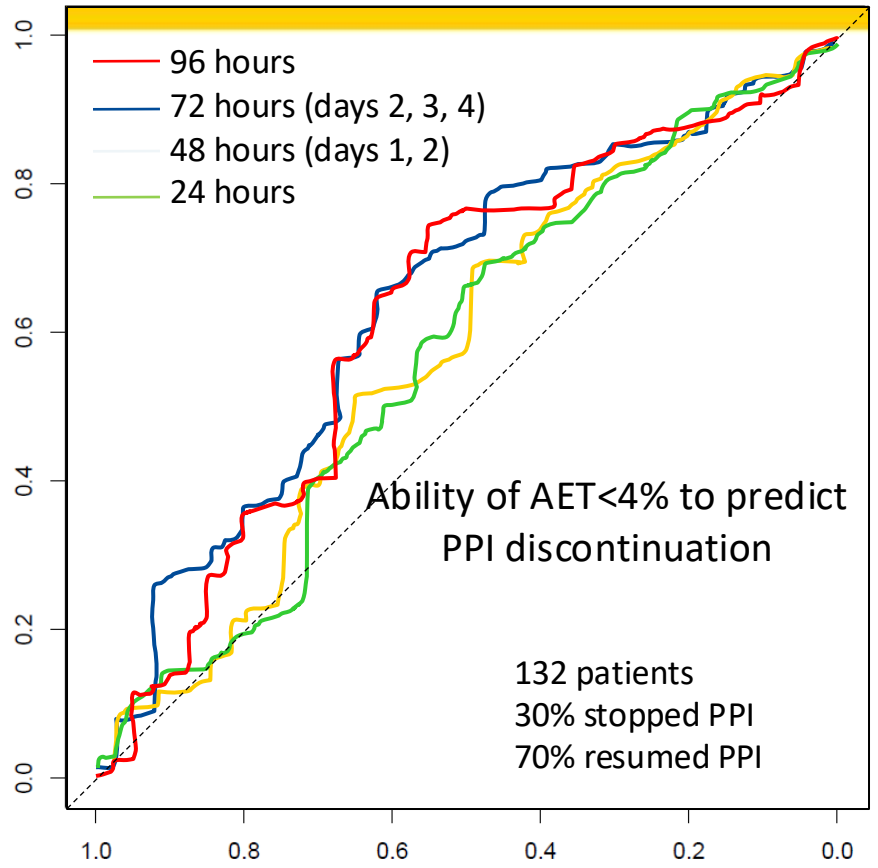
Value of Prolonged pH Monitoring



14 did not meet inclusion criteria
12 had EoE
3 had advanced grade esophagitis
7 had insufficient reflux monitoring time
6 were lost to follow up

Able to discontinue PPI *n=34 (34.0%)*	Unable to discontinue PPI *n=66 (66.0%)*
RESQ-eD 12.0 [SD 9.6]*	RESQ-eD 17.8 [SD 11.7]*
GERDQ 7.2 [SD 3.0]*	GERDQ 9.3 [SD 4.6]*
AET 4.3 [SD 3.6]*	AET 6.6 [SD 3.6]*

Physiologic AET on multiple consecutive days rules out pathologic GERD and allows PPI discontinuation

**p<0.05*

Yadlapati R, et al. *Am J Gastroenterol*. 2022;117:1573-1582; Yadlapati R, et al. *Gastroenterology*. 2021;160:174-182.e1.

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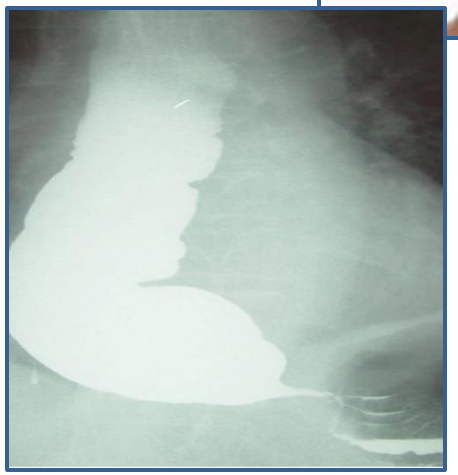
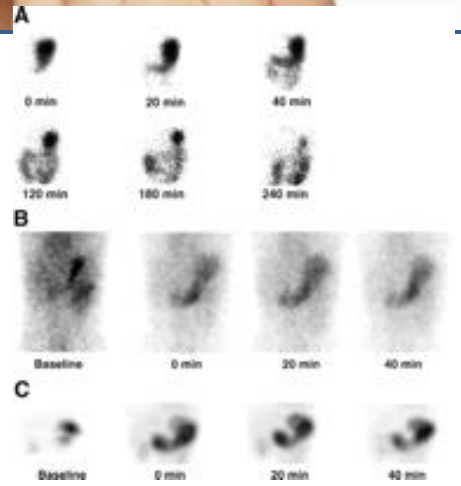
Why Is My Patient Still Symptomatic?

If the patient has normal reflux monitoring :

1. Rumination
2. Aerophagia
3. Motility Disorder (Achalasia)
4. Delayed Gastric Emptying (Gastroparesis)
5. EoE (1-6%)
6. Functional





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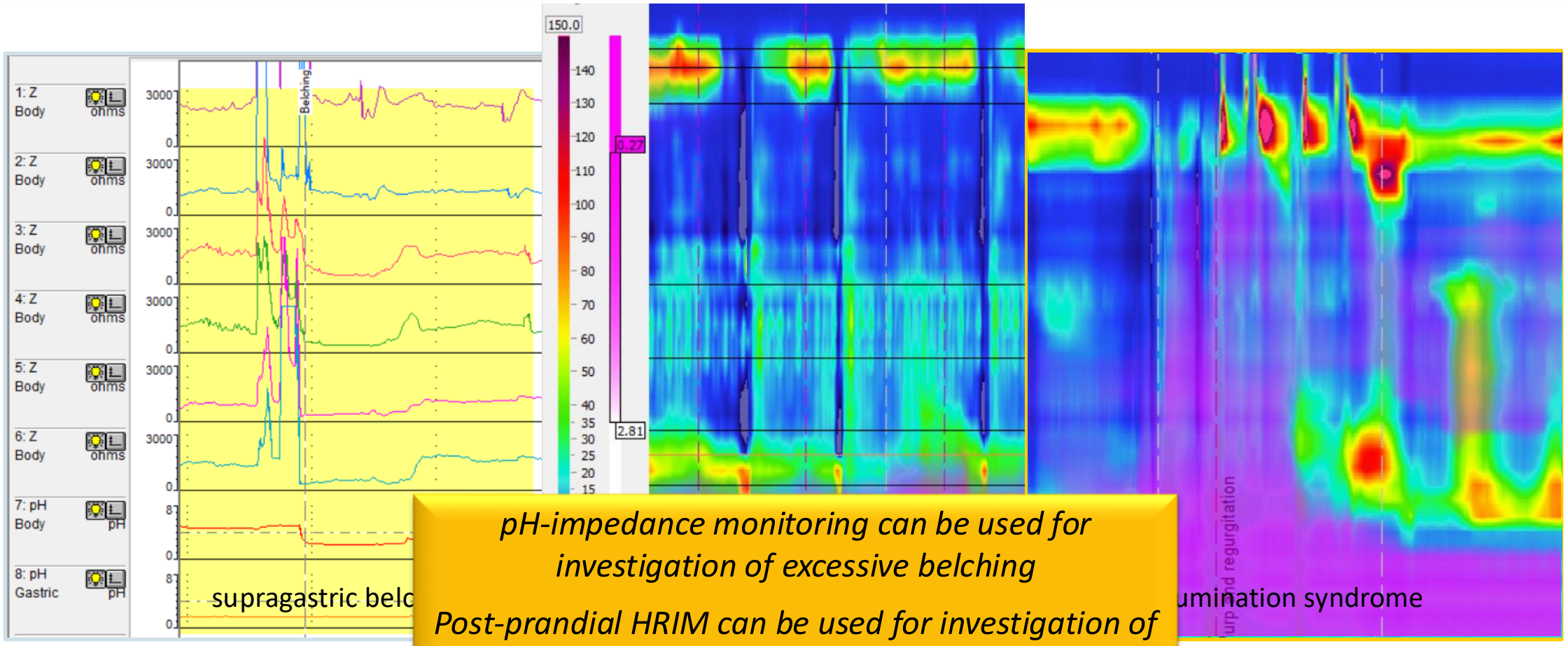
pH Impedance Monitoring: Behavioral Syndromes



pH-impedance monitoring can be used for investigation of excessive belching

Post-prandial HRIM can be used for investigation of suspected rumination

Yadlapati R, et al. *Clin Gastroenterol Hepatol*. 2018;16:211-218.e1; DeLay K, et al. *Neurogastroenterol Motil*. 2021;33:e14106.

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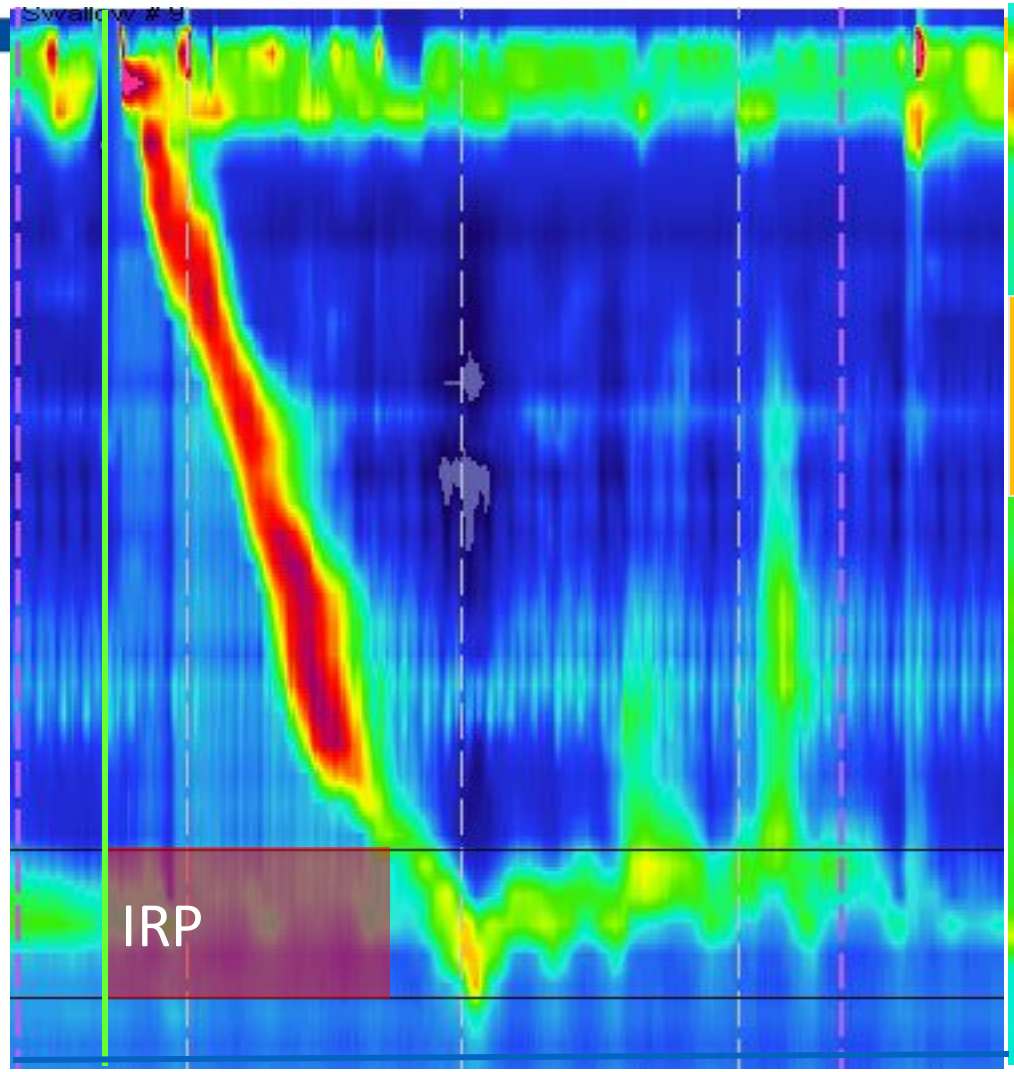
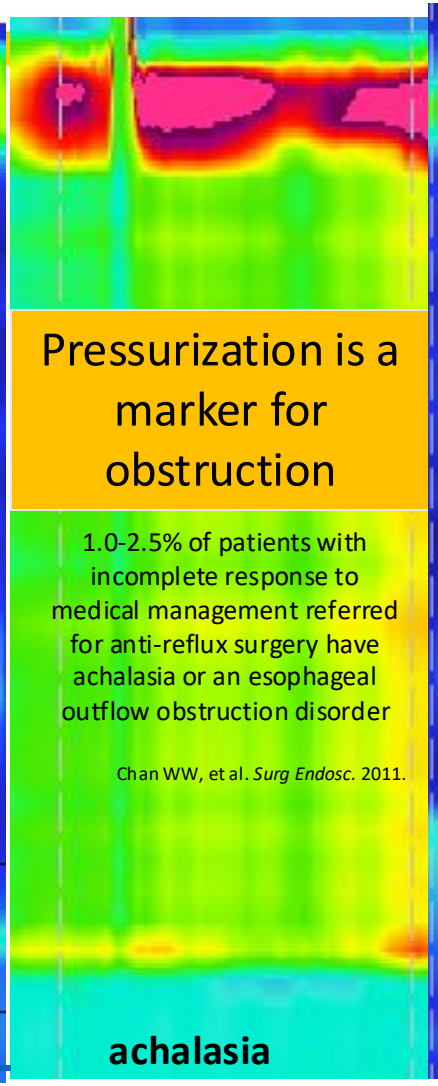
Value of High Resolution Manometry



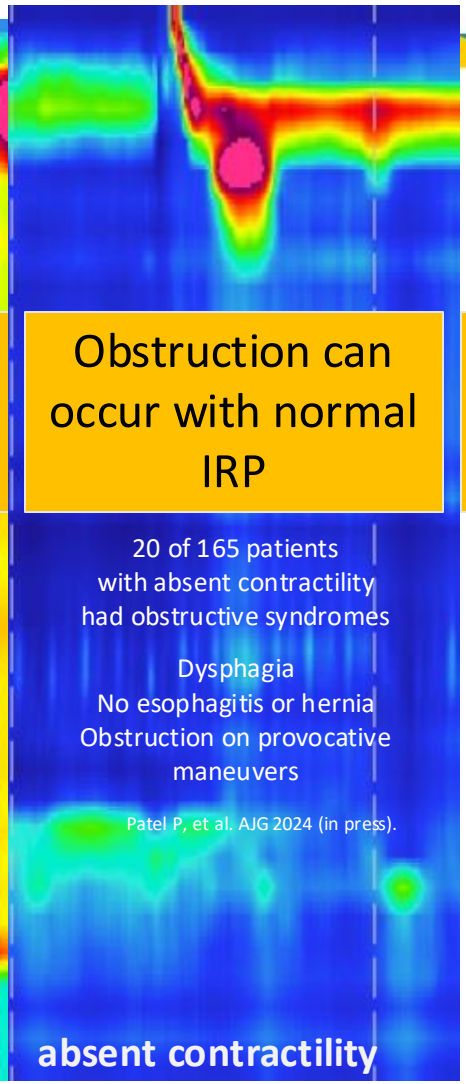


Pressurization is a marker for obstruction

1.0-2.5% of patients with incomplete response to medical management referred for anti-reflux surgery have achalasia or an esophageal outflow obstruction disorder

Chan WW, et al. *Surg Endosc.* 2011.

achalasia



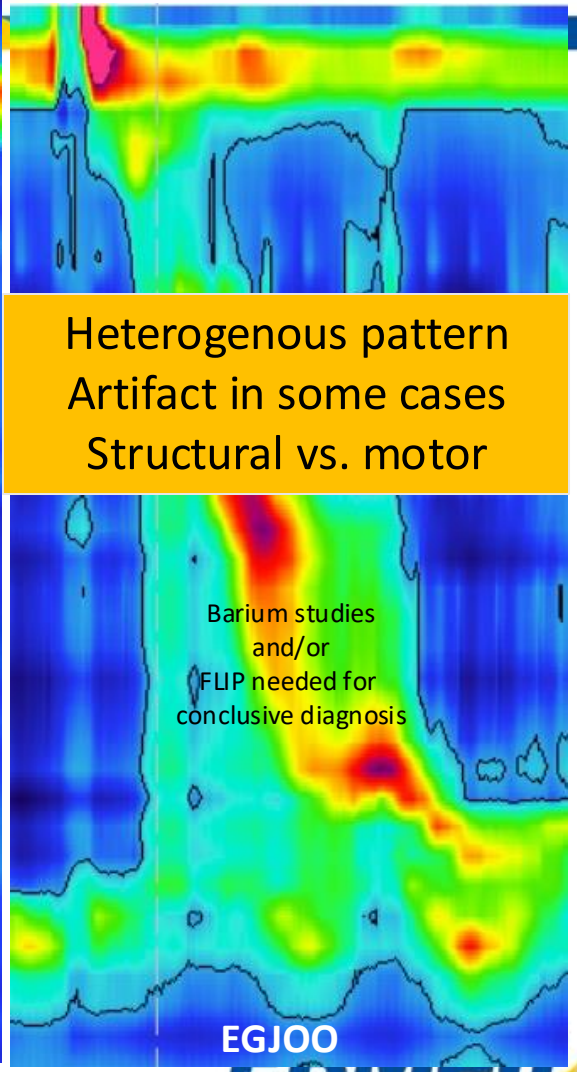
Obstruction can occur with normal IRP

20 of 165 patients with absent contractility had obstructive syndromes

Dysphagia
No esophagitis or hernia
Obstruction on provocative maneuvers

Patel P, et al. AJG 2024 (in press).

absent contractility



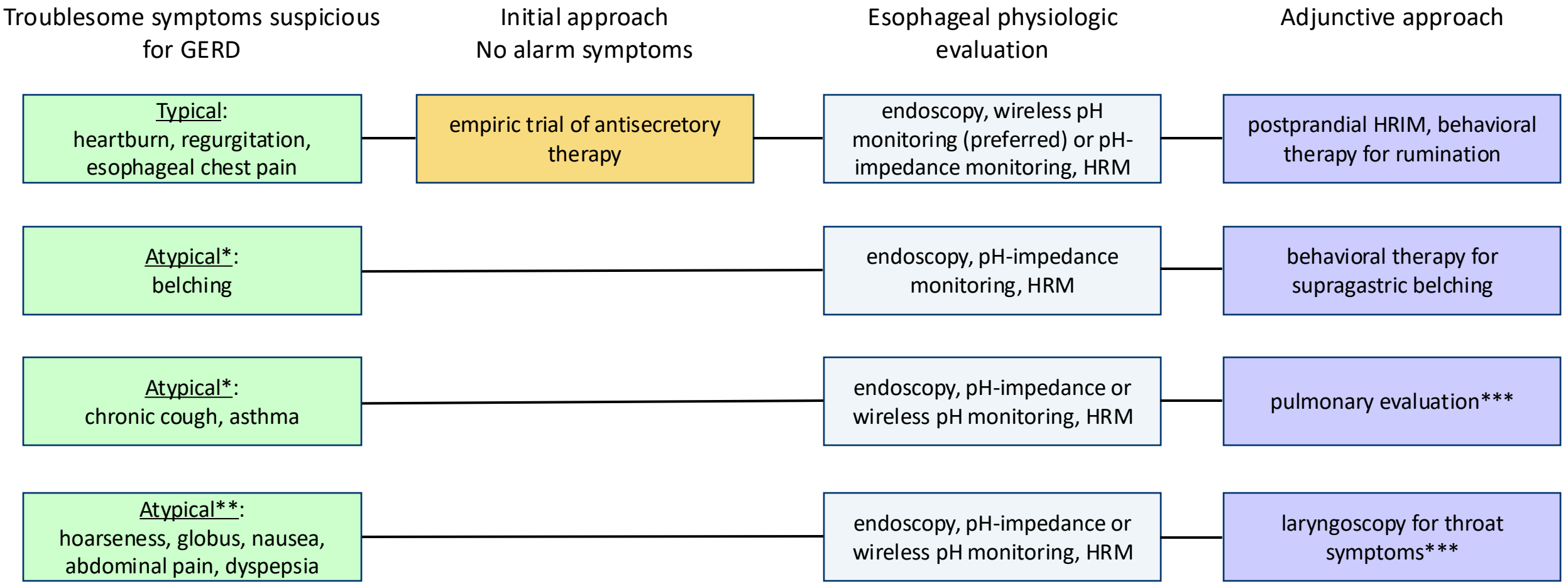
Heterogenous pattern
Artifact in some cases
Structural vs. motor

Barium studies and/or FLIP needed for conclusive diagnosis

EGJOO

Gyawali CP, et al. *Neurogastroenterol Motil.* 2013;25:99-133; Kahrilas PJ, et al. *Neurogastroenterol Motil.* 2015;27:160-174; Chan WW, et al. *Surg Endosc*. 2011;25:2943-2949; Patel P, et al. *Am J Gastroenterol*. 2024;119:2189-2197. .

What Should be the Diagnostic Approach Based on Symptoms



* likelihood of GERD is lower than with typical symptoms, testing is performed to identify or rule out a reflux basis for symptoms

** likelihood of GERD is very low, upfront testing is typically not recommended except to rule out a reflux basis for symptoms

***adjunctive approaches may precede esophageal evaluation to rule out primary pulmonary and laryngeal disorders

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

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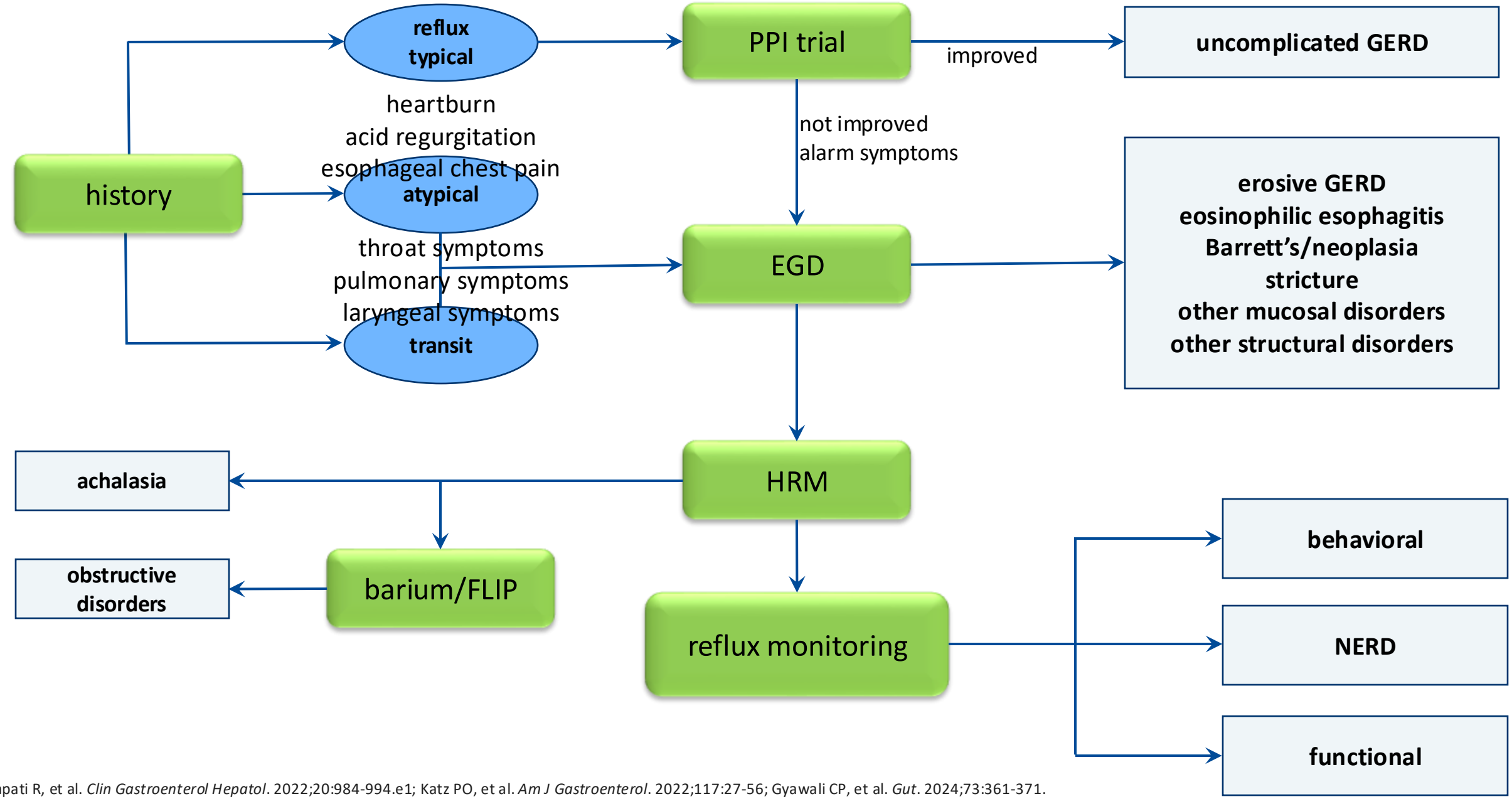

Yadlapati R, et al. *Clin Gastroenterol Hepatol*. 2022;20:984-994.e1; Katz PO, et al. *Am J Gastroenterol*. 2022;117:27-56; Gyawali CP, et al. *Gut*. 2024;73:361-371.

Use the Diagnostic Toolbox

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Great Debates

Feel the Burn: Diagnostic Testing vs Empiric PCAB in PPI Resistant Non-Erosive GERD

John E. Pandolfino, MD, MSCI
Hans Popper Professor of Medicine
Feinberg School of Medicine,
Northwestern University
Chief, Division of Gastroenterology and Hepatology
Northwestern Medicine
Northwestern Memorial Hospital

Reflux Testing Versus Empiric PCAB

How do you debate someone who is one of the most likable people in your field (certainly more likable than you) and is also taking the position that reflects a major component of your life's work?

You ask Chat GPT

Reflux Testing Versus Empiric PCAB

Debating someone who is both widely liked and aligned with your core beliefs—at least in part—requires a strategic and thoughtful approach. Here's how to navigate this challenge:

1. **Frame It as a Collaborative Exploration, Not a Battle**
2. **Distinguish Your Position with Nuance and acknowledge their points**
3. **Find a Higher Purpose and bigger picture**
4. **Appeal to Logic and Evidence, Not Just Charisma**
5. **Maintain Warmth and Respect**

Clinical Context and Treatment Issues
Reflux testing versus Empiric PCAB

35 year old woman with GERD (Heartburn) and Normal Endoscopy - Experiencing limited Relief with PPIs.

Why we should start with a short trial of PCABs instead of going to reflux testing in this patient?

We both want to do the best thing for the patient and either approach is likely OK and it may boil down to patient preference.

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Clinical Context and Treatment Issues

Reflux testing versus Empiric PCAB

35 year old woman with GERD and Normal Endoscopy- Experiencing limited Relief with PPIs

- Demographics
- Symptoms
- EGD results
- Response to PPI

Where does she fit in the algorithm most follow?

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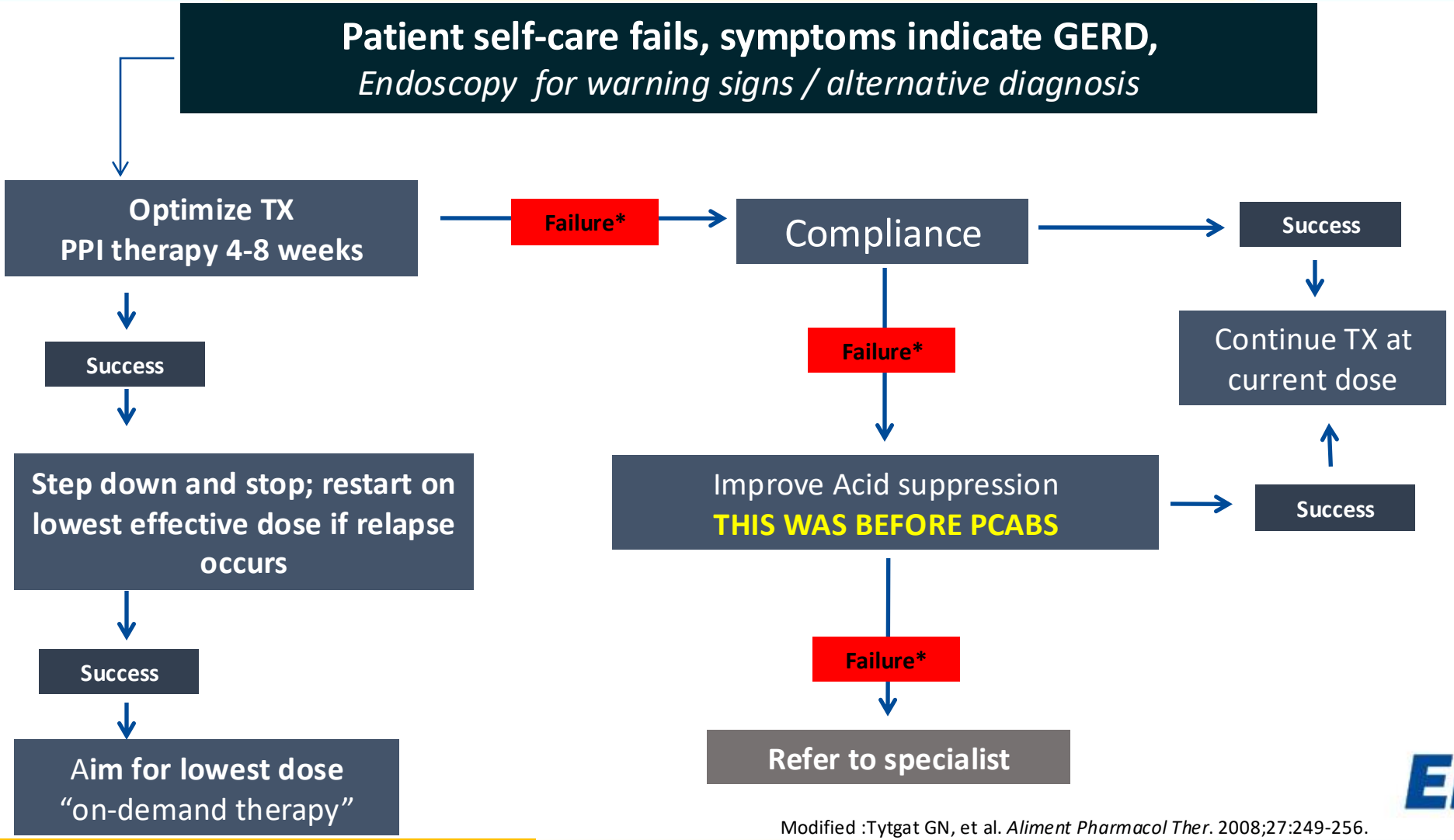
Empiric Therapy is Easy and Can Be Diagnostic



Modified :Tytgat GN, et al. *Aliment Pharmacol Ther*. 2008;27:249-256.

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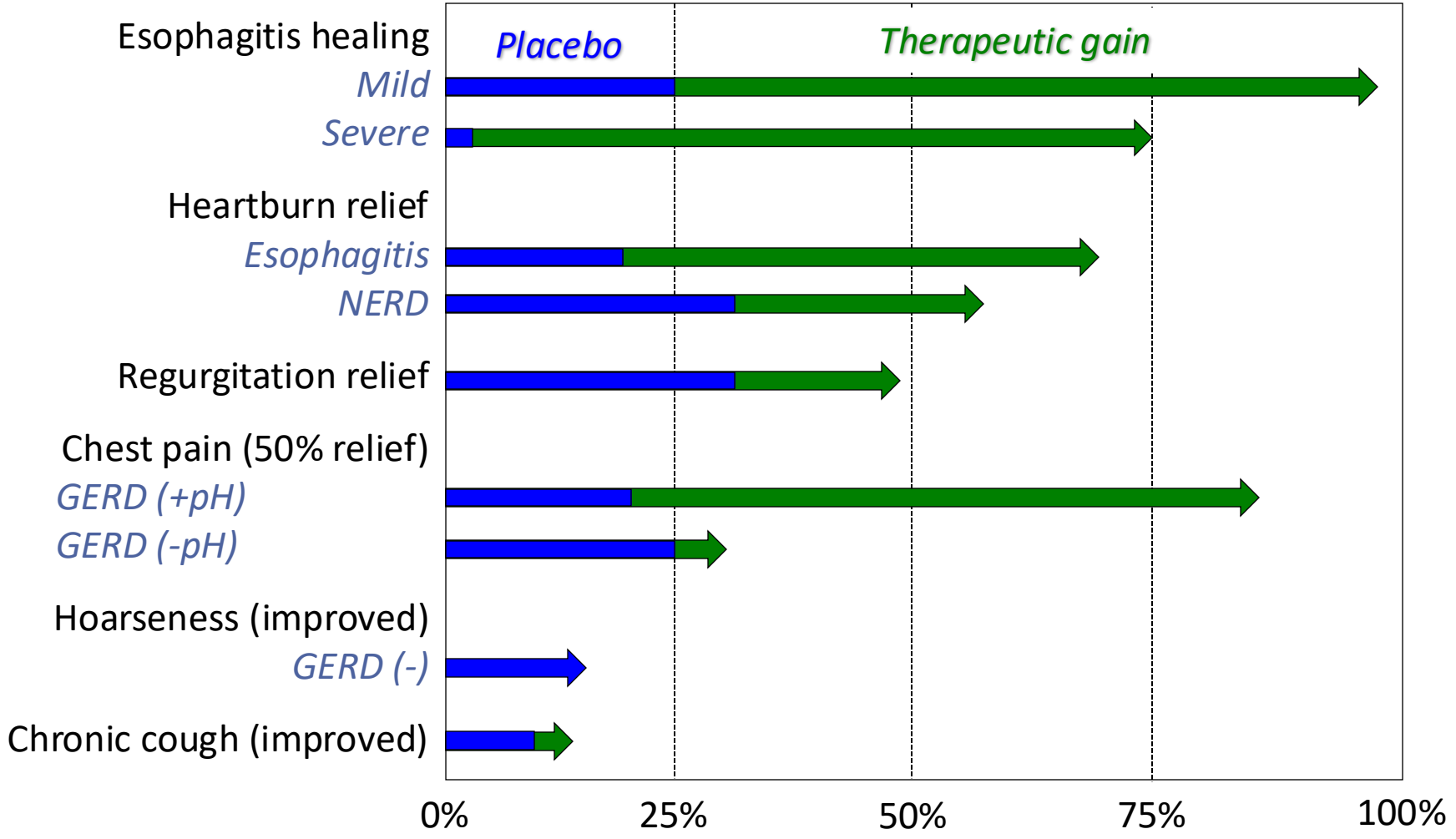
* Always consider alternative diagnosis when treatment failure occurs

PPIs work 100% - 60% of the time
Limiting the effectiveness of PPI test- improved with PCAB



Kahrilas PJ.... AJG, 2011;106(8):1419-25;

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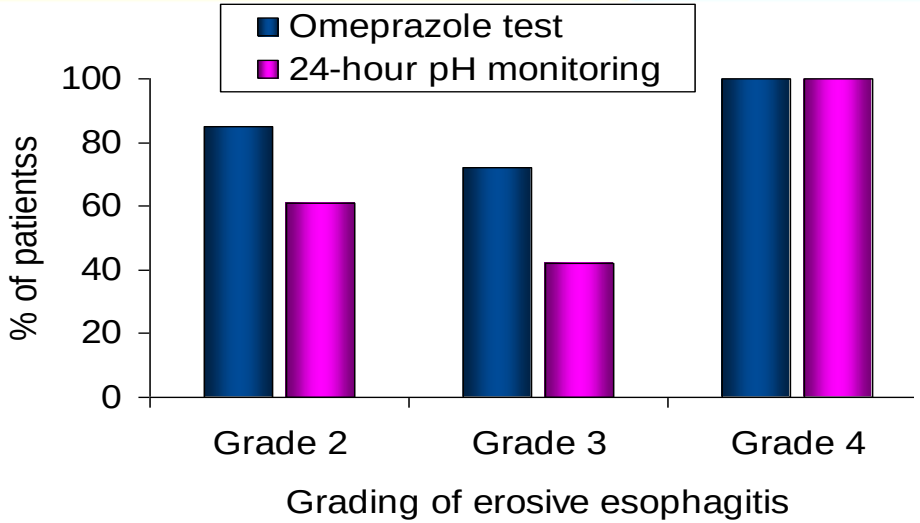
Empiric Therapy is Can be Diagnostic

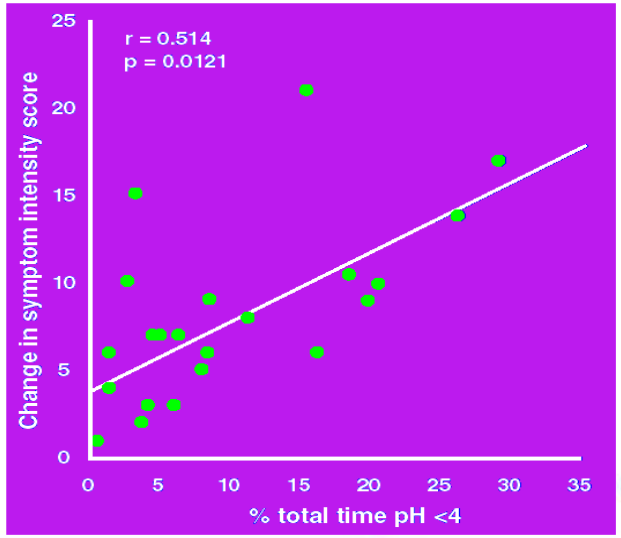
TABLE 1. Proposed PPI Test Characteristics for GERD and NCCP

Characteristics	GERD	NCCP
Duration (d)	7-14	7-14
Dose of PPI (X standard dose)	X2 – X3	X2 – X3
Schedule	AM + PM	AM + PM
Positivity of test (symptom improvement)	> 50%	> 50%
Which PPI	All	All

GERD indicates gastroesophageal reflux disease; NCCP, noncardiac chest patient; PPI, proton pump inhibitor.



Comparator PPI TEST	Sensitivity 0.80	Specificity 0.50
24-hr pH	0.78 (0.66-0.86)	0.54 (0.44-0.65)
EGD	0.68 (0.56-0.79)	0.46 (0.34-0.59)



Gasiorowska A, Fass R. J Clin Gastroenterol. 2008 Sep;42(8):867-74
Fass et al., J Clin Gastroenterol, 1999; Numans et al Ann Int Med 2004 140:518-27

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PPI Pharmacologic Features That Limit Speed of Onset and Acid Inhibiting Efficacy

PPIs are vulnerable to degradation by gastric acid

Enteric coating protects them from acid but delays absorption

PPIs are prodrugs

Must be activated by gastric acid to bind covalently to proton pumps

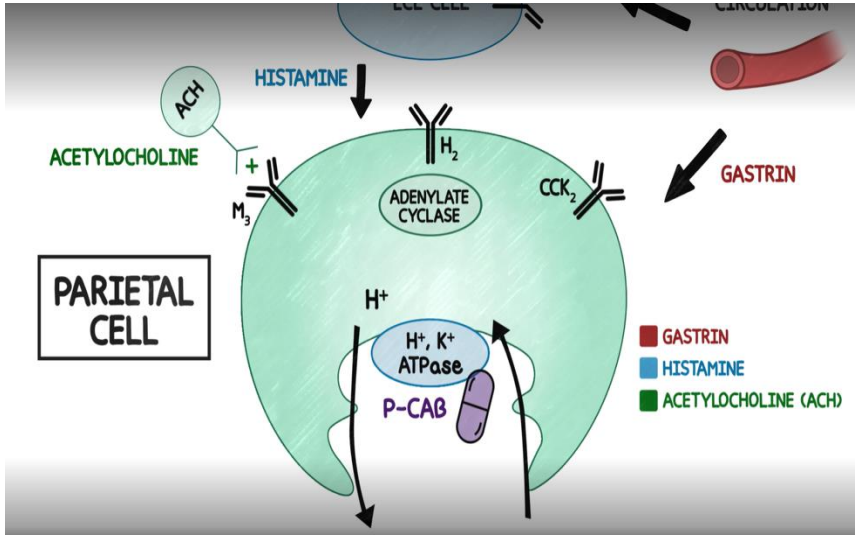
Only actively secreting parietal cells affected by PPIs

Fasting: only ≈5% of proton pumps actively secreting
With meals: 60% to 70% of proton pumps actively secreting

Short plasma half-life (2 to 3 hours)

Stomach constantly making new proton pumps (25% replaced in 24 hours)
Repeated administration required

Individual variability in rate of metabolism by CYP2C19



Kinoshita Y, et al. J Neurogastroenterol Motil. 2018;24:182-196.

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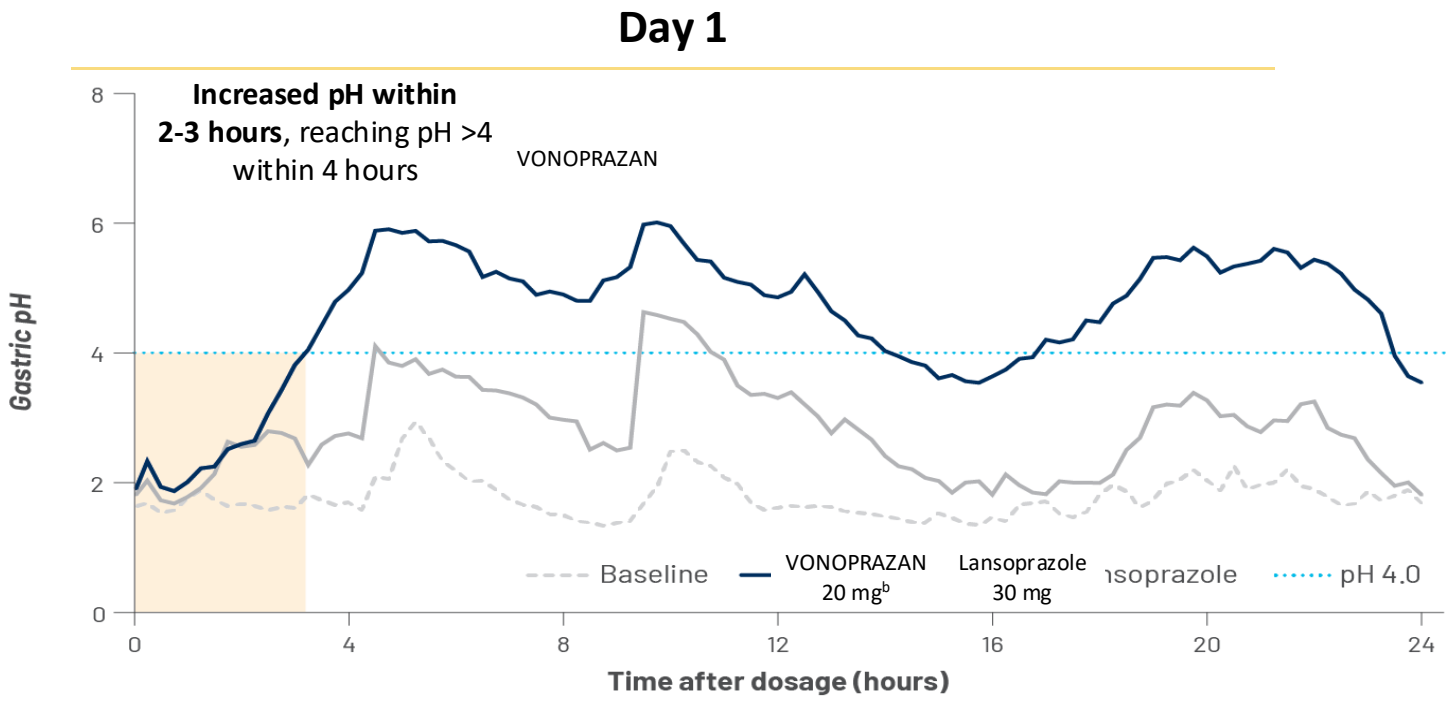
Rapid, Potent, and Durable Acid Suppression Perfect for an Empiric Trial

In a phase 1, open-label, crossover study with 44 healthy volunteers receiving VOQUEZNA 20 mg once daily, Vonoprazan has been shown to provide rapid, potent, and durable acid suppression[a]



Patients not responding will likely not have an acid mediated disease

Laine L et al. *Am J Gastroenterol*. 2022;117:1158–1161.

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AGA Clinical Practice Recommendation

Best practice advice

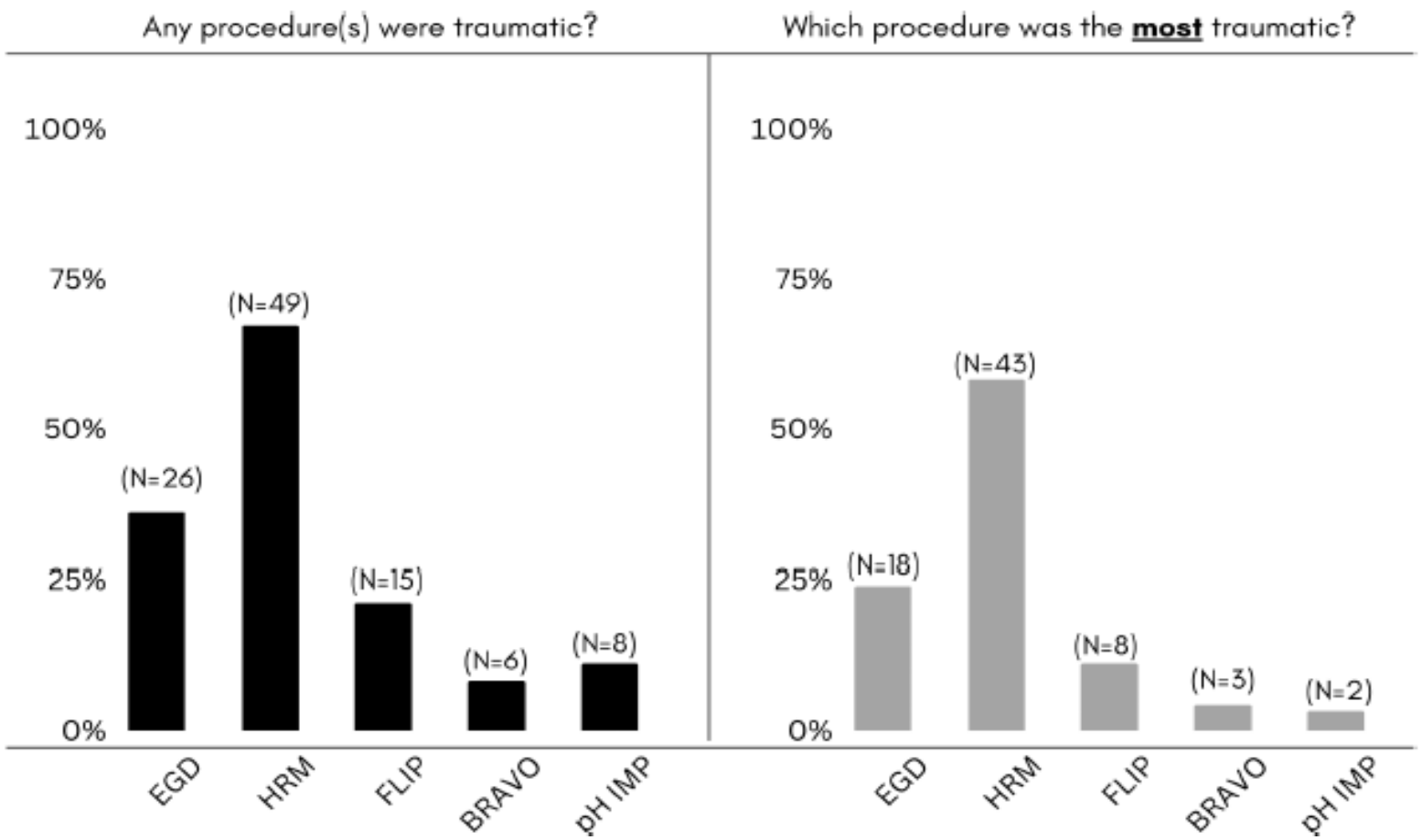
- **AGA**: Clinicians should provide patients presenting with troublesome heartburn, regurgitation, and/or non-cardiac chest pain without alarm symptoms a 4- to 8-week trial of single-dose PPI therapy
- With inadequate response, dosing can be **increased to twice a day** or switched to a more effective acid suppressive agent once a day. – **WHY NOT PCAB**
- When there is adequate response, PPI should be tapered to the lowest effective dose
- **ACG**

Table 1. Summary and strength of recommendations

	GRADE quality of evidence	GRADE strength of recommendation
Diagnosis of GERD		
For patients with classic GERD symptoms of heartburn and regurgitation who have no alarm symptoms, we recommend an 8-wk trial of empiric PPIs once daily before a meal.	Moderate	Strong
We recommend attempting to discontinue the PPIs in patients whose classic GERD symptoms respond to an 8-wk empiric trial of PPIs.	Low	Conditional

Yadlapati R et al. Clin Gastroenterol Hepatol 2022;20:984-94
Katz et al. The American Journal of Gastroenterology 117(1):p 27-56, January 2022. | DOI: 10.14309/ajg.0000000000001538

Tolerability of Esophageal Diagnostics
Huge Drawback



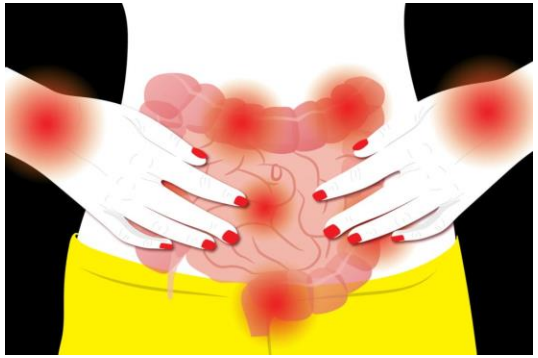
Taft et al. NGM Nov 2022. DOI: 10.1111/nmo.14540

Empiric Therapy With a PCAB is Reasonable Clinical Pragmatism

- Easy and patient friendly in the right patient (35 y/o)
  - *2 week trial- escalation of acid suppression guideline recommended*
- Likely cost effective and more generalizable
  - *Reduce reflux testing and endoscopy*
    - *You can't bring everyone back- cost prohibited*
- Will likely improve diagnostic capability
  - *Less false negatives due to inadequate acid suppression*
- Access to reflux testing is limited
  - *Can always perform testing later*

Yadlapati R et al. Clin Gastroenterol Hepatol 2022;20:984-94
Katz et al. The American Journal of Gastroenterology 117(1):p 27-56, January 2022. | *DOI:* 10.14309/ajg.0000000000001538

How I Do It: Irritable Bowel Syndrome



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Disclosures

- Advisory Board/Honoraria:
  - Ironwood Pharmaceuticals
  - Vibrant
  - Ardelyx pharmaceuticals
- Research Support
  - National Institutes of Health, NIDDK
  - Vibrant
  - Biora Therapeutics

Objectives

- Define IBS and its subtypes
- Understand their multifactorial pathophysiology
- Review latest treatment options using a pathophysiologic and Evidence-based approach
  - IBS-D
  - IBS-C

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Irritable Bowel Syndrome

- Disorder of Gut and Brain Interaction (DGBI)
  - Chronic recurrent problem
  - Abdominal pain or discomfort
  - Diarrhea
  - Constipation
  - Prevalence ~ 15% of population
- Gastrointestinal disorder
  - Gas and Bloating
  - Prevalence 13.9% of population
- Symptoms are often exacerbated by Food or Stress
- Coexisting conditions are common
  - Gastrointestinal: Functional dyspepsia, Heartburn, Bloating
  - Extra GI; Fibromyalgia, Headaches, Interstitial Cystitis, Chronic Fatigue etc

Lacy BE, et al. *Am J Gastroenterol*. 2021;116(1):17-44; Ballou S, et al. *Clin Gastroenterol Hepatol*. 2019;17(12):2471-2478.e3; Oh JE, et al. *Clin Gastroenterol Hepatol.* 2023;21(9):2370-2377; Rao SSC, et al. *Practical Gastroenterology*. 2024;48:38-46.

Irritable Bowel Syndrome/Unexplained GI Symptoms SUBTYPES

Bristol Stool Form Scale

Type 1
Separate hard lumps, like nuts

Type 2
Sausage-shaped but lumpy

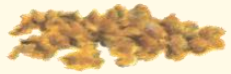
IBS-C

Type 3
Like a sausage but with cracks on its surface

Type 4
Like a sausage or snake, smooth and soft

IBS-M

Type 5
Soft blobs with clear-cut edges



Type 6
Fluffy pieces with ragged edges; mushy stool

Type 7
Watery, no solid pieces; entirely liquid

IBS-D

Gas & Bloating

Lacy BE, et al. *Am J Gastroenterol*. 2021;116(1):17-44; Rao SSC, et al. *Clin Transl Gastroenterol*. 2019;10(10):e00078; Rao SSC, et al. *Practical Gastroenterology*. 2024;48:38-46.

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Rome IV Criteria for Irritable Bowel Syndrome

Recurrent abdominal pain at least 1 day/week
In the last 3 months associated with 2 or more:

- **Related to defecation**

and

- **Onset associated with a change in frequency of stool**

and

- **Onset associated with a change in form (appearance) of stool**

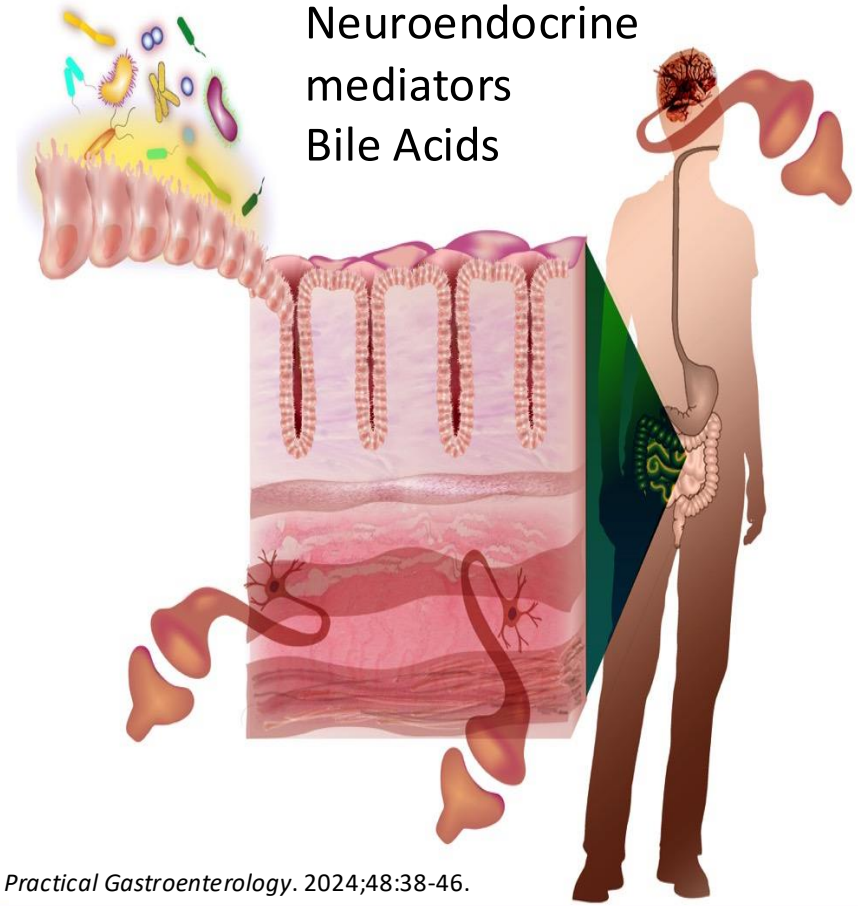
Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407.e5.

IBS Pathophysiology

Luminal Factors

Dysbiosis
Neuroendocrine mediators
Bile Acids



Host Factors

Altered GI Motility
Visceral Hypersensitivity
Altered brain & gut interactions
Gut mucosal immune interactions
Increased intestinal permeability

Environmental Factors

Psychosocial distress
Food
Antibiotics
Enteric infection

Chey WD, et al. *JAMA*. 2015;313(9):949-958; Rao SSC, et al. *Practical Gastroenterology*. 2024;48:38-46.

ACG Guidelines on Diagnostic Testing in IBS

Recommended	IBS population
Positive diagnostic strategy vs. diagnosis of exclusion	All IBS
Celiac serologies	IBS-D
C-reactive protein	IBS-D
Fecal calprotectin	IBS-D
Anorectal physiology testing	IBS with suspected PFD and/or refractory constipation

Not recommended
Routine stool testing
Routine colonoscopy < 45 year
Food allergy or insensitivities testing

Strength/type of recommendation

Strong | Conditional | Consensus

Lacy BE, et al. *Am J Gastroenterol*. 2021;116(1):17-44.

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Searching for IBS-D: Differential Diagnoses

Bile acid diarrhea

Microscopic colitis

Celiac disease

Non-celiac wheat intolerance

Food allergy

Disaccharidase deficiency

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AGA Guidelines for IBS-D Treatment

Drug	Class	N	Dose	Side effects	Efficacy (drug vs placebo)
Eluxadoline	Mixed μ/κ agonist & δ antagonist	1617 (2 RCT)	75 /100 mg qd	Constipation, nausea, pain	27.2 vs 16.7 %, RR 0.87 (0.8-0.9)
Rifaximin	Nonabsorb. broad spectrum antibiotic	1258 (3 RCT)	550 mg tid	Nausea, URI, UTI	RR 0.85% (0.8-0.9)
Rifaximin	Antibiotic	2438/636 (1 RCT- 2 phases)	550 mg/tid	Nausea, URI, UTI, N. Pharyngitis	38% vs 31%; RR 0.9(0.8-1)
Alosetron	5 HT_3 antagonist	4227 (8 RCT)	0.5-1 mg bid	Ischem. colitis, constipation	RR 0.6 (0.5-0.67)
Loperamide	μ agonist	2883 (2 RCT)	2 or 6 mg bid	Headache, nausea, diarrhea	RR 0.4 (0.2-0.8)
Ami/Des/Imip	TCA	523 (8 RCT)	variable	Constip/ sleep/ High Withdrawal rate	RR 0.67 (0.5-0.8)
Fluox/Parox	SSRI	7 RCT	variable	Weight gain, dreams	RR 0.74(0.5-1.06)
12 drugs (Cochrane)	Antispasmodics	2983 (22 RCT)	variable	Dry mouth, dizziness, vision	RR 0.74 (0.59-0.9)

Lembo A, et al. *Gastroenterology*. 2022;163:137-151.

AGA Guidelines for IBS-D Treatment

New or updated recommendations[a]	Strength of recommendation	Certainty in evidence
1. In patients with IBS-D, the AGA suggests using eluxadoline Implementation remark: eluxadoline is contraindicated in patients without a gallbladder or those who drink more than 3 alcoholic beverages per day	Conditional	Moderate
2a. In patients with IBS-D, the AGA suggests using rifaximin	Conditional	Moderate
2b. In patients with IBS-D with initial response to rifaximin who develop recurrent symptoms, the AGA suggests retreatment with rifaximin	Conditional	Moderate
3. In patients with IBS-D, the AGA suggests using alosetron	Conditional	Moderate
4. In patients with IBS-D, the AGA suggests using loperamide	Conditional	Very low
5. In patients with IBS, the AGA suggests using TCAs	Conditional	Low
6. In patients with IBS, the AGA suggests against using SSRIs	Conditional	Low
7. In patients with IBS, the AGA suggests using antispasmodics	Conditional	Low

[a]For all recommendation statements, the comparator was no drug treatment.

Lembo A, et al. *Gastroenterology*. 2022;163:137-151.

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AGA Guidelines for Treatment of IBS-C

Drug	Class	N	Dose	Side effects	Efficacy
Tenapanor	NHE3 channel inhibitor	1372 (3 RCT)	50 mg bid	Diarrhea,	34 vs 27%, RR, 0.84 (0.79-0.94)
Plecanatide	Guanylate cyclase C (GCC) agonist	1632 (3 RCT)	3 mg daily	Diarrhea, bloating	RR, 0.87 (0.83-0.92)
Linaclotide	GCC agonist	2443 (3 RCT)	290 mcg/day	Diarrhea, bloating	RR, 0.81 (0.77-0.85)
Lubiprostone	ClC_2 blocker	1154 (3 RCT)	8 mcg bid	Nausea, diarrhea	RR, 0.88 (0.79-0.96)
Tegaserod	$5HT_4$ agonist	2883 (4 RCT)	2 or 6 mg bid	Headache, nausea, diarrhea	35 vs 24 %,RR, 0.87 (0.81-0.93)
PEG	Osmotic	139 (1 RCT)	30 g daily	Bloating, diarrhea	RR, 0.9 (0.66-1.2
Ami/Nor/Imi/ Desimipramine	TCA	523 (8 RCT)	variable	Constipation, sleep	RR,0.67 (0.54-0.82)
Parox/Citalo	SSRI	7 RCT	variable	Weight gain, dreams	RR, 0.74 (0.52-1.06
12 drugs (Cochrane)	Antispasmodics	2983 (22 RCT)	variable	Dry mouth	RR, 0.67 (0.55-0.80)

Chang L, et al. *Gastroenterology*. 2022;163(1):118-136.

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AGA Guidelines for Treatment of IBS-C

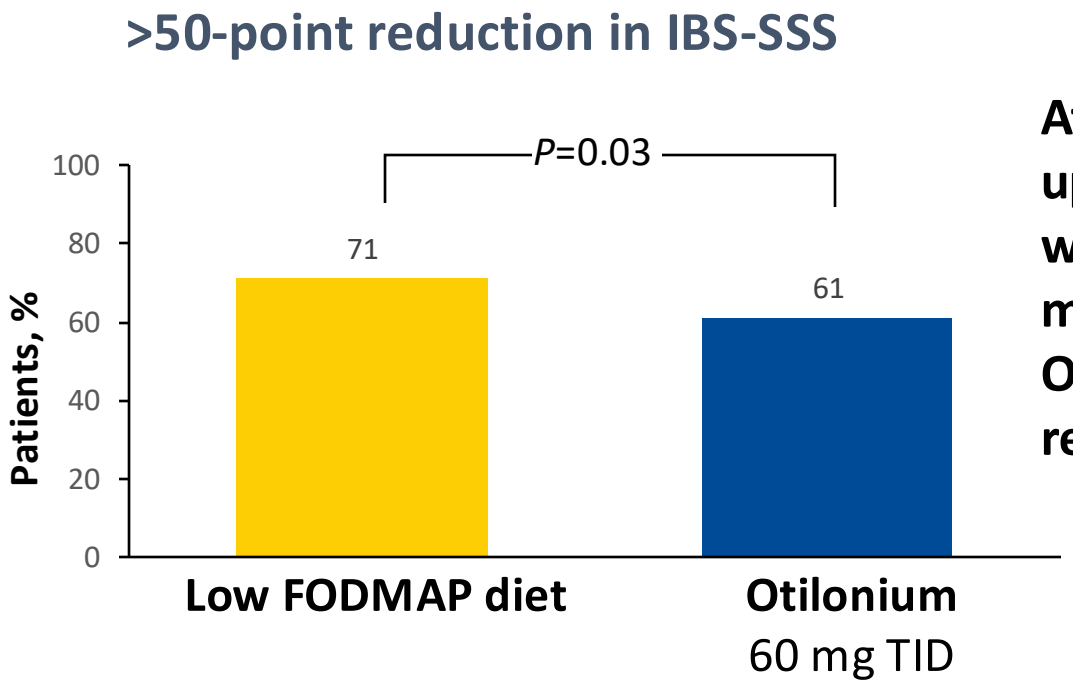
New or updated recommendations[a]	Strength of recommendation	Certainty of evidence
1. In patients with IBS-C, the AGA suggests using tenapanor	Conditional	Moderate
2. In patients with IBS-C, the AGA suggests using plecanatide	Conditional	Moderate
3. In patients with IBS-C, the AGA recommends using linaclotide	Strong	High
4. In patients with IBS-C, the AGA suggests using tegaserod Implementation remark: Tegaserod was reapproved for women under the age of 65 years without a history of cardiovascular ischemic events (such as myocardial infarction, stroke, TIA, or angina)	Conditional	Moderate
5. In patients with IBS-C, the AGA suggests using lubiprostone	Conditional	Moderate
6. In patients with IBS-C, the AGA suggests using PEG laxatives	Conditional	Low
7. In patients with IBS, the AGA suggests using TCAs	Conditional	Low
8. In patients with IBS, the AGA suggests against using SSRIs	Conditional	Low
9. In patients with IBS, the AGA suggests using antispasmodics	Conditional	Low

[a]For all recommendation statements, the comparator was no drug treatment.

Chang L, et al. *Gastroenterology*. 2022;163(1):118-136.

Diet or Medication for IBS: Domino Study

69 GPs from Europe and Australia recruited 459 IBS patients (76% F) who were randomized to Otilonium bromide (40 mg tid) or a low FODMAP diet (LFD) delivered using a smart phone app x 8 weeks



At 6 months follow-up, the LFD Group was significantly more likely than the OB Group to still be responders

Take-home point

App-based LFD should be considered a first-line treatment choice for primary care IBS

Carbone F, et al. *Gut*. 2022;71:2226-2232.

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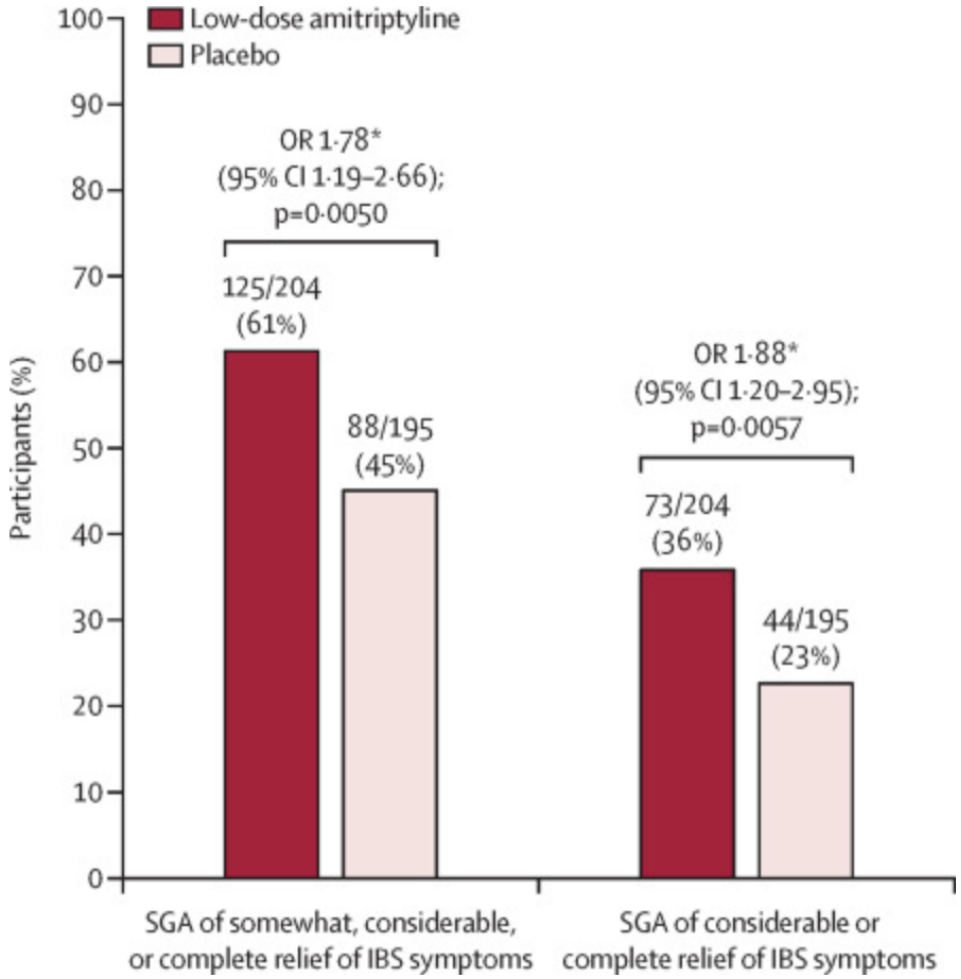
Amitriptyline for IBS in Primary care (ATLANTIS Trial): 463 patients;Amitriptyline (232 pts),10-30 mg/day



Ford AC, et al. *Lancet*. 2023;402(10414):1773-1785.

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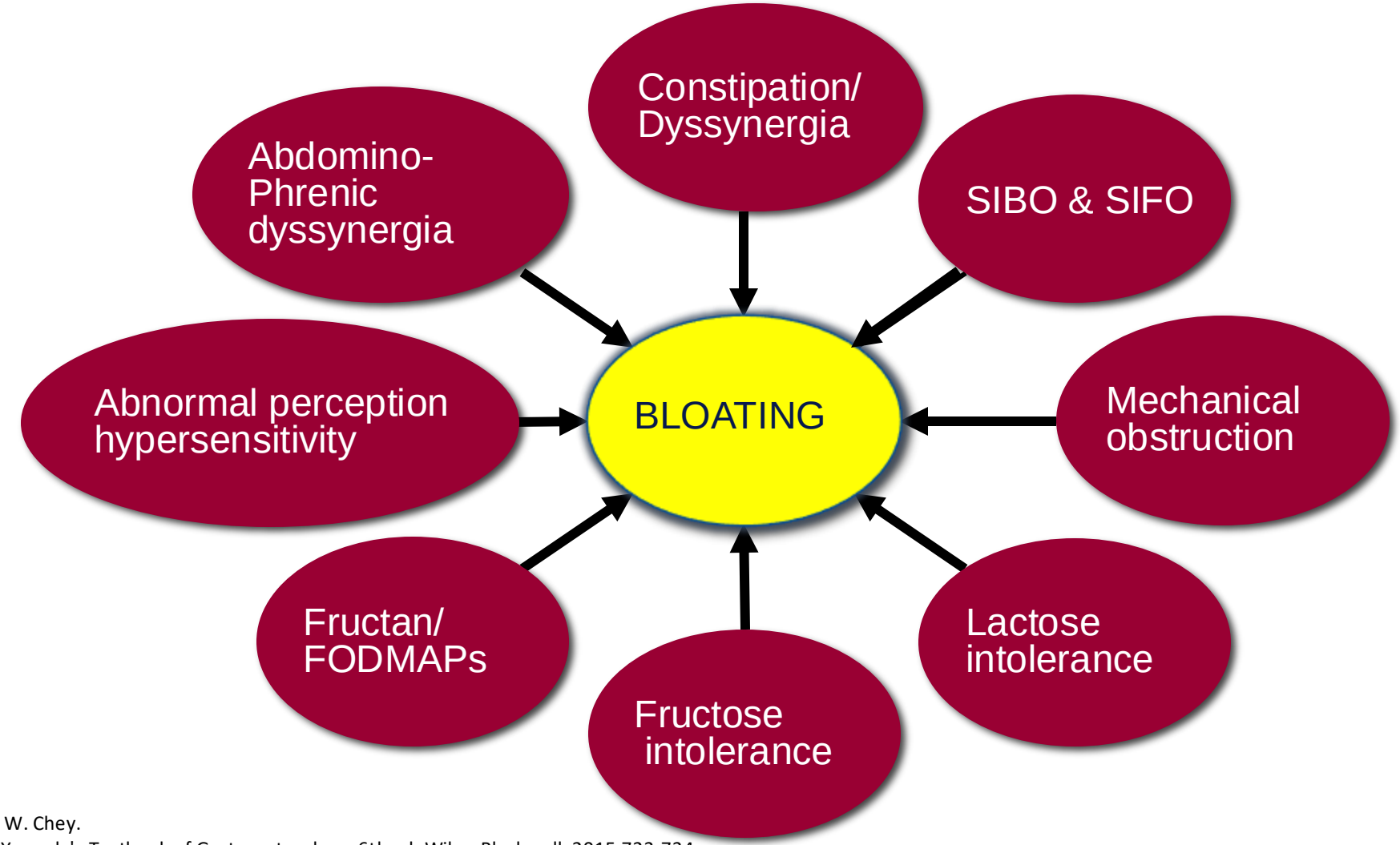
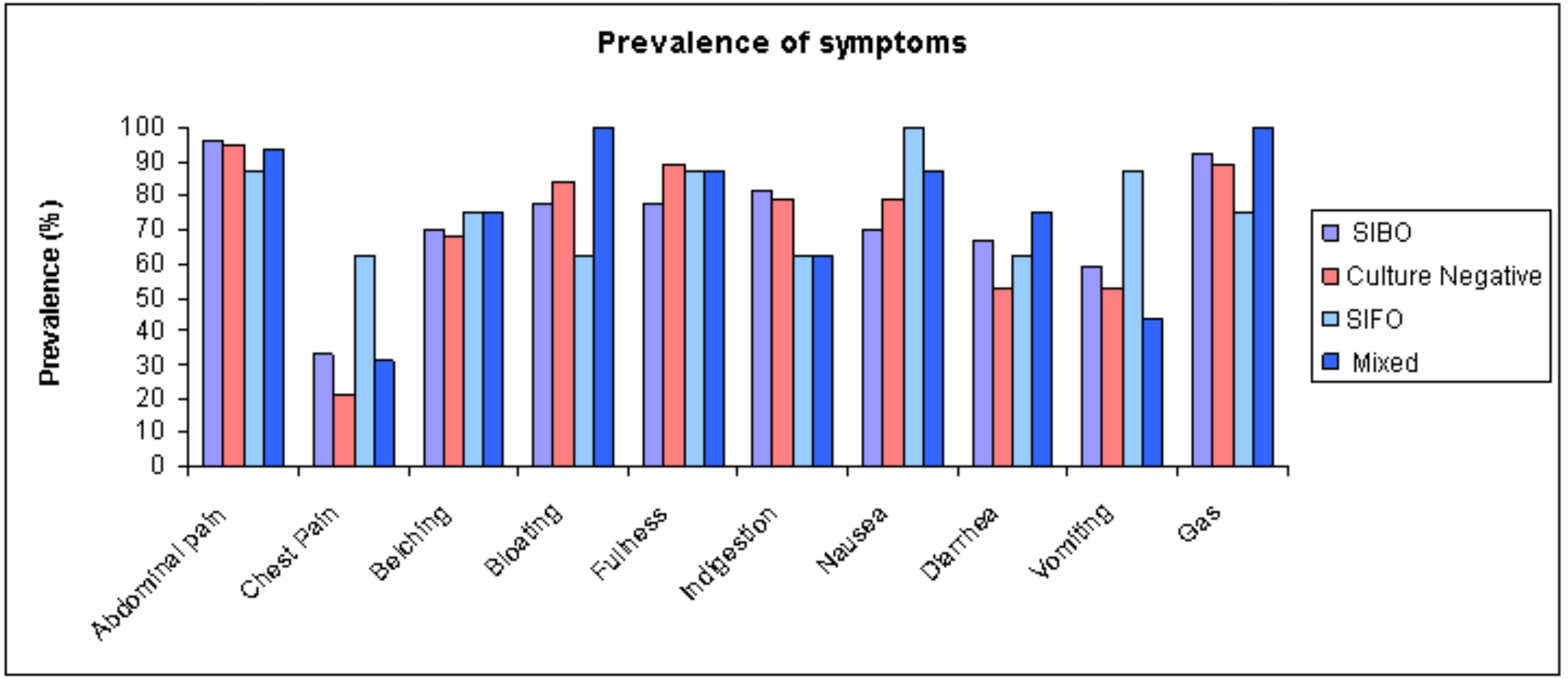
Causes of Bloating



Courtesy of Dr W. Chey.

Rao SSC, et al. Yamada's Textbook of Gastroenterology. 6th ed. Wiley-Blackwell; 2015:723-734.

Can Symptoms Identify SIBO or SIFO? (n=124)



SIBO = Small Intestinal Bacterial Overgrowth; SIFO = Small Intestinal Fungal Overgrowth.

Jacobs C, et al. *Aliment Pharmacol Ther*. 2013;37(11):1103-1111.

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How to Investigate Gas & Bloating?

Empirical

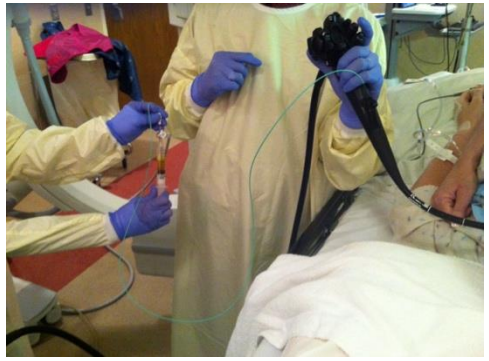
- Detailed History
- Symptom response after empirical antibiotic trial
- Symptom response after CHO exclusion/Low FODMAP diet
- Stool Tests

Evidence-Based

- Breath Tests
  - Glucose/Lactulose Breath Test
  - Fructose/Lactose/Sucrose/Fructan Breath Test
- Duodenal/Jejunal Aspirate/Culture
- Disaccharidase Enzyme assay

Newer

- Newer modalities
  - SCBDS capsule
  - Gas sensing capsule
  - Confocal Microscopy after food challenge



Rao SSC, et al. *Clin Transl Gastroenterol.* 2019;10(10):e00078; Rao SSC, et al. *Practical Gastroenterology*. 2024;48:38-46; Kemple B, Rao SS. *Clin Transl Gastroenterol.* Published online January 10, 2025; In Press: Lee N, et al. *Neurogastroenterol Motil.* 2025; Sonu I, et al. *Curr Gastroenterol Rep*. 2024;26(6):157-165.

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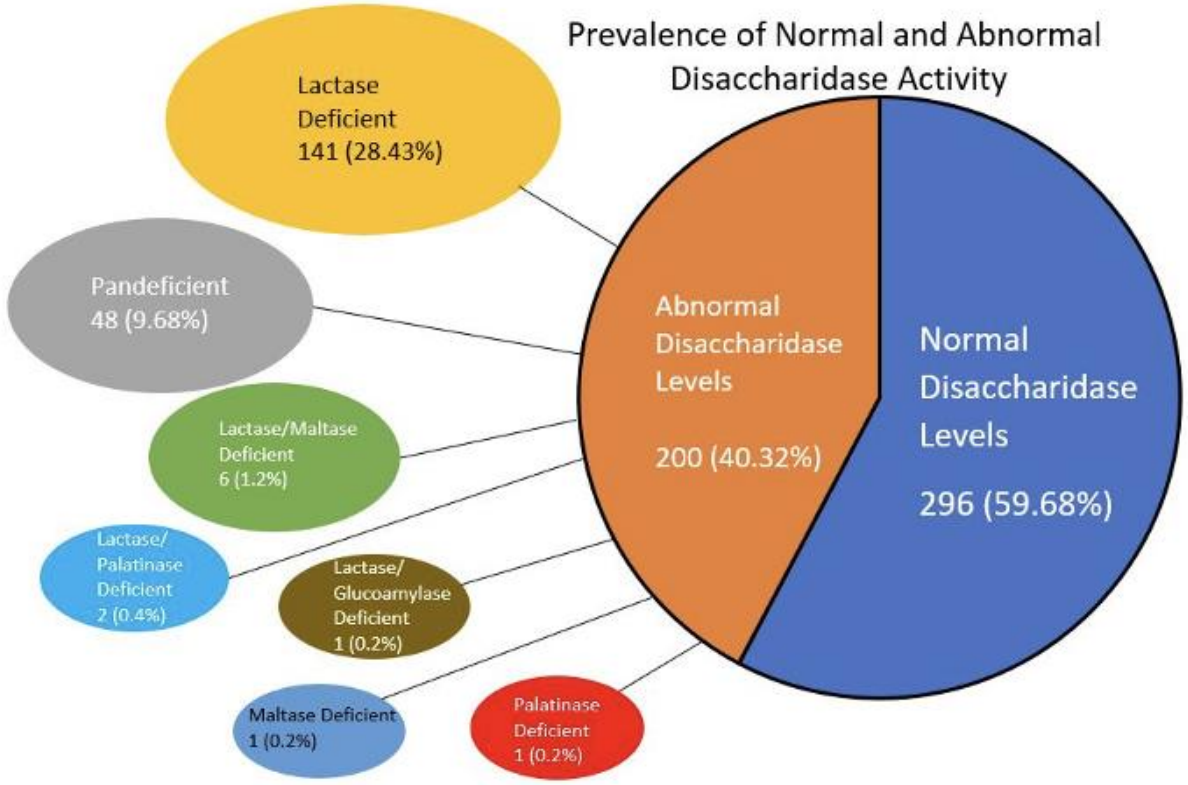
Intestinal Disaccharidases Deficiency in Adults: Prevalence, n=496



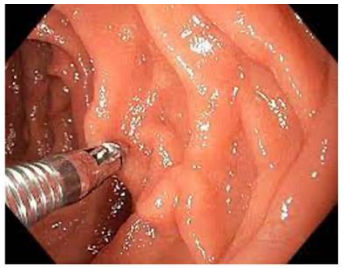


Image 1A

Kemple B, Rao SS. *Clin Transl Gastroenterol*. Published online January 10, 2025.

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Treatment of SIBO- ACG guidelines

Antibiotic	Recommended Dose	Efficacy
Rifaximin	550 mg tid	61-78%
Amoxicillin-Clavulanic acid	875 mg bid	50%
Ciprofloxacin	500 mg bid	43-100%
Doxycycline	100 mg qd-bid	-
Metronidazole	250 mg tid	43-87%
Neomycin	500 mg bid	33-55%
Norfloxacin	400 mg qd	30-100%
Tetracycline	250 mg qid	87.5%
Trimethoprim-Sulfamethoxazole.DS	160/800 mg bid	95%

Pimentel M, et al. *Am J Gastroenterol.* 2020;115:165-178

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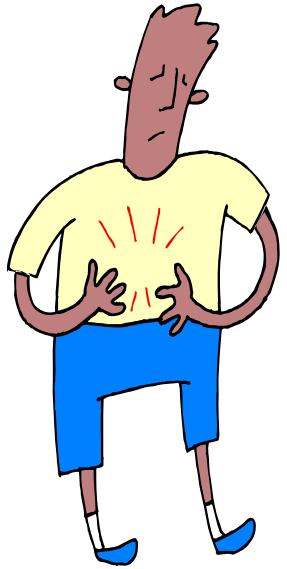
IBS: Take Home Points

- Make a Positive Diagnosis: Physician-patient communication is key
- Abdominal Pain, Visceral hypersensitivity are Key features
- All Bloating & Gas is not IBS
- Not essential to give a diagnosis at first visit
- Evaluate for Alarming features and treat symptomatically
- Specific Management: Tailor therapy to specific symptoms
  - IBS-D: Rifaximin, Eluxodoline, Alosetron, Amitriptyline
  - IBS-C: Linaclotide, Plecanatide, Lubiprostone, Tenapanor
  - Pain: Peppermint oil, antispasmodics, TCAs, SNRI
  - Psychological Therapies: CBT, Home CBT, Hypnosis
  - Bloating/Gas: CHO deficiency- Enzymes or Diet exclusion (specific CHO)
    - SIBO (Antibiotics), SIFO (Antifungals)



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So You Want to be a Gastroenterologist?

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Question #1

- How many of you are medical students?
- How many of you are interns/residents?
- How many of you are GI Fellows?
  - -1st year
  - -2nd year
  - -3rd year
  - -4th year
  - -5th year or more (ARE YOU KIDDING ME?)

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Question #2

- What will you need to do to become a Gastroenterologist?

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Answer

You will need a

J

O

B

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Yes That's Right

A JOB!!!

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Getting The Job – 5 Steps

1. Know thyself and what you want
2. Narrow the field
3. Pre-visit planning
4. Visit and Interview
5. Post-visit due diligence

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Choosing your JOB

How will you make a choice

1- ?

2- ?

3- ?

4- ?

5- ?

ETC., ETC.,ETC…….

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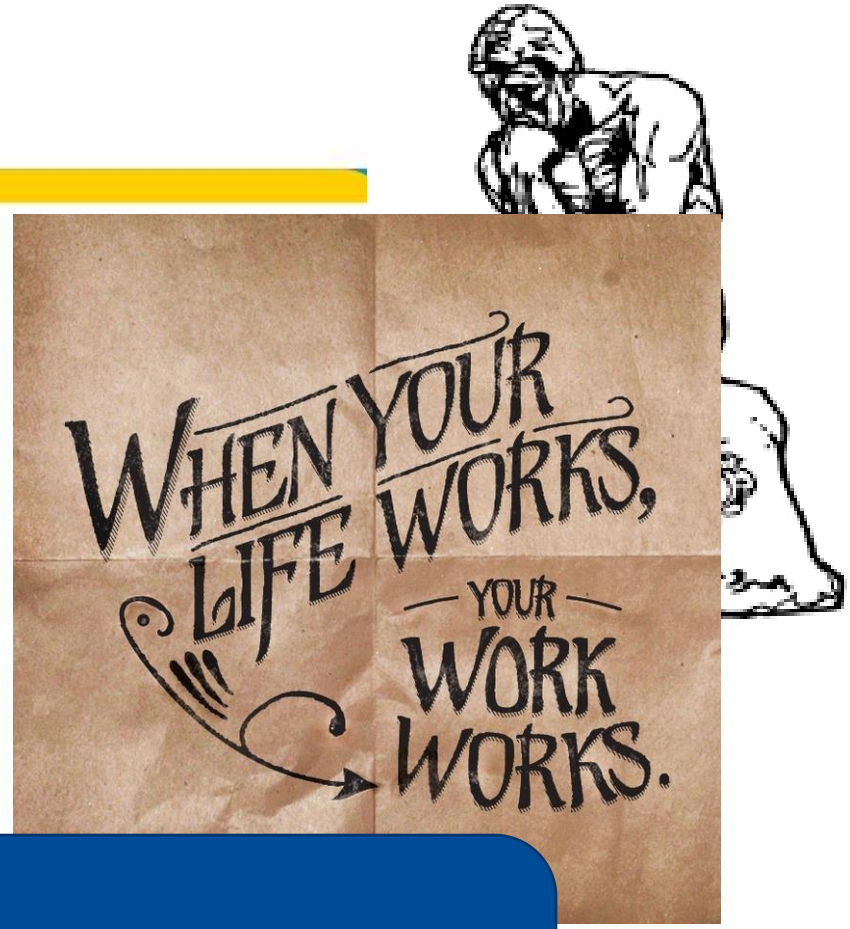
Know Thyself

- Where do you want to do it?
- What are your family's needs?
- What do you want to be doing?



What is most important if you cannot have it all?

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Know Thyself

- What do you want to be doing?
- Where do you want to do it?
- What are your family's needs?

- What practice type/setting appeals to you?
  - Academia vs non-academic
  - Large group vs small group, rural vs urban, hospital based or not
  - Interventional endoscopy vs general GI vs other

When You Know What You Want, Narrow The Field

- Co-workers, faculty, prior fellows
- Word of mouth, social media, LinkedIn, etc
- National and regional GI meetings
- ASGE, ACG, AGA, AASLD websites & journals
- Recruiting firms (?)
- BEST PLACE TO START IS….?

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When You Know What You Want, Narrow The Field

- Reviews
- Physician profiles (age, age range, training, experience, expertise, APPs
- Web site
- Services (Endo centers, path, anesthesia, infusion, etc)
- Hospitals

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The Visit

- Contact targets- set up interviews. Start early!!
- What to look for (Indirect and direct clues)
- Come with questions (First date vs Second date)

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When You Visit

- Multi-task: you are performer AND audience
  - Observe behaviors of physicians and staff
  - Have conversations with MDs (old and young), APPs, nurses, administrators, practice staff, hospital staff, community physicians, everyone
  - Pose same question to different people - Do you get consistent answers?
- Is the visit organized? Is their an agenda? Is there a schedule time in a social setting(dinner)?
- In the end: do the “personalities” match?

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Post-Visit Due Diligence

- Weighing pros & cons
  - Write a ‘thank you’ note either way
- When negotiating an employment contract remember

1-they want you and you want them

2-don’t take the negotiations personally

3-keep your eye on the ball.

- Consult an attorney!
  - Experience in health care and employment law (state-specific issues!)
  - Do not sign anything without prior legal review!

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Stephen Covey's 7 Habits of Highly Successful People

1- Be Proactive (Take initiative, Take responsibility for your life)

2- Begin with end in mind

3- Put first things first

4- Think win/win

5- Seek to understand first then be understood (Be a good listener and learner)

6- Synergize (Networking and cooperation)

7- Sharpen the saw (Continue to learn and improve)

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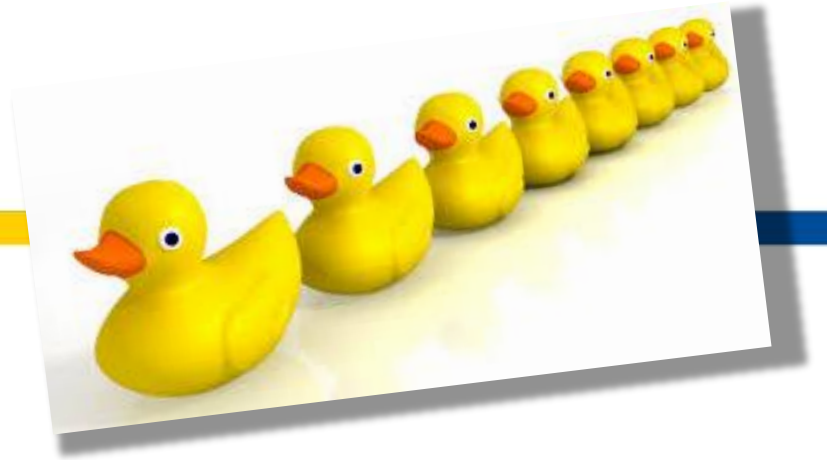
"We're looking for someone with the wisdom of a 50-year-old, the experience of a 40-year-old, the drive of a 30-year-old and the pay scale of a 20-year-old."

3. Pre-Visit Planning



- What type of practice are you visiting?
  - Have a general understanding of that practice setting
- Collect information on the target practice
  - …via practice website, personal contacts, consider a phone call
  - Group size? Physician ages? Leadership? Ownership?
  - Competitive environment?
- What questions are you planning to ask?
  - Write them down and take them with you

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Questions to Explore

- Understand PEOPLE, STRUCTURE, ENVIRONMENT
  - What motivates members of the group?
  - What do they like and dislike about the group? What needs to change?
  - Who owns what? (ASC, path, anesthesia, infusion, etc.)
  - Hospital partners? Competitors? Payer mix (Medicare vs Commercial)

Questions to Explore

- Understand PEOPLE, STRUCTURE, ENVIRONMENT
  - What motivates members of the group?
  - What do they like and dislike about the group? What needs to change?
  - Who owns what? (ASC, path, anesthesia, infusion, etc.)
  - Hospital partners? Competitors? Payer mix (Medicare vs Commercial)
- How do YOU fit in?
  - Why is the practice hiring? What is their overall strategic plan?
  - What do they expect of you? How will you get referrals to build your practice?
  - Path to partnership/career advancement? Who decides, when, and how?
  - Compensation? Call schedule? – The nitty gritty

Things To Do Now (Before the End of Fellowship)

- Close gaps in your procedural training
  - Decompressions, dilations, foreign bodies, Minnesota tubes
  - Think “emergencies, on-call situations”
- Get up to speed
  - 30-minute procedure slots are common
- **Build your network!**
  - Contact infos from attendings and peers
  - Get involved with ASGE and other professional societies

Case Studies in Esophageal Disorders

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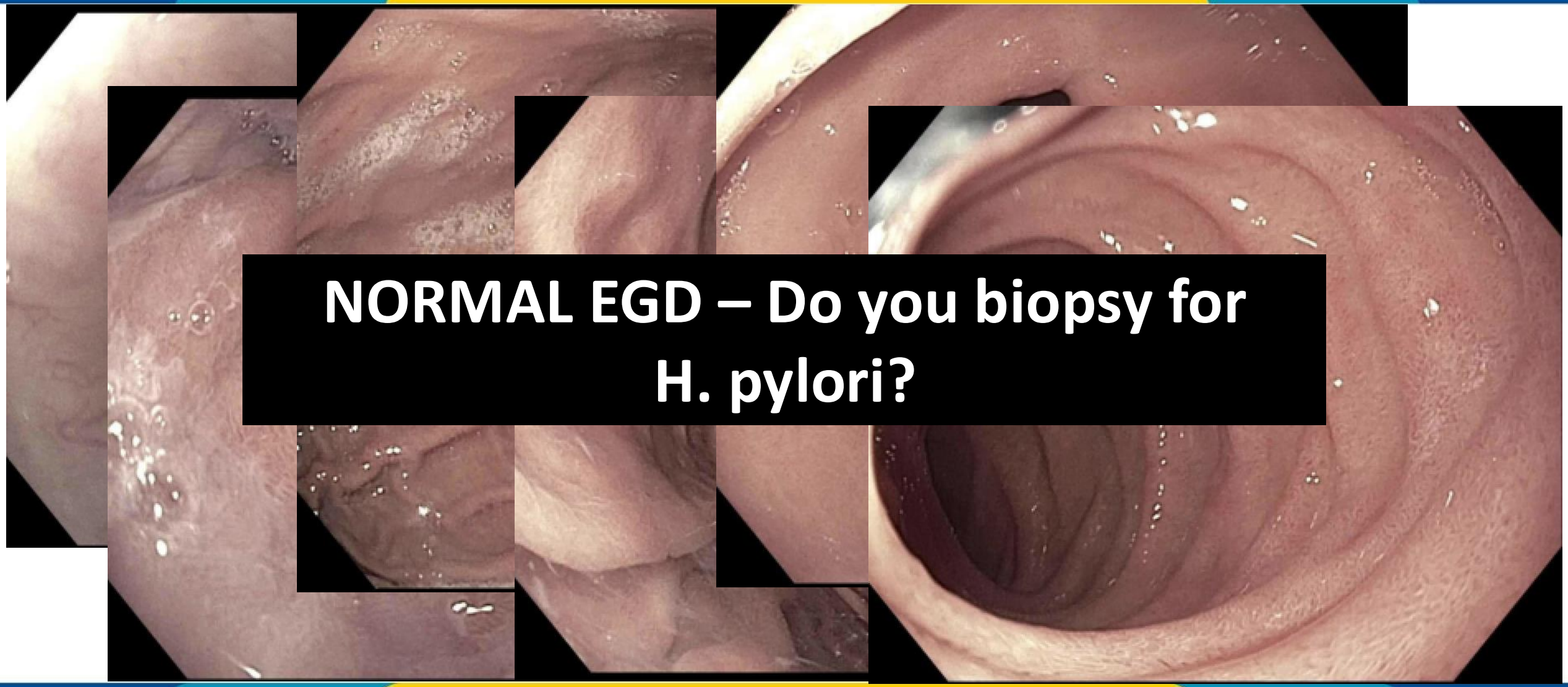
Case

A 50-year-old Chinese gentleman with HTN presented for an EGD after complaining of bloating.

- Abdominal bloating has been going on for 6 months, worse by the end of the night.
- Denies increased belching or flatulence.
- Denies early satiety, weight loss, nausea, changes in bowel habits, and heart burn symptoms.
- FHx: Father with “stomach cancer” (estranged)

EGD



Gastric biopsy -> H. Pylori +

What would the experts recommend in treating this patient?

Additional information:

- Born and raised in Saint Louis, Missouri
- No known allergies
- No prior antibiotic exposure

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Follow-up

- Bismuth quadruple therapy was prescribed
  - Tetracycline was too expensive and doxycycline was taken as substitute
  - GI discomfort/food tasted badly with metronidazole so he skipped some doses

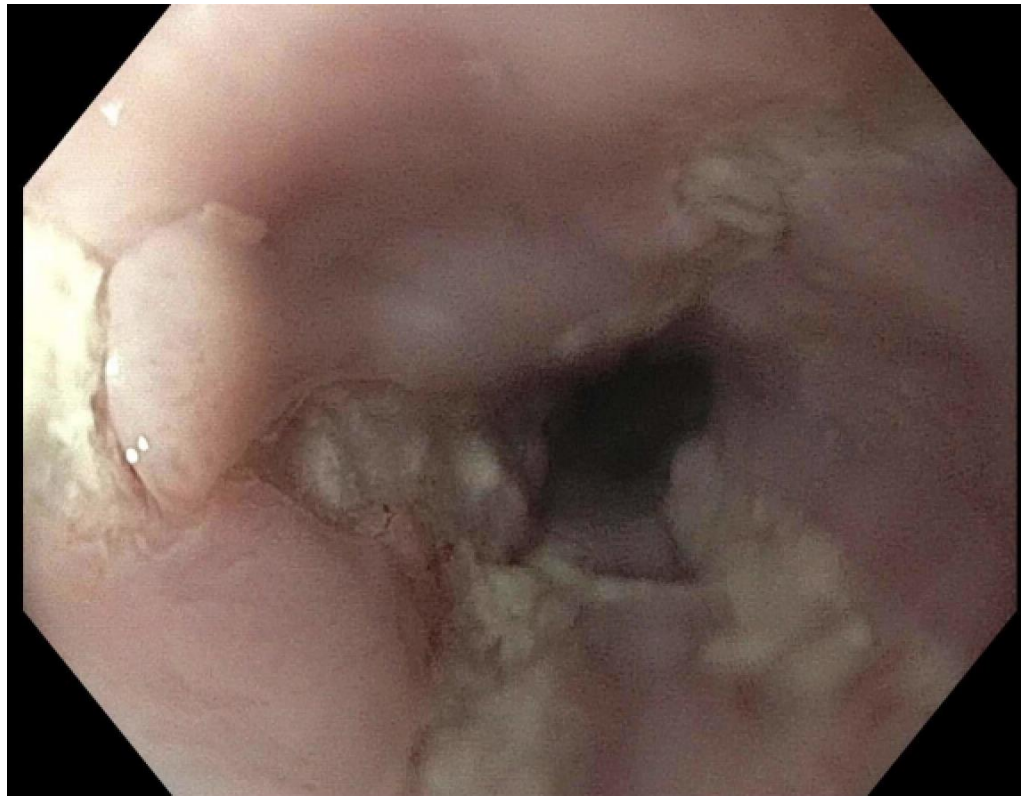
- H. pylori Breath Test - positive

What would be the next steps in treatment?

If adherent to medications and unable to eradicate in the future, at what point would antibiotic susceptibility testing be warranted?

Case

- A 75-year-old woman follows up in your clinic to discuss her long-standing heart burn.
- Last year, she underwent an EGD for her symptoms and found to have LA Grade D esophagitis.
  - She started Omeprazole 20mg BID and repeat EGD after 3 months showed resolved inflammation.
  - She continued Omeprazole 20mg daily for symptom control



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History

- Past medical History
  - Diabetes – Metformin, Glipizide
  - Hypertension – Enalapril
  - Osteopenia – Calcium/Vit. D
  - Chronic kidney disease, Stage 2
- She lives in a nursing facility.
- Her nephrologist recommended stopping PPI

Data?

What are the data behind long-term PPI use and its side effects?

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Continued concern

- She was still very concerned about PPI use and kidney disease, so she stopped the medication.
- However, her reflux worsened and her nephrologist recommended famotidine twice daily.
- Symptoms persisted after 1 month and she returns to you to discuss alternatives.

Is a PCAB an option for her?

What is the safety profile of long-term use of PCABs?

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Questions & Answers

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Break

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Future of AI in Gastroenterology

Austin L Chiang, MD MPH
Chief Medical Officer, Medtronic Endoscopy

2025

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Disclosures

- Medtronic (employment)

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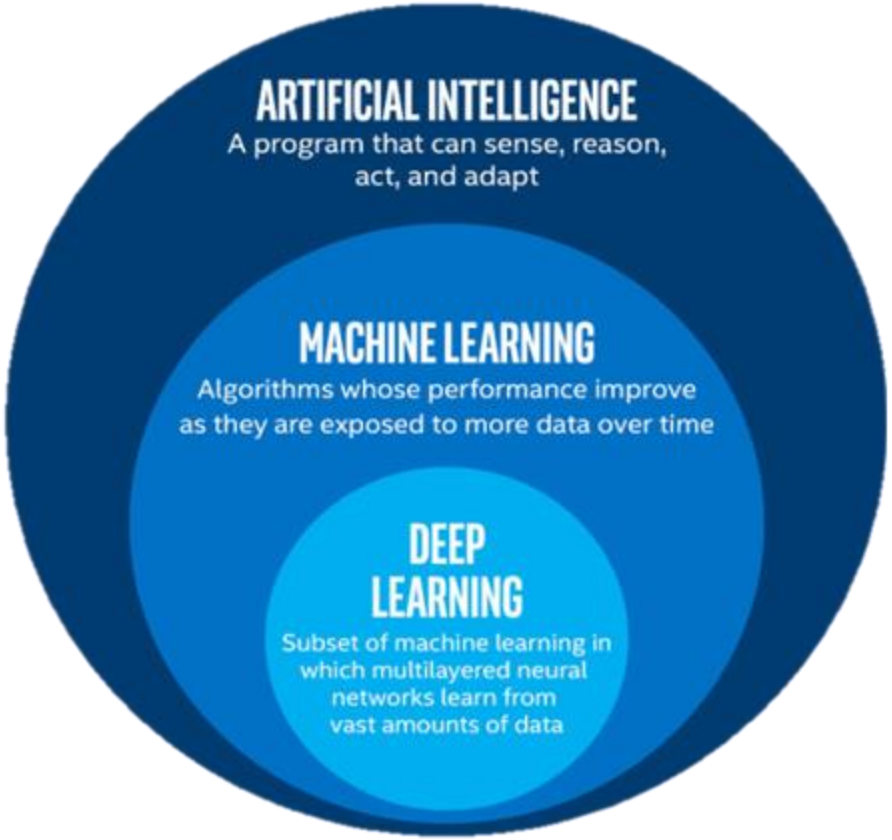
Agenda

- Understanding AI
- Current landscape
- Future of AI in GI



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AI Affects Us Everyday

- Content moderation
- Email filtering
- Fraud detection
- Language translation
- SEO
- Navigation
- Face recognition
- Voice assistants

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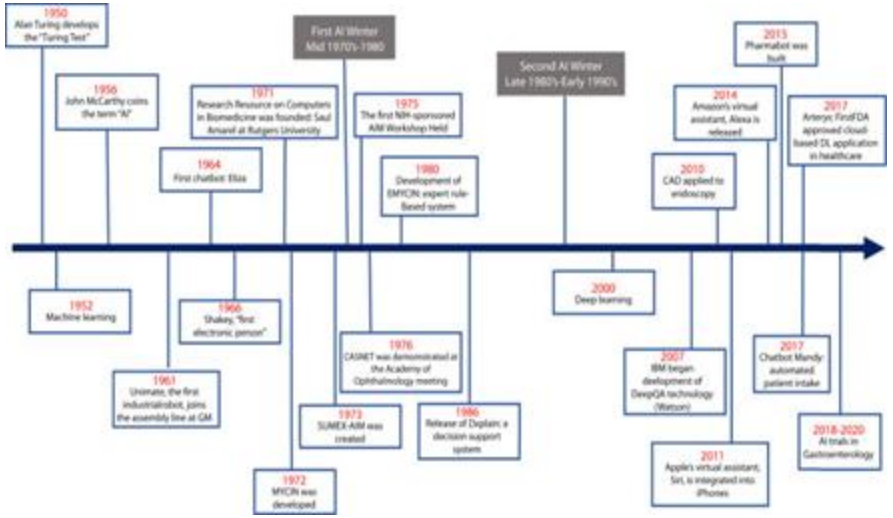
AI in GI Has a Long History, but We're Just Getting Started

- 2019 – Global AI in GI and Endoscopy Summit
- 2020 – ASGE AI Task Force Position Statement on priorities
- 2021 – 1st FDA cleared CADe system for colonoscopy
- 2021 – MRI analysis of intestinal motility FDA cleared
- 2024 – CT detection of hepatic steatosis FDA cleared
- 2024 – ASGE announces AI Institute



Kaul V, et al. *Gastrointest Endosc*. 2020;92:807-812.

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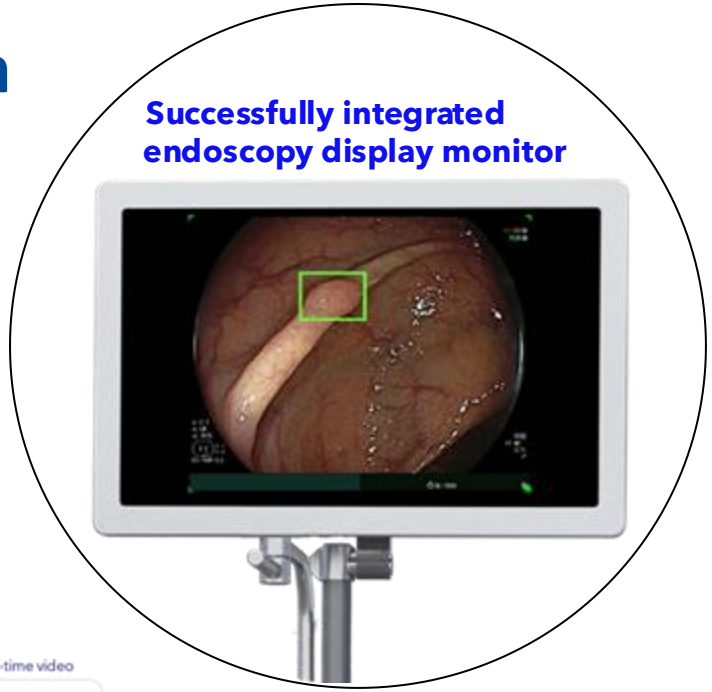
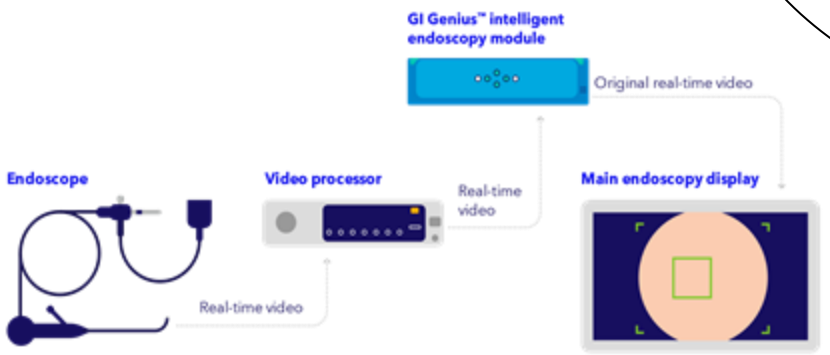
GI Genius™

Seamless integration into your existing workflow





- No data acquired
- No PHI acquired
- Doesn't learn in real-time

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AI Improves Polyp Detection and Reduces Missed Polyps

- Pivotal trial (2020)
  - 685 subjects (1:1 randomization)
  - **54.8% with AI** vs 40.4% control
  - No change in withdrawal time
  - No differences by morphology or location

- Adenoma miss rate (2022)
  - **15.5% with AI** vs. 32.4%
  - False neg: **6.8% with AI** vs 29.6%

AI Improves Polyp Detection and Reduces Missed Polyps

- Markov model q10yr starting age 50 until 80, 60% screening uptake
- CRC incidence **44.2% with AI** vs 48.9% without AI
- CRC mortality RR redux **52.3% with AI** vs 48.7% without AI
- Cost per screened: $3343 with AI vs $3400
- 7194 CRC cases, 2089 deaths prevented = $290M annual savings

Cost-effectiveness of artificial intelligence for screening colonoscopy: a modelling study

Miguel Areia, Yuichi Mori*, Loredana Correale, Alessandro Repici, Michael Bretthauer, Prateek Sharma, Filipe Taveira, Marco Spadaccini, Giulio Antonelli, Alanna Ebigbo, Shin-ei Kudo, Julia Arribas, Ishita Barua, Michal F Kaminski, Helmut Messmann, Douglas K Rex, Mário Dinis-Ribeiro*, Cesare Hassan**

Areia M, et al. *Lancet Digital Health* 2021. https://doi.org/10.1016/S2589-7500(22)00042-5

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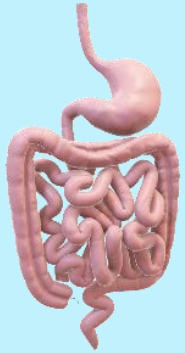
Where This Can Go



More disease states

More applications within disease states, existing tech

More breadth along care continuum

Enable other technologies

Hardware and software improvements

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Challenges and Limitations

Innovation challenges

Ethical/legal

Adoption

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The Role You Play

- Be a clinical champion
- It’s still early to be a leader
- Advocacy within societies
- Advocacy externally
- Adapting with dynamic environment

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Thank You

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The Future of AI in GI

Brennan Spiegel, MD MSHS
Cedars-Sinai

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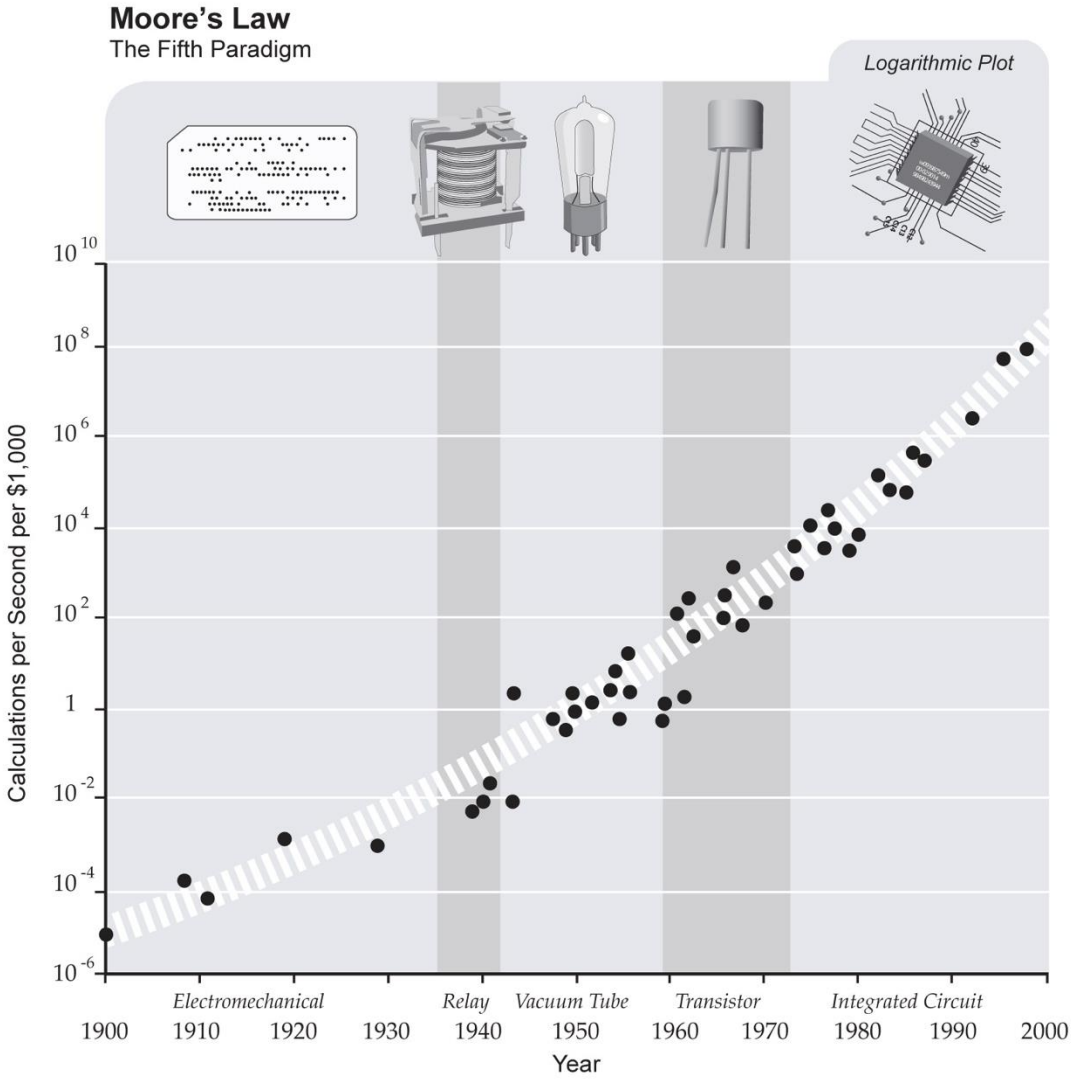
Moore’s Law

> The number of transistors on a chip will double approximately every two years

Gordon Moore, Co-Founder
Intel Corporation, 1965



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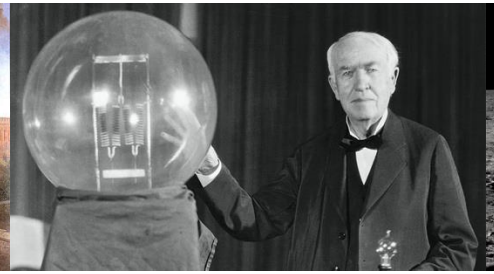
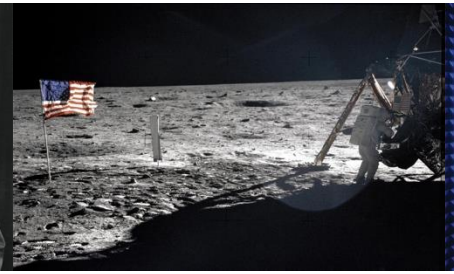
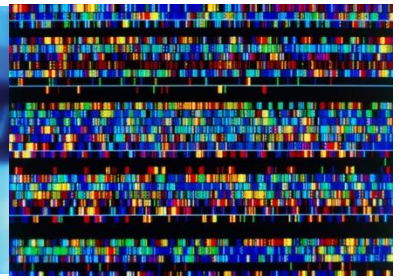
Exponential Growth of Technological Breakthroughs

Agricultural Revolution → (8,000 years) → Industrial Revolution → (120 years) → Lightbulb → (90 years) → Moon Landing → (22 years) → Internet → (9 years) → Human Genome Sequenced



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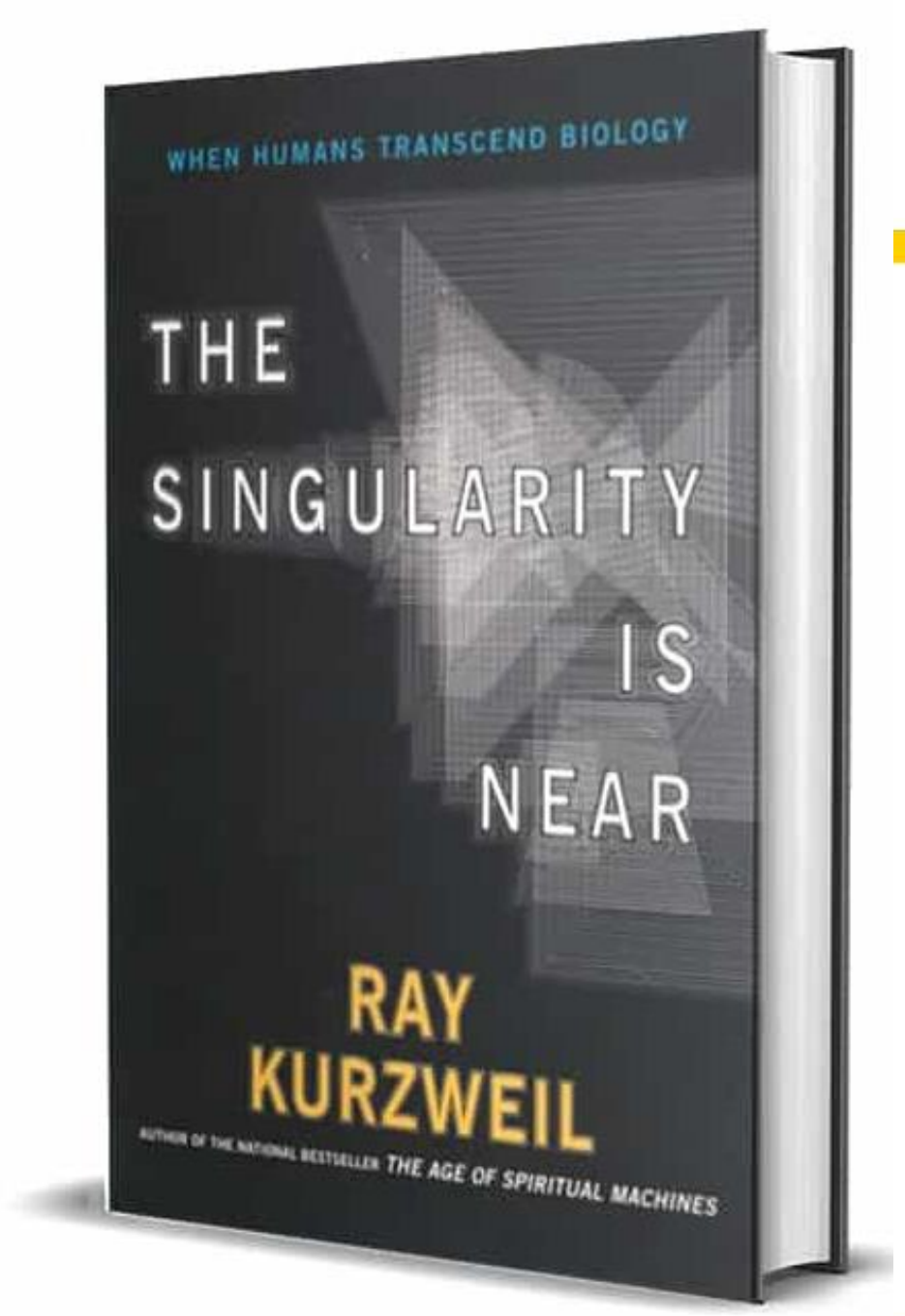
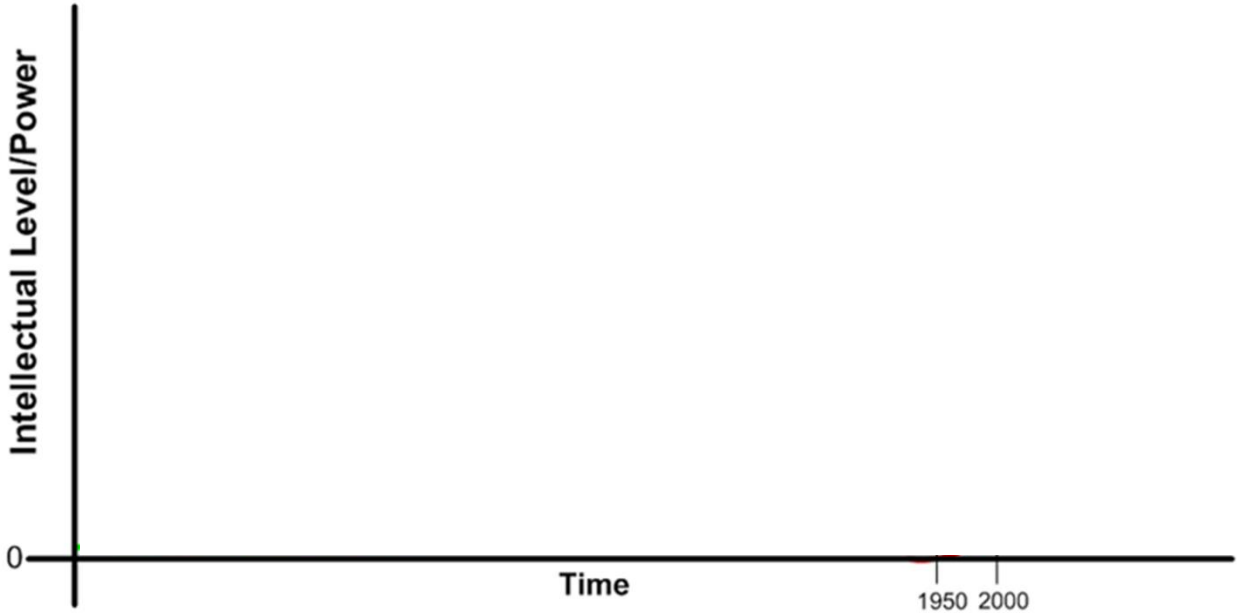
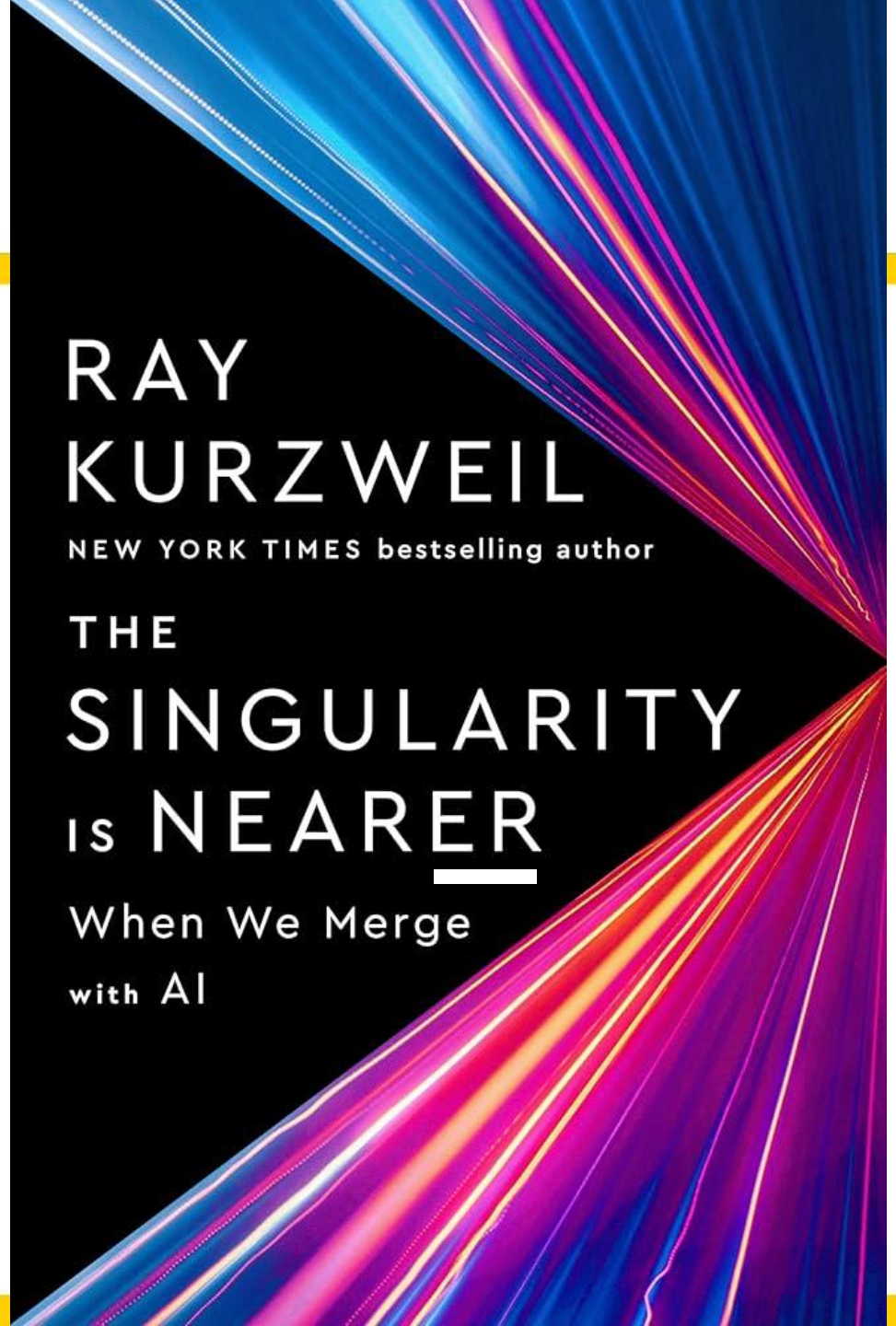
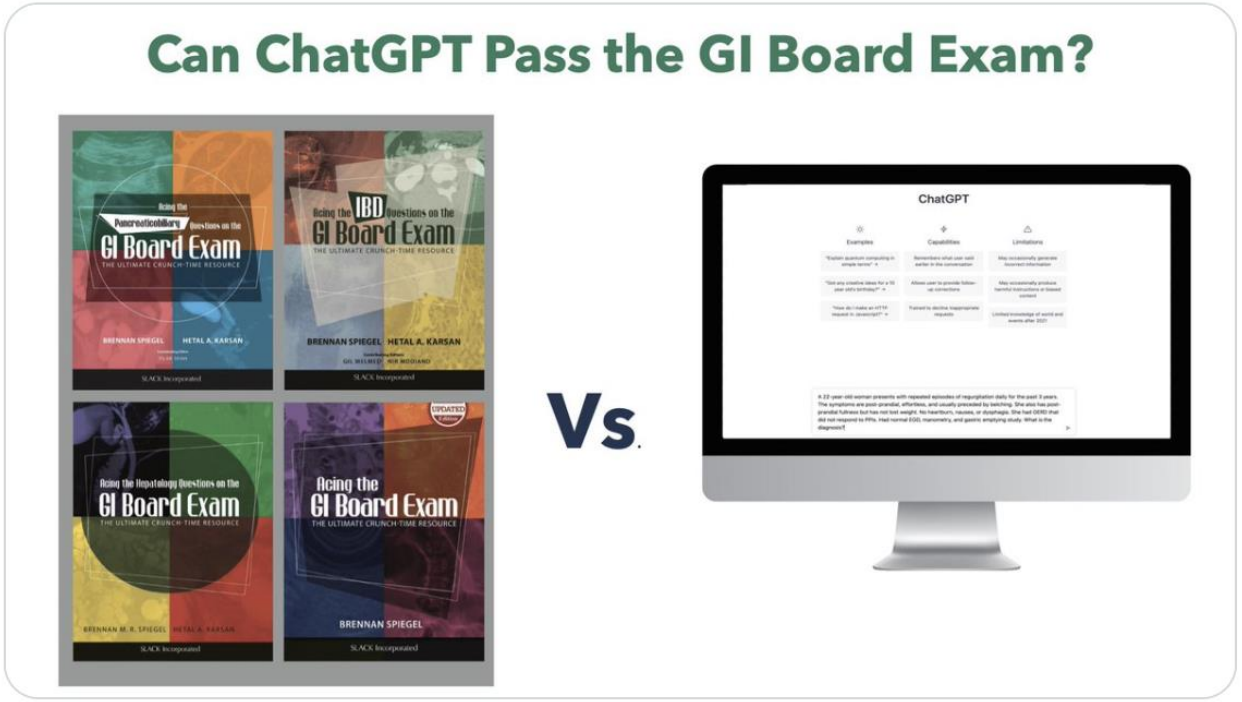






Brennan Spiegel, MD, MSHS
@BrennanSpiegel

Can #AI pass a medical board exam? I administered a 16-question exam to #ChatGTP based on my GI board review books. The computer answered confidently. How did it do? Well...the responses are both fascinating and troubling. Watch: youtube.com/watch?v=BQsYWl... #GITwitter #MedTwitter

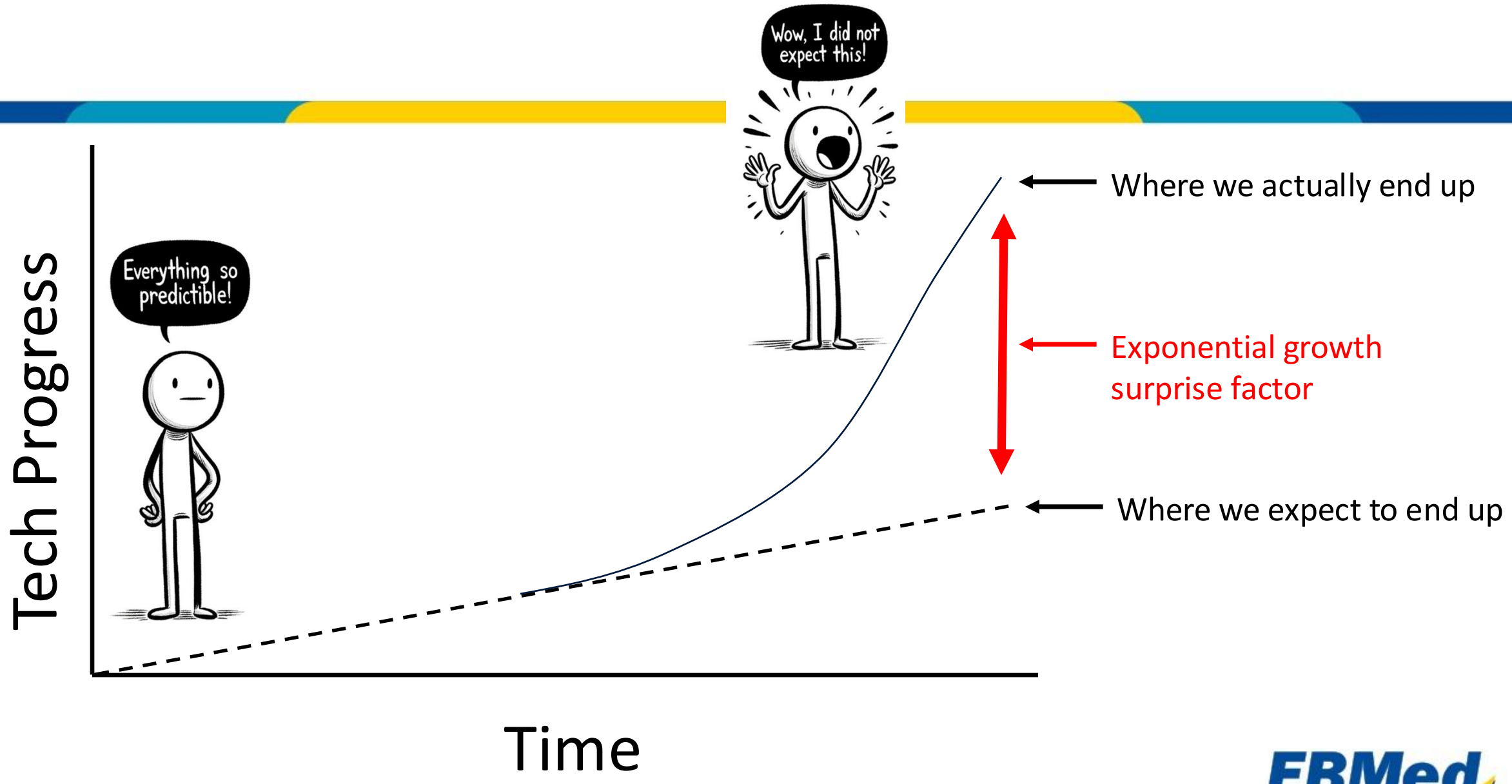


11:17 AM · Dec 11, 2022

Brennan Spiegel, MD, MSHS
@BrennanSpiegel

I subjected the #ChatGPT to a 16-question GI board exam and it scored ~35% correct. Watch here: youtube.com/watch?v=BQsYWl.... So, today I asked #AI to draw an oil painting of itself struggling through a medical board exam, and it drew this depiction of itself taking the test:

12:04 PM · Dec 15, 2022 · **7,449** Views



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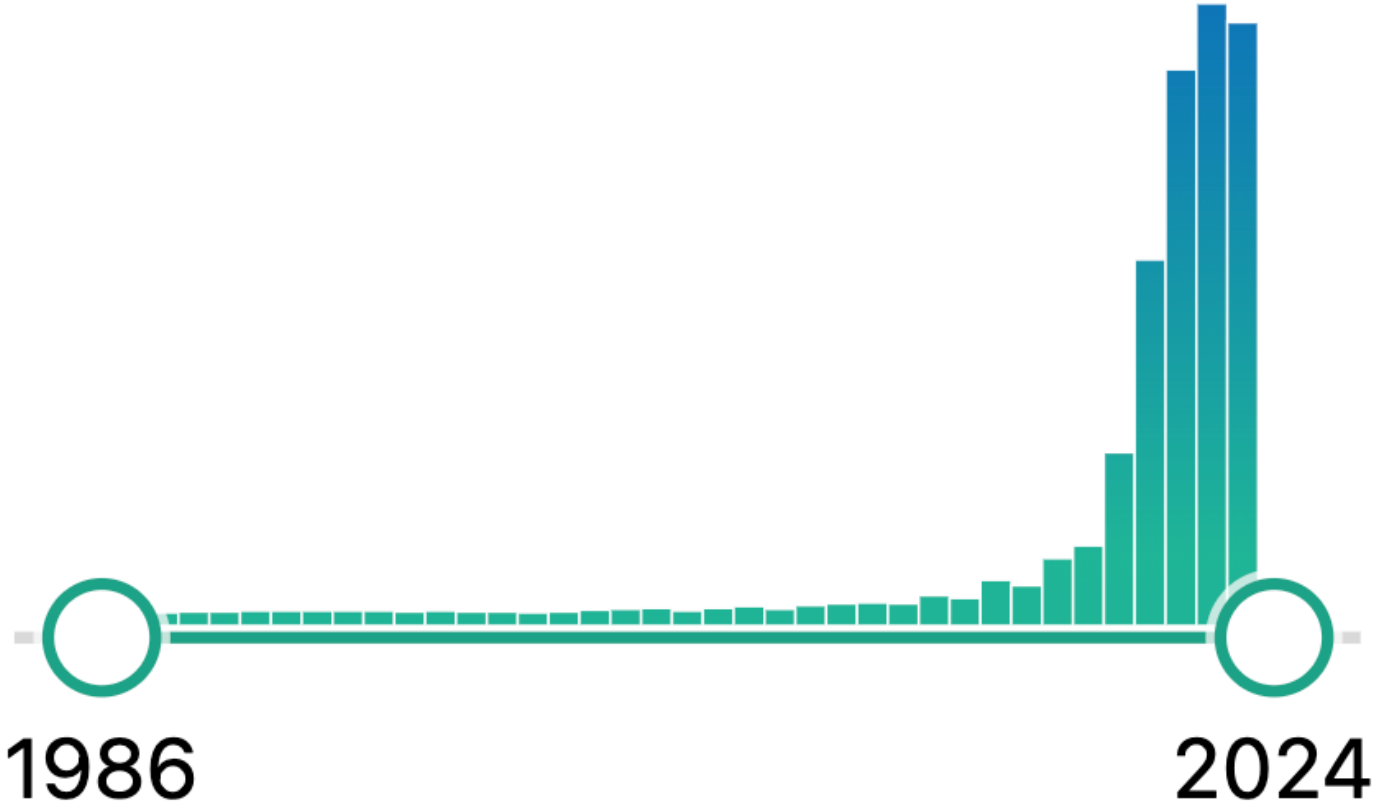
Annual Mentions of “Artificial Intelligence” Together with “Gastroenterology” on PubMed: Jan ‘85 Through Dec ‘23



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Deep Learning Localizes and Identifies Polyps in Real Time With 96% Accuracy in Screening Colonoscopy

Gregor Urban,[1,2] Priyam Tripathi,[4] Talal Alkayali,[4,5] Mohit Mittal,[4] Farid Jalali,[4,5] William Karnes,[4,5] and Pierre Baldi[1,2,3]

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

The benefit of colonoscopy for colorectal cancer prevention depends on the adenoma detection rate (ADR). New strategies are needed to increase the ADR during colonoscopy.

NEW FINDINGS

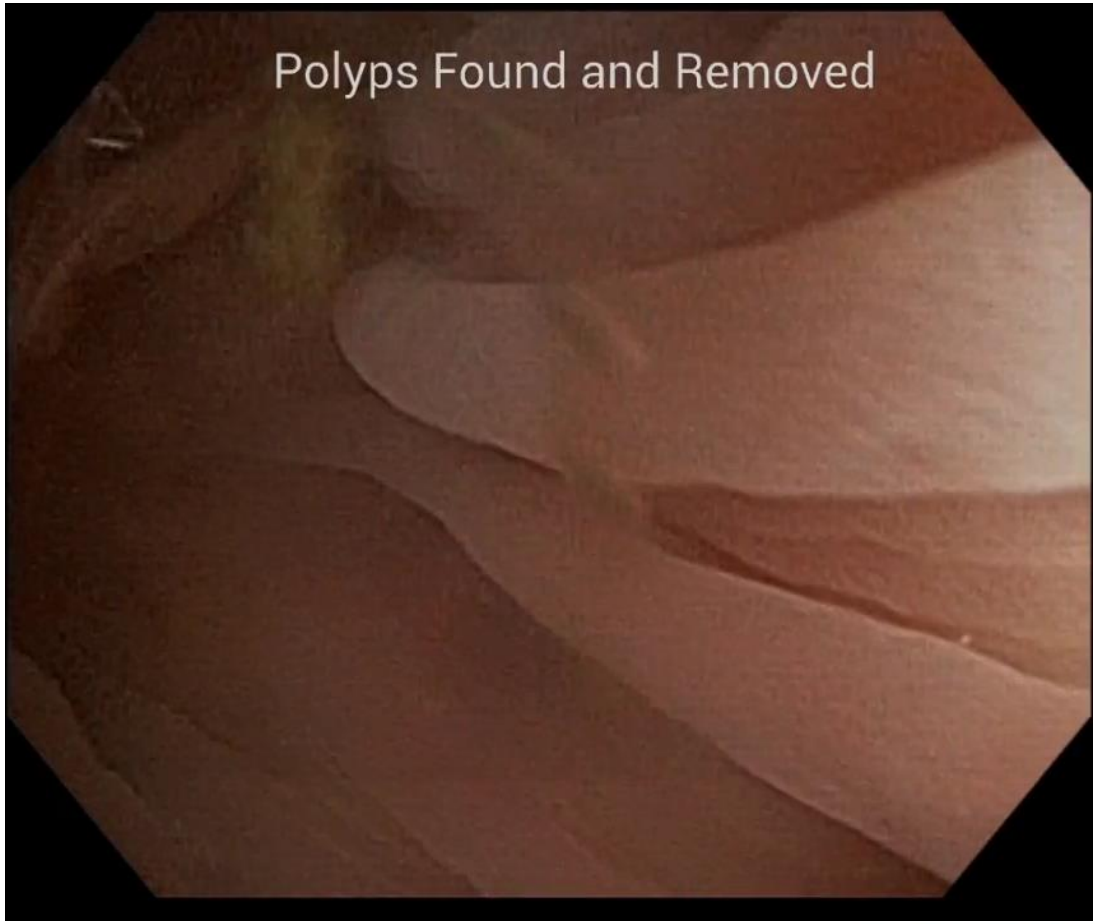
A system of convolutional neural networks (CNN) called Deep Learning was able to process colonoscopy images at high speed in real time, identifying polyps with a cross-validation accuracy of 96.4% and ROC-AUC value of 0.991.

LIMITATIONS

Possible effects of the CNN on inspection behavior by colonoscopists are not known. The anonymized videos excluded information about patient history. CNN performance may vary by indication (screening vs surveillance).

IMPACT

This technology may assist colonoscopists in finding precancerous polyps in real-time and with high accuracy.

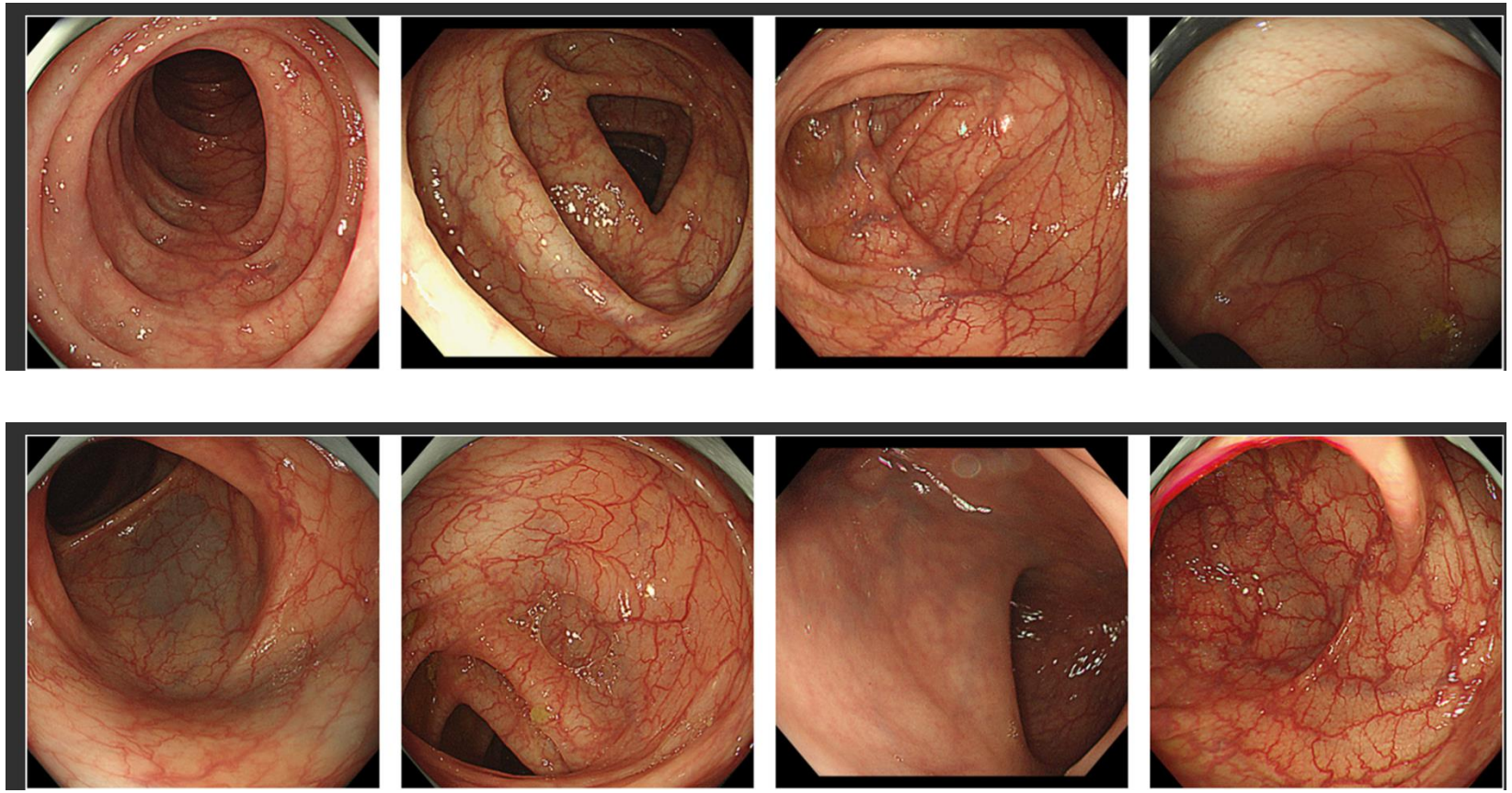


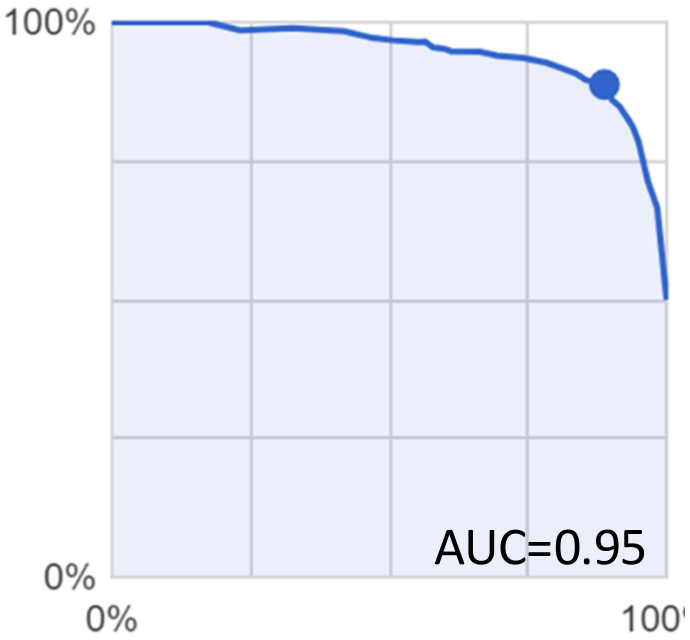
Artificial intelligence model for analyzing colonic endoscopy images to detect changes associated with irritable bowel syndrome

Kazuhisa Tabata, Hiroshi Mihara, Sohachi Nanjo, Iori Motoo, Takayuki Ando, Akira Teramoto, Haruka Fujinami, Ichiro Yasuda

Published: February 17, 2023 • https://doi.org/10.1371/journal.pdig.0000058

PLOS DIGITAL HEALTH



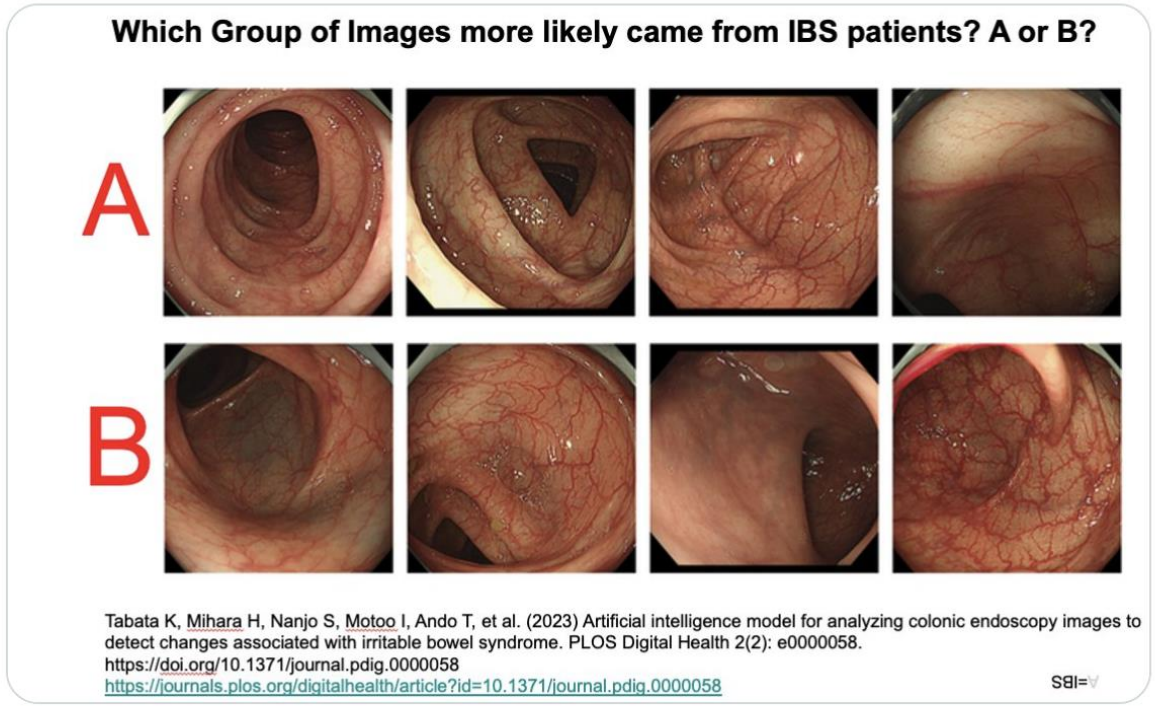


Kewin Siah
@KewinSiah

📢🔥AI is coming to #FGIDs! Using the image #AI model, colonoscopy images of #IBS could be discriminated from healthy subjects at AUC 0.95.

Now, can you see what AI sees? (Answer Right🔽corner)

🔓 Study by Uni. Toyama 🇯🇵
journals.plos.org/digitalhealth/...
#gitwitter #medtwitter #DGBIs



You and 9 others

5:35 PM · Feb 23, 2023 · **50.4K** Views

You and this Tweeter share some mutual follows

Alexander Ford
@alex_ford12399

Replying to @KewinSiah @RomeGastroPsych and 9 others

But given we should not be colonoscoping people to make a diagnosis of IBS seems like a pointless exercise to me.

10:32 AM · Feb 25, 2023 · **2,231** Views

1 Quote Tweet **21** Likes

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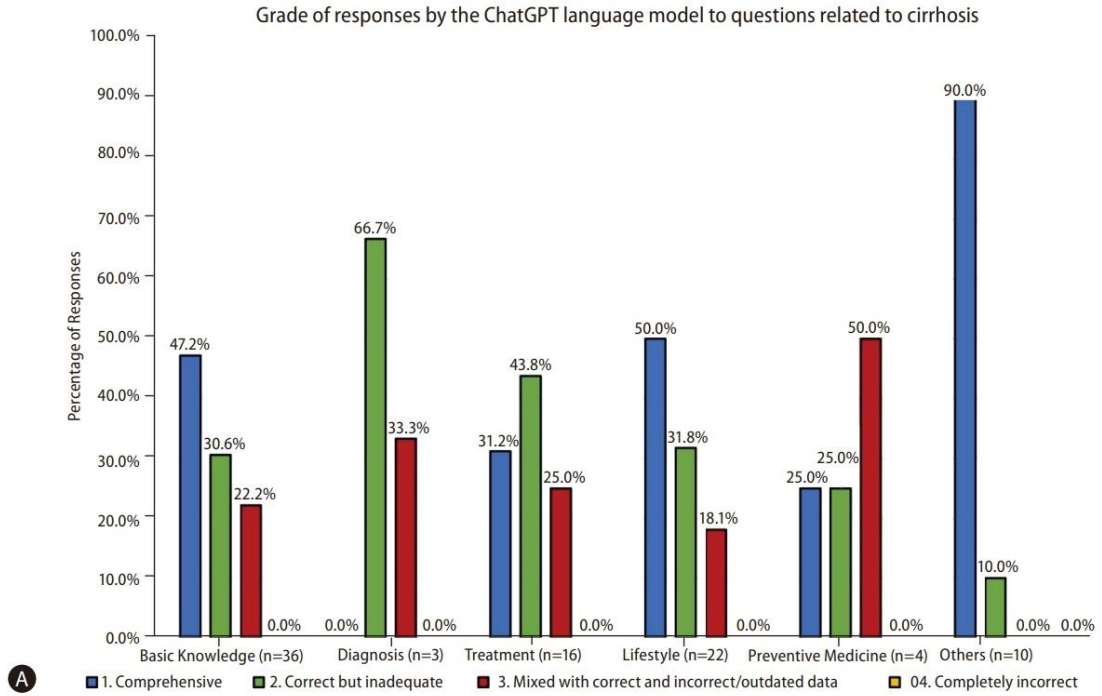
Clin Mol Hepatol. 2023 Jul;29(3):721-732. doi: 10.3350/cmh.2023.0089. Epub 2023 Mar 22.

Assessing the performance of ChatGPT in answering questions regarding cirrhosis and hepatocellular carcinoma

Yee Hui Yeo [1], Jamil S Samaan [1], Wee Han Ng [2], Peng-Sheng Ting [3], Hirsh Trivedi [1 4], Aarshi Vipani [1], Walid Ayoub [1 4], Ju Dong Yang [1 4 5], Omer Liran [6 7], Brennan Spiegel [1 7], Alexander Kuo [1 4]



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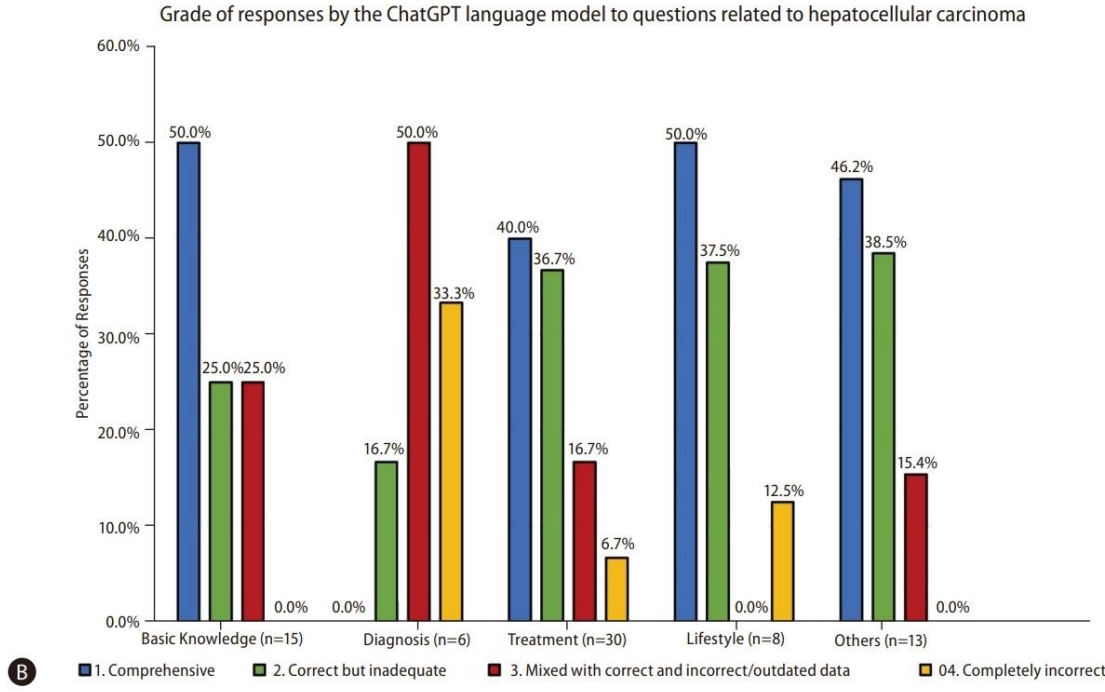

B

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Original Investigation

April 28, 2023

Comparing Physician and Artificial Intelligence Chatbot Responses to Patient Questions Posted to a Public Social Media Forum

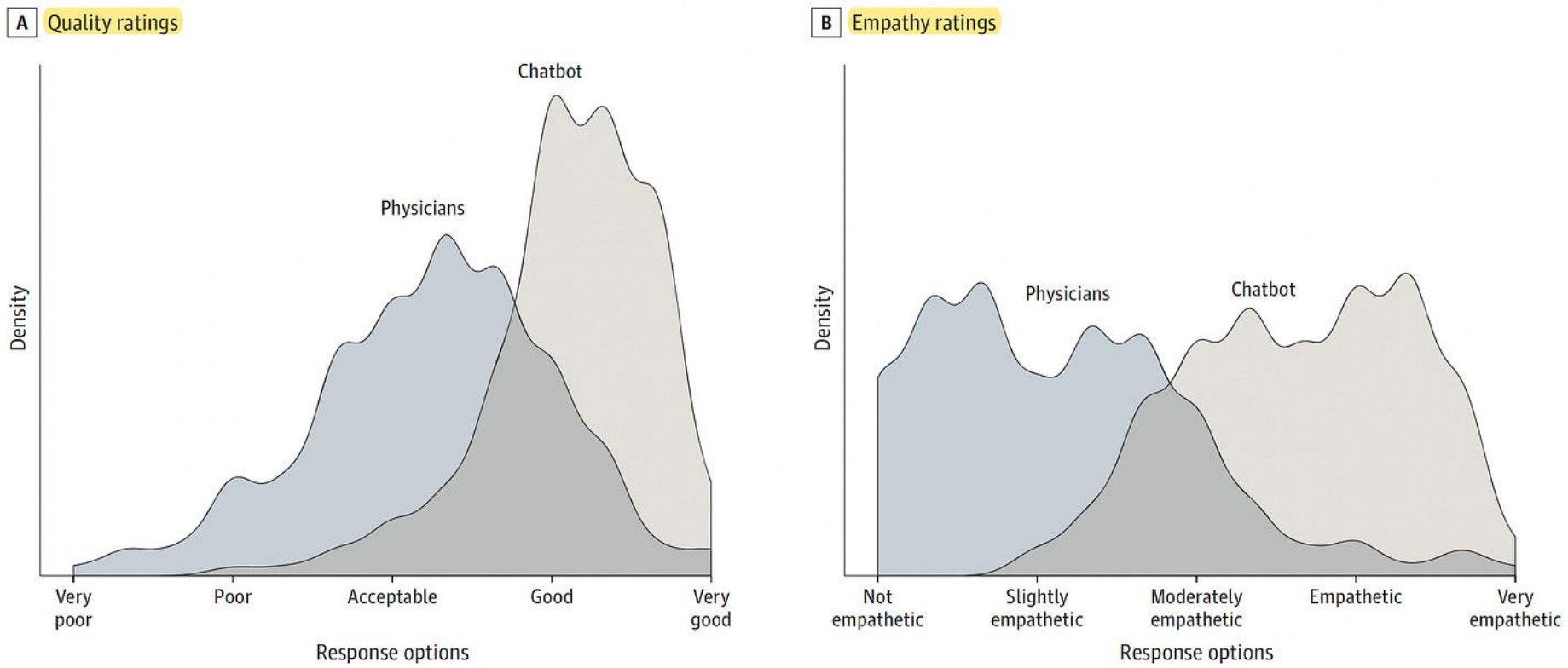
John W. Ayers, PhD, MA[1,2]; Adam Poliak, PhD[3]; Mark Dredze, PhD[4]; et al

» Author Affiliations | Article Information

JAMA Intern Med. 2023;183(6):589-596. doi:10.1001/jamainternmed.2023.1838

JAMA Internal Medicine

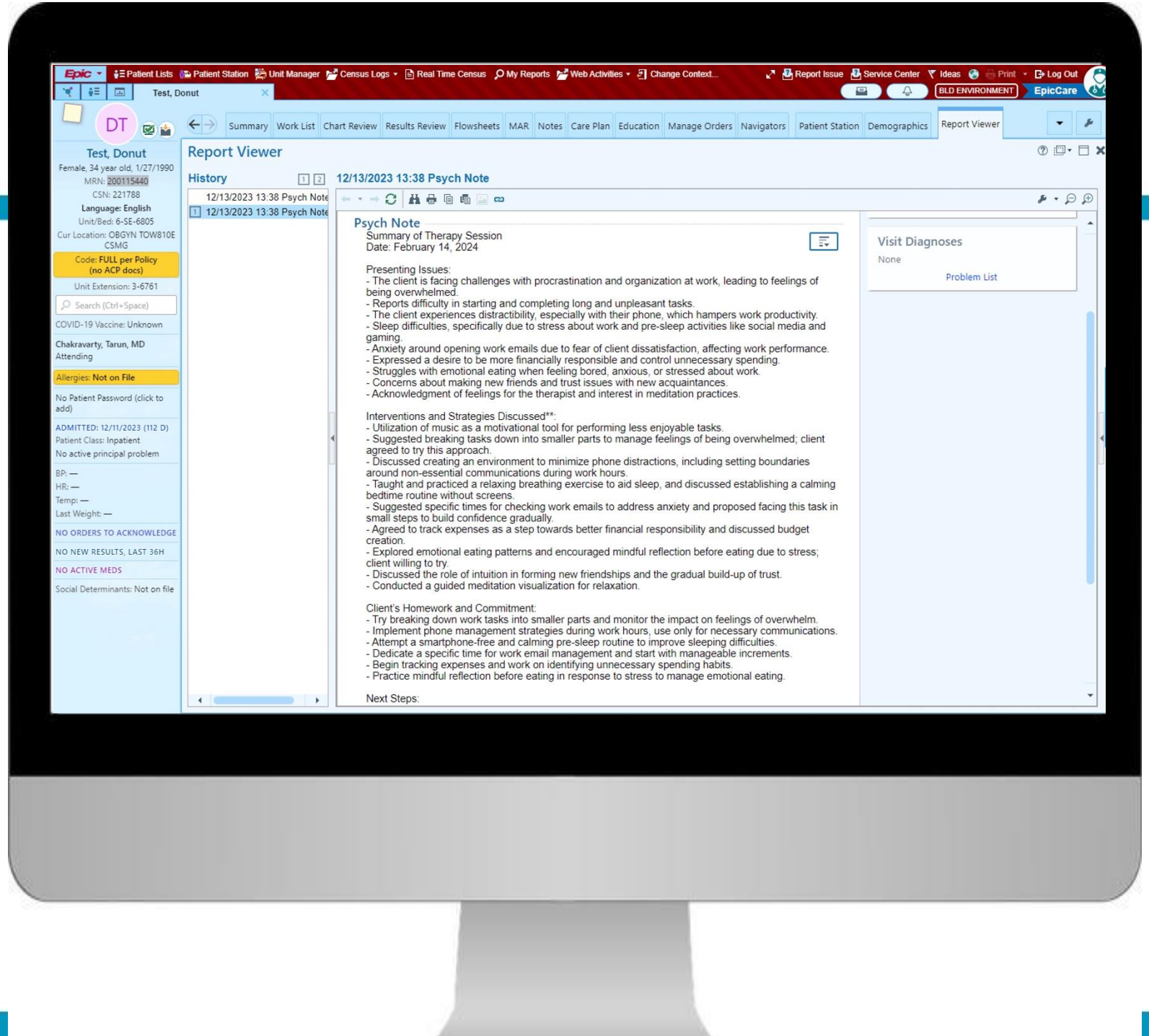
Figure. Distribution of Average Quality and Empathy Ratings for Chatbot and Physician Responses to Patient Questions



BRIEF COMMUNICATION OPEN

Feasibility of combining spatial computing and AI for mental health support in anxiety and depression

Brennan M. R. Spiegel[1,2]✉, Omer Liran[1,3], Allistair Clark[1], Jamil S. Samaan[2], Carine Khalil[1], Robert Chernoff[3], Kavya Reddy[2] and Muskaan Mehra[1]



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⏳ Waiting for response...

Pause Session

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AI ⟷ Human

AI	Human
Takes a technical history	Looks people in the eyes
Interprets an X-ray	Lays hands on the patient
Reads an endo image	Performs the endoscopy
Generates a list of diagnoses	Communicates & collaborates
Knows stuff	Shares wisdom

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Thank you!

@BrennanSpiegel

@VirtualMedConf

Cedars Sinai

Inflammatory Bowel Disease

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#EvidenceIsPower

Guideline Updates- Ulcerative Colitis

Oriana M. Damas, MD MSCTI
Associate Professor of Medicine
Interim Director for the Crohn's and Colitis Center
Director of Translational Studies for the Crohn's and Colitis Center
University of Miami Miller School of Medicine

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Disclosures

- Research Funding from: Pfizer
- Consulting and advisory board for: AbbVie, Janssen
- Educational content for Equip-q

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Objectives

1. Review the latest guidelines on ulcerative colitis (UC) from the American Gastroenterological Association (AGA) and the American College of Gastroenterology (ACG).
2. Examine the latest literature and evidence on the positioning of therapies and guideline recommendations for UC

AGA Living Guidelines 2024: *What's new*

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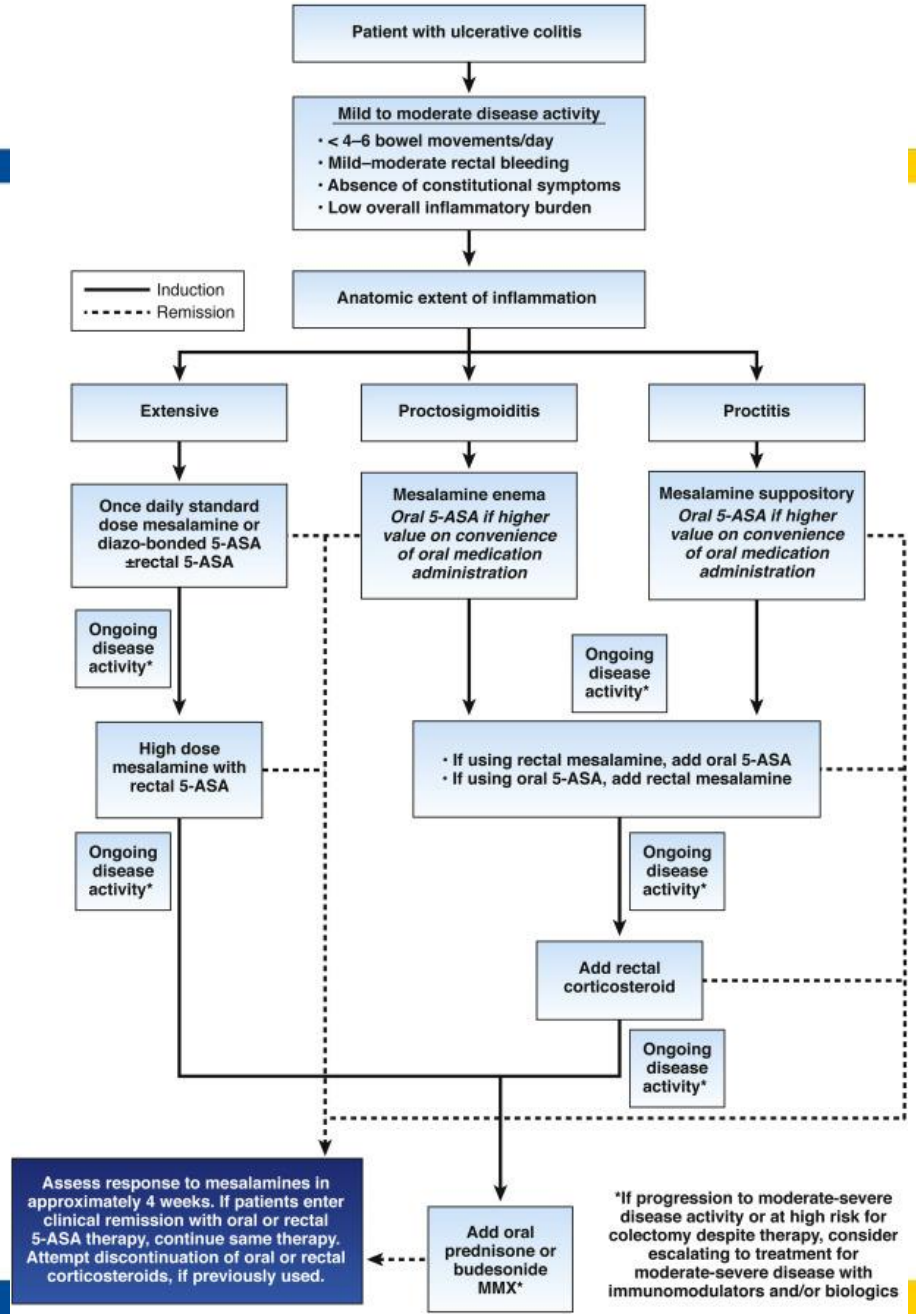
In mild to moderate ulcerative colitis



Important factors to consider in the management of patients with :

What determines mild-mod UC?

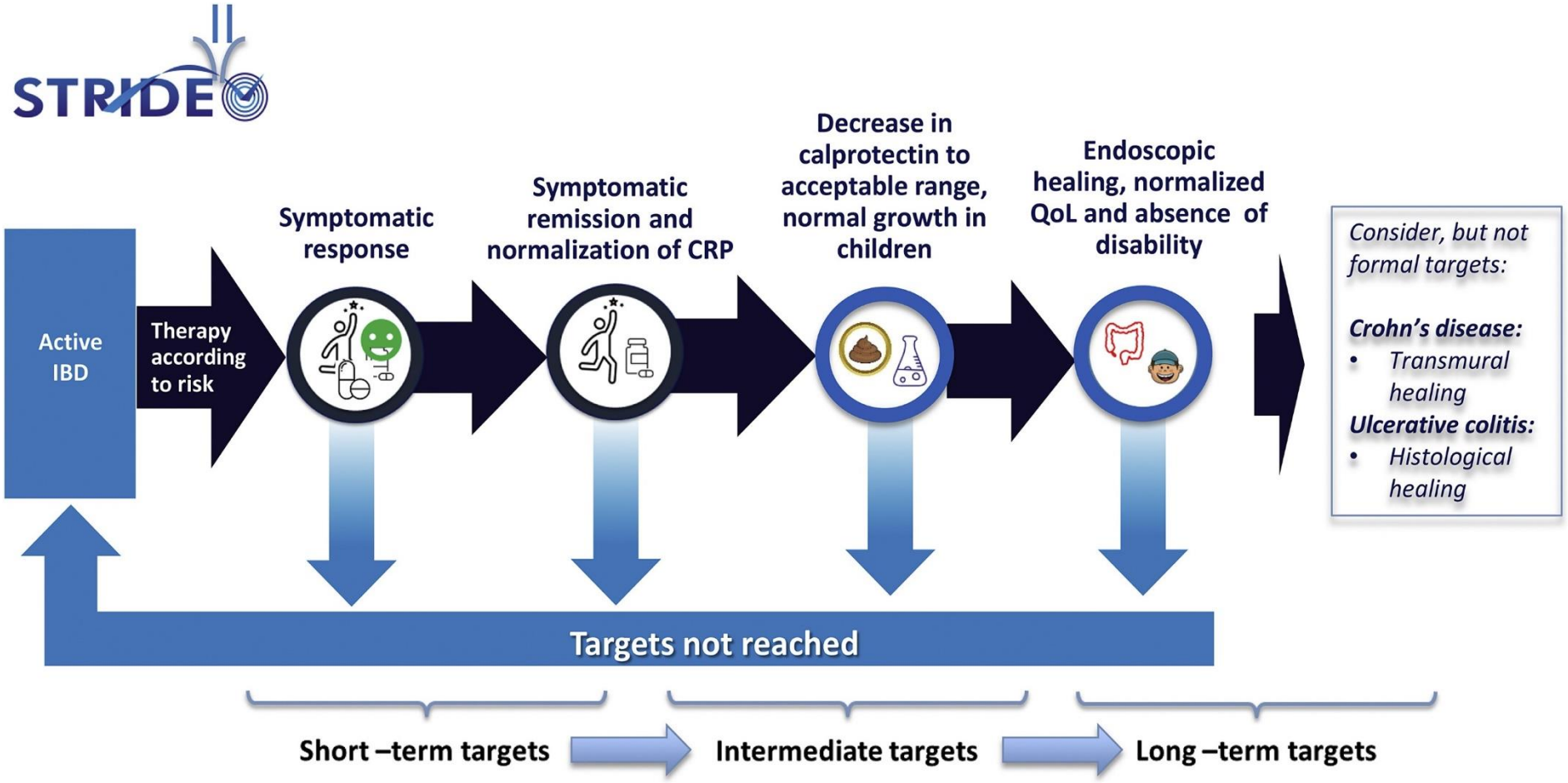
- ✓ Extent of disease
- ✓ Disease activity at present
- ✓ Inflammatory burden
- ✓ History of disease

In patients with mild-moderate UC:

- ✓ First-line therapy is 5-ASA (oral or supp/enema)
- ✓ Re-assess in ~4 weeks to determine improvement
- ✓ Can bridge with steroids (pred, budesonide MMX, or rectal depending on disease phenotype and disease activity)
- ✓ Re-assess whether phenotype is now mod-UC and start advanced therapy

Singh S, et al. *Gastroenterology*. 2024;167:1307-1343.

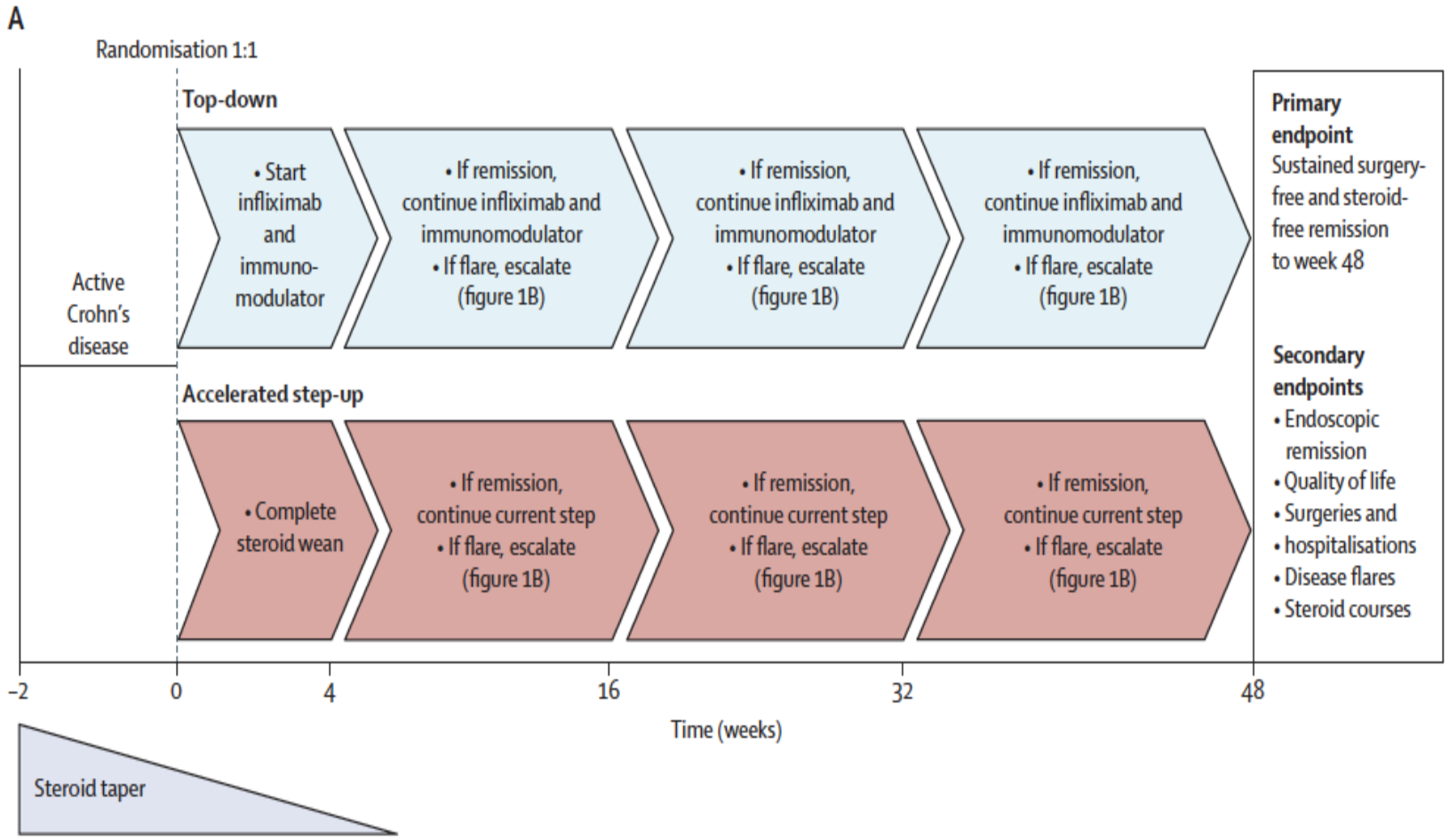
STRIDE II



QoL= quality of life.

Turner D, et al. *Gastroenterol*. 2021;160:1570-1583.

Top-down treatment with combination infliximab plus immunomodulator achieved substantially better outcomes at 1 year (top-down therapy) than accelerated step-up treatment: Results of the PROFILE



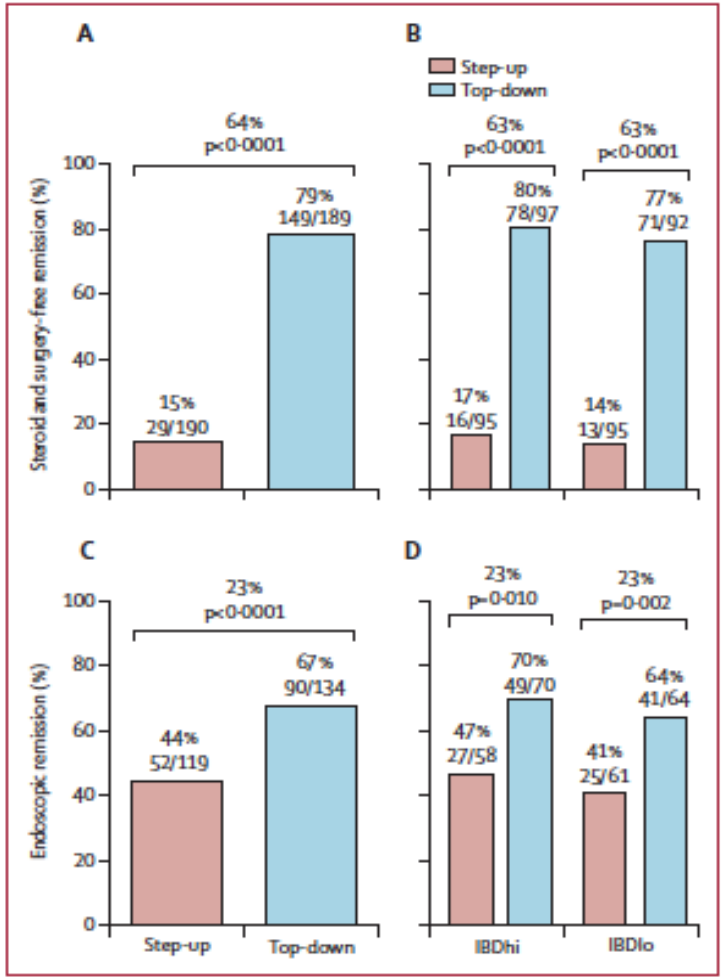


Figure 3: **Primary endpoint and key secondary endpoint**
(A) Sustained steroid-free and surgery-free remission until week 48 for treatment groups. (B) Sustained steroid-free and surgery-free remission until week 48 for biomarker–treatment subgroups. (C) Endoscopic remission (absence of ulceration) at week 48 for treatment groups. (D) Endoscopic remission (absence of ulceration) at week 48 for biomarker-treatment subgroups.

Noor M. PROFILE. Lancet 2024

Adult outpatients with moderate to severely active ulcerative colitis

Better to treat early with advanced therapy

Moderate to severely active UC defined as:

-Moderate to severe symptoms with Mayo endoscopy sub-score 2 or 3

-Mild symptoms, with high burden of inflammation or poor prognostic features

-Patients with corticosteroid-dependence, or refractory to oral corticosteroids

- SUGGEST early use of advanced therapies and/or immunomodulator therapy, rather than the gradual step up after failure of 5-aminosalicylates

  Conditional recommendations, very low certainty of evidence

- RECOMMEND using any of the following, over no treatment:

  Infliximab, Golimumab, Vedolizumab, Tofacitinib, Upadacitinib, Ustekinumab, Risankizumab, Guselkumab, Ozanimod, Etrasimod

  Strong recommendation, moderate certainty of evidence

Which medication should we start with?

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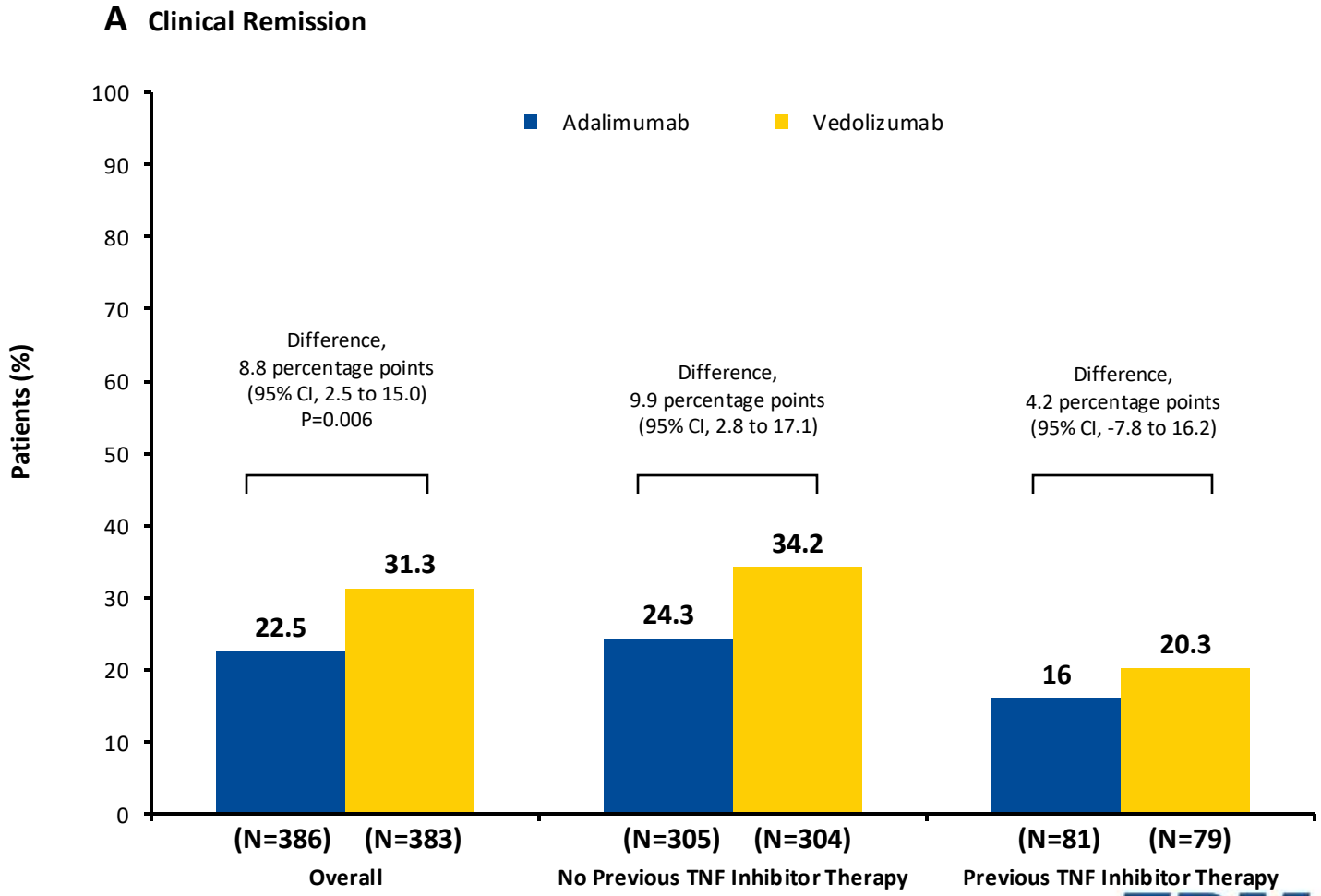
VARSITY: Which Agent to Use as First Line in UC?

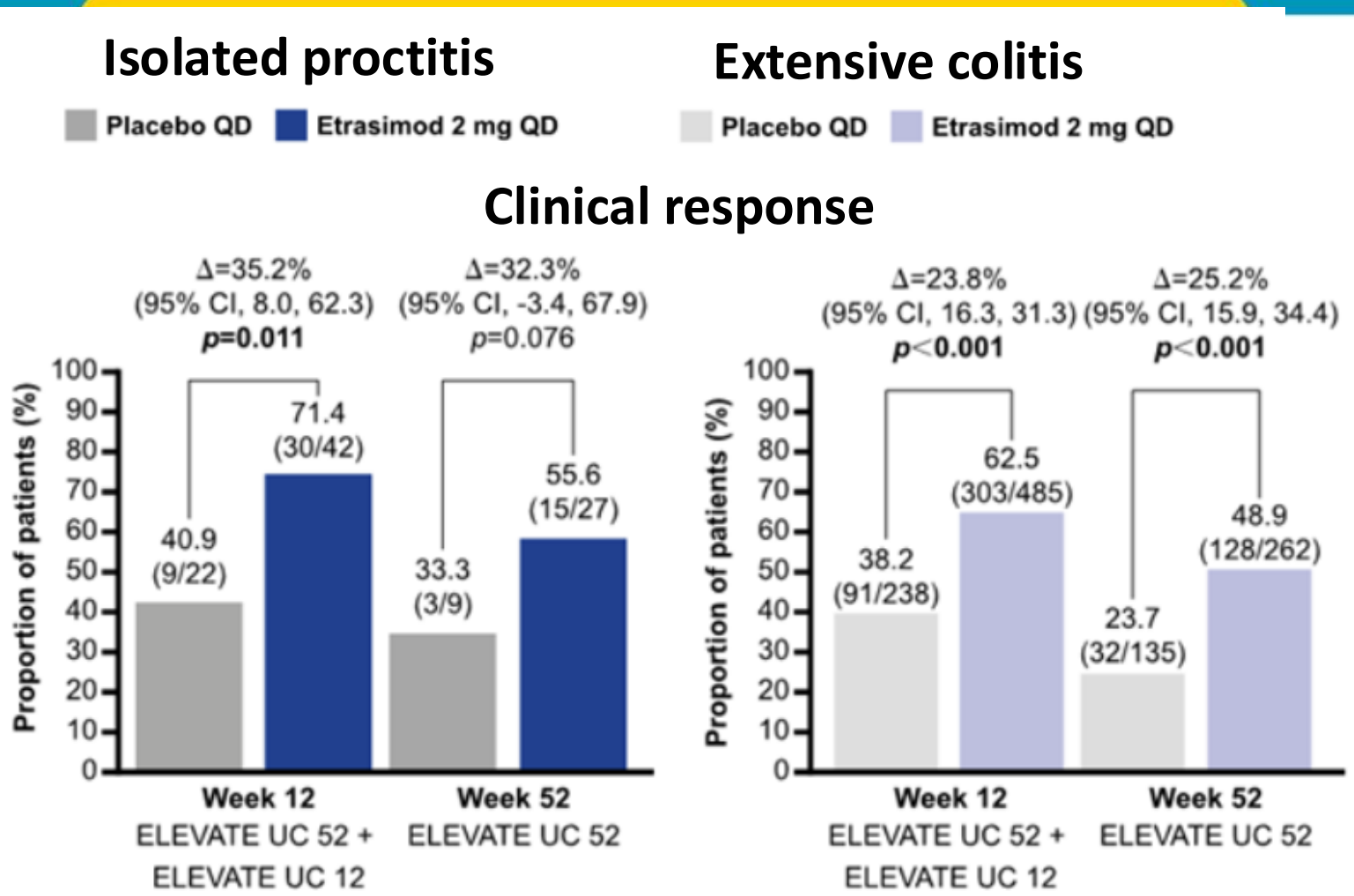
- Phase 3b, randomized, double-blind, double-dummy, active-controlled study comparing *vedolizumab* versus *adalimumab*
- Adults with moderate to severe UC failing conventional therapy
- Exposure to one prior antiTNF (not ADA) capped at 25%



N Engl J Med. 2019 Sep 26; 381(13):1215-1226.

EBMed #EvidenceIsPower

Etrasimod: Efficacy Proctitis vs Extensive Colitis from ELEVATE UC



Peyrin-Biroulet L, et al Presented at: ACG 2023 Annual Meeting; October 24, 2023; Vancouver, Canada. P3603. (S1165).

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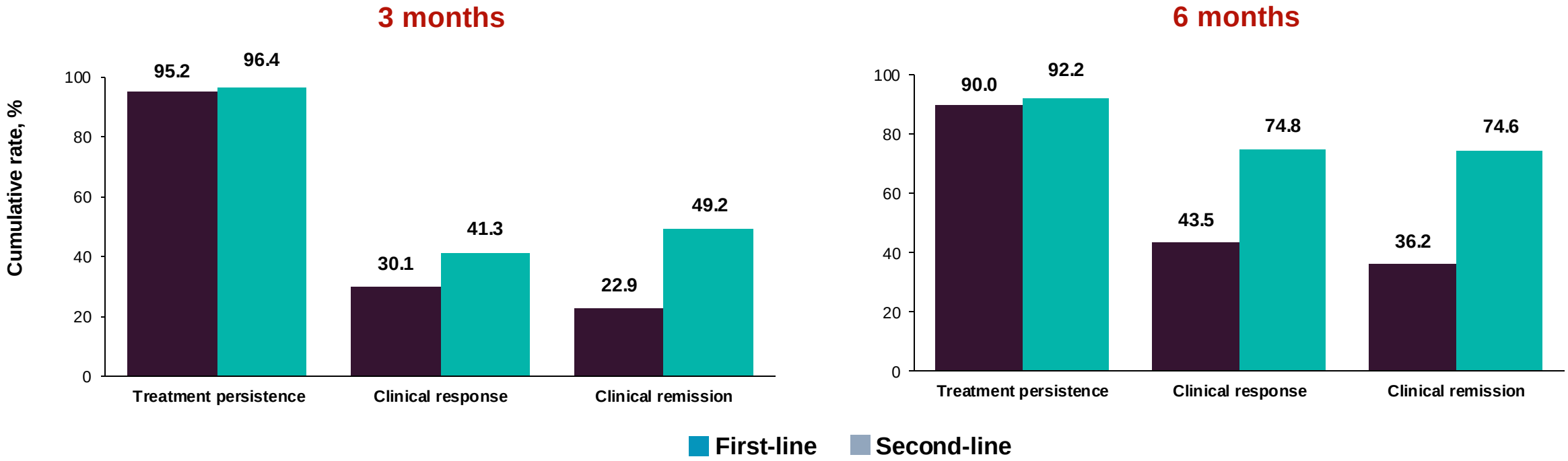
Real-World Data Suggests That First-line VDZ May Not Impact The Effectiveness of Subsequent Anti-TNFα Treatment

EVOLVE (N=1,095)

Cumulative rates of treatment persistence and clinical effectiveness in second-line cohort were similar to rates in first-line anti-TNFα cohort[1]



37 sites: First-line anti-TNFα (n=497).[2]

*number at risk.[1]

CD, Crohn's disease; TNFα, tumour necrosis factor alpha; VDZ, vedolizumab.

1. Bressler B et al. *J Crohns Colitis*. 2021; 15:1694-706 (supplementary appendix); 2. Bressler B et al. *J Crohns Colitis*. 2021; 15:1694-706.

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Advanced Therapies Are Affected by Prior Exposure To Anti-TNF Therapy in IBD

Clinical remission: Absolute difference versus placebo

	Anti-TNF-naïve	Anti-TNF-exposed
Adalimumab (Week 56, CHARM)[1,2]	42.0%	31.0%
Vedolizumab (Week 52, GEMINI 2)[3,4]	22.1%	14.9%
Ustekinumab (Week 8, UNITI-1 and -2)[5,6]	20.6%	13.6%

Adalimumab, vedolizumab, and ustekinumab demonstrated **decreased efficacy in anti-TNF–exposed patients with CD**[1–3]

*The adalimumab 40 mg every other week dosing regimen cohort data was used.[1]

CD, Crohn's disease; CHARM , Crohn's Trial of the Fully Human Antibody Adalimumab for Remission Maintenance; TNF, tumour necrosis factor.

1. Colombel JF et al. *Gastroenterology*. 2007; 132:52-65; 2. Humira® (adalimumab) SmPC. European Medicines Agency. October 2022. Available at: https://www.ema.europa.eu/en/documents/product-information/humira-epar-product-information_en.pdf. Accessed October 2023; 3. Sands BE et al. *Inflamm Bowel Dis.* 2017; 23:97-106; 4. Entyvio® (vedolizumab) SmPC. European Medicines Agency. September 2023. Available from: https://www.ema.europa.eu/en/documents/product-information/entyvio-epar-product-information_en.pdf. Accessed October 2023; 5. Feagan BG et al. *N Engl J Med.* 2016; 375:1946-60 (supplementary appendix); 6. Stelara® (ustekinumab) SmPC. European Medicines Agency. July 2023. Available from: https://www.ema.europa.eu/en/documents/product-information/stelara-epar-product-information_en.pdf. Accessed October 2023.

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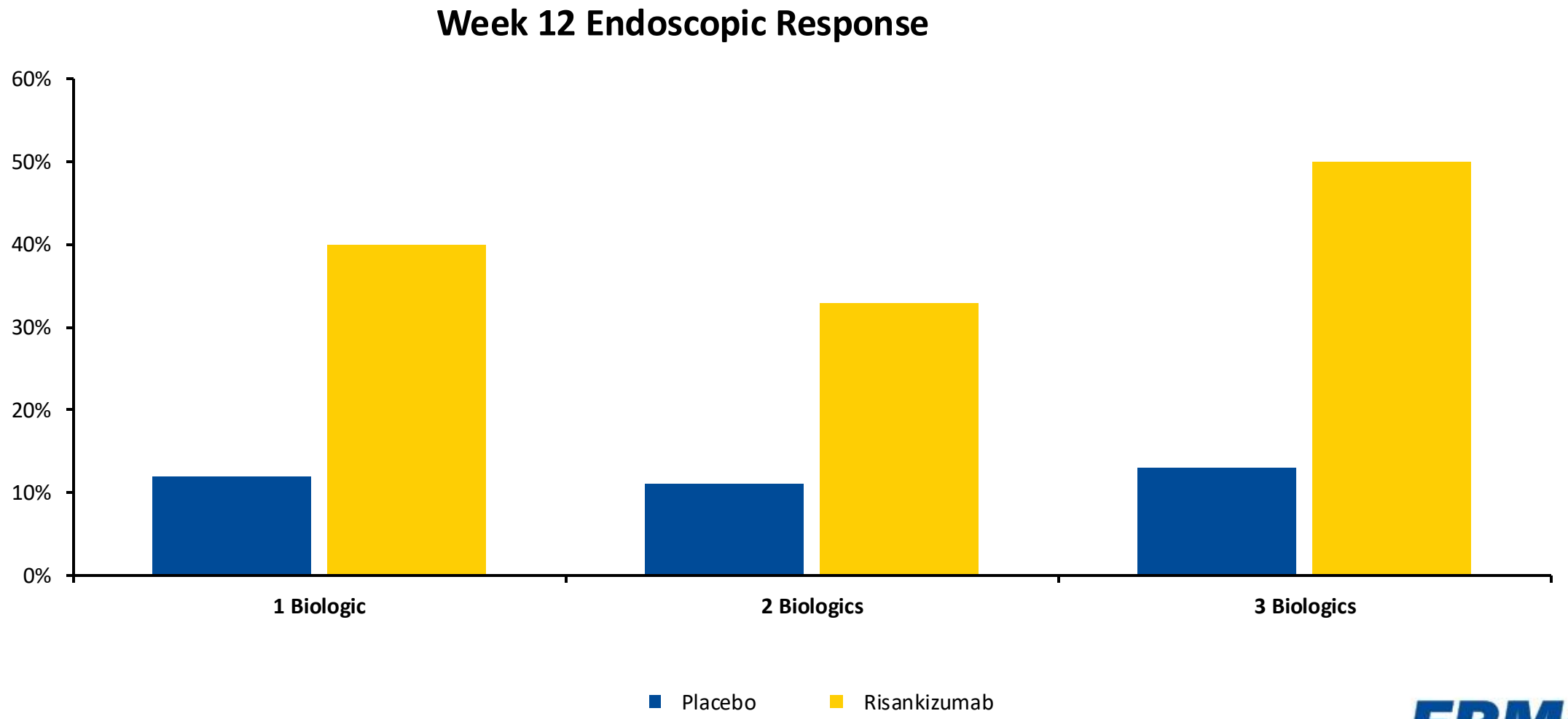
Efficacy of Risankizumab in Prior Biologic Exposures



D'Haens et al. *Lancet*. 2022.

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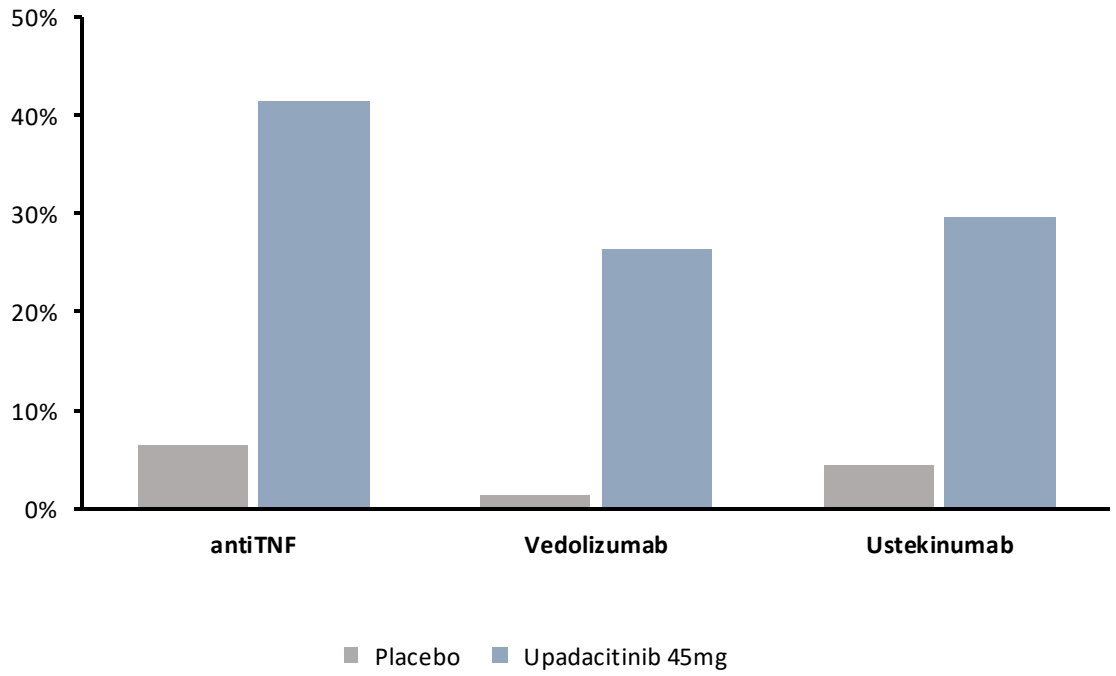
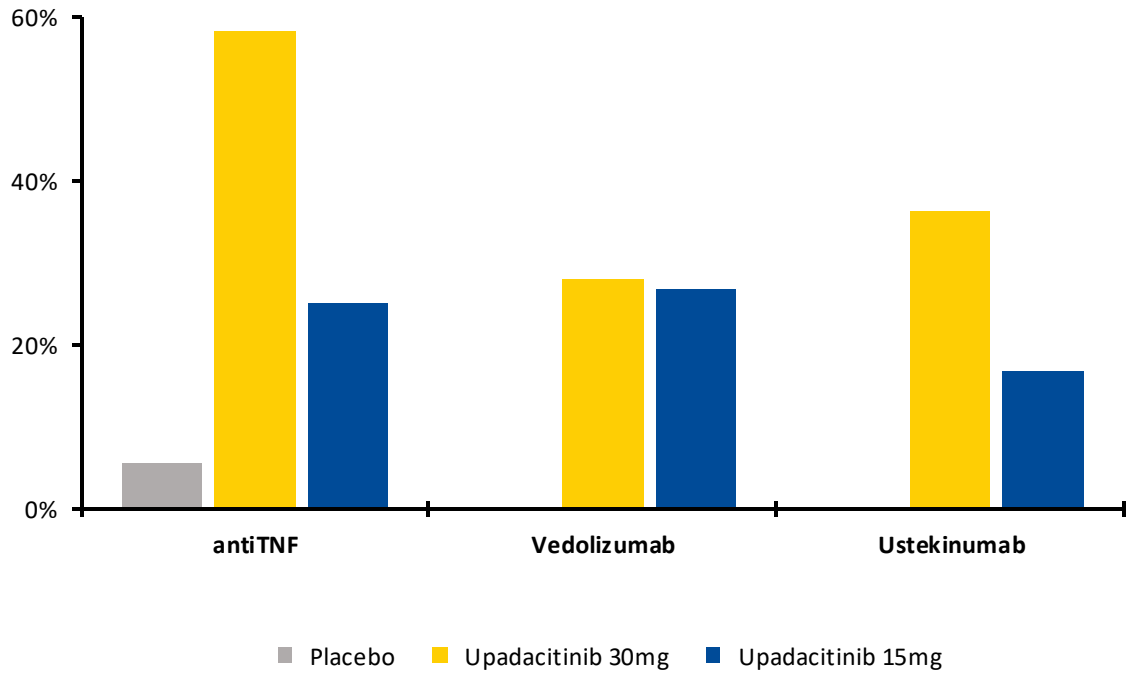
Efficacy of Upadacitinib in Prior Biologic Exposure

U-EXCEED/EXCEL –
Week 12 Endoscopic Response



U-ENDURE –
Week 52 Endoscopic Response



Loftus EV et al. *NEJM*. 2023.

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AGA Living Guidelines

ADVANCED THERAPY-NAÏVE PATIENTS (FIRST LINE THERAPY)

Suggest using a HIGHER efficacy, or INTERMEDIATE efficacy medication, rather than a lower efficacy medication.

(*Conditional recommendation, low certainty of evidence*)

HIGHER EFFICACY MEDICATIONS: Infliximab, vedolizumab, ozanimod, etrasimod, Upadacitinib, Risankizumab, guselkumab

INTERMEDIATE EFFICACY MEDICATIONS: Golimumab, Ustekinumab, tofacitinib, filgotinib, mirikizumab

LOWER EFFICACY MEDICATIONS: Adalimumab

PRIOR EXPOSURE TO ONE OR MORE ADVANCED THERAPIES, PARTICULARLY TNF ANTAGONISTS

Suggest using a HIGHER efficacy, or INTERMEDIATE efficacy medication, rather than a lower efficacy medication.

(*Conditional recommendation, low certainty of evidence*)

HIGHER EFFICACY MEDICATIONS: Tofacitinib, Upadacitinib, Ustekinumab

INTERMEDIATE EFFICACY MEDICATIONS: Filgotinib, Mirikizumab, Risankizumab, Guselkumab

LOWER EFFICACY MEDICATIONS: Adalimumab, Vedolizumab, Ozanimod, Etrasimod,

Singh S. et al, Gastro 2024; 167:1307-1343.

There Are Many Additional Factors in Treatment Decision-Making

- Patient Factors
- Disease Factors
- Treatment Factors

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How to Choose the "Right" Agent?

- **Disease-specific factors**
  - *Severity of disease*
  - *EIM*
  - Perianal disease
  - *Associated conditions* (psoriasis, RA)
- **Patient-specific factors**
  - Age
  - Co-morbidities (CHF, renal disease, recent cancer); pregnancy
  - *Patient preference*

Insurers / payers

- **Medication-specific factors**
  - *Efficacy* (clinical remission, endoscopic healing, perianal, EIM)
  - *Safety*
  - Rapidity of onset
  - Durability of remission
  - Immunogenicity
  - Availability and data on TDM
  - How it is administered
  - Time on market (devil you know)
  - Cost?

Physician comfort

RA = rheumatoid arthritis; CHF = congestive heart failure; EIM = extra-intestinal manifestations.

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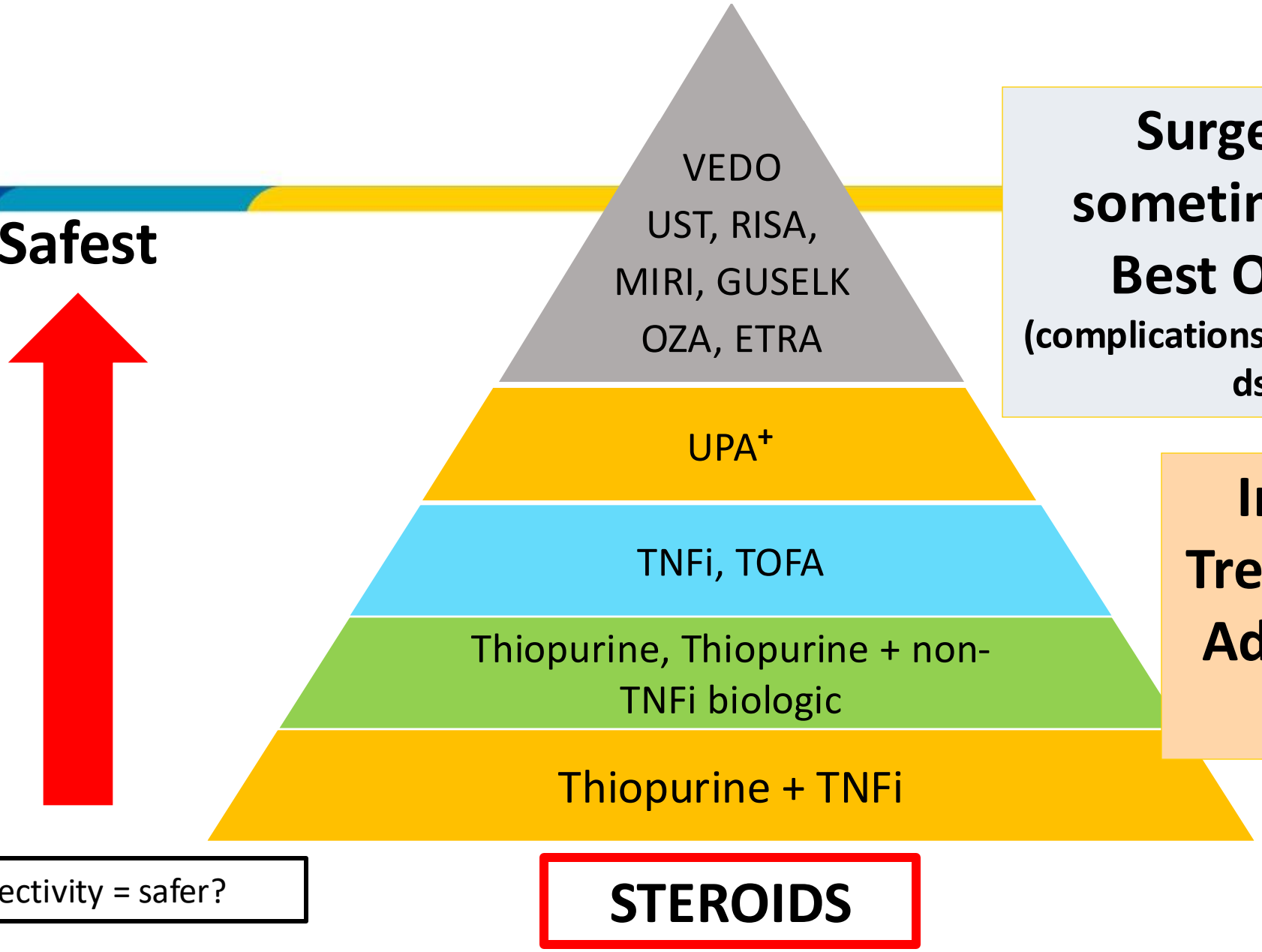
Safest



STEROIDS

Surgery is sometimes the Best Option
(complications or isolated TI ds)

Inadequate Treatment is an Adverse Event

+Does selectivity = safer?

Adapted Bhat, Click, Regueiro IBDj. 2023.

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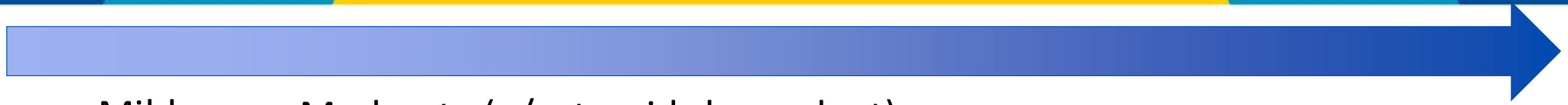
ACG Guidelines: Positioning Key Concept Statements

1. There are **no validated therapeutic biomarkers or companion diagnostic tests** to enhance selection or predict response to treatment for the patient with active UC.
2. Patients with UC should have available all medical options as recommended by their doctor and healthcare team. **Third party payers and requirements for step therapy should not come between the patient and their healthcare team in making decisions about treatment for UC.**
3. Patients with moderately to severely active UC have higher rates of response and remission with their first therapies than after failure of one or more advanced therapies.
4. Given the expanding number of therapies per mechanistic class, **a distinction between primary non-response and secondary non-response is important** in order to select the next therapeutic option.
5. Post hoc subgroup analyses and network meta-analyses provide hypothesis-generating data but are not sufficient to stratify therapies for individual patients.
6. Infliximab is the preferred anti-TNF therapy for patients with moderately to severely active UC.
7. Some patients with moderately to severely active UC who are at higher risk for infectious complications may benefit from vedolizumab or an anti-IL-23 strategy over more systematically immunosuppressive medical options.
8. Initial and subsequent therapies for moderately to severely active UC may be chosen based on extra-intestinal manifestations, including the involvement of joints and skin, in which therapies which have efficacy in both UC and in EIM.

Rubin, David. Updated Ulcerative Colitis Practice Guidelines in Adults: ACG, Practice Parameters Committee. In review

Synthesizing Choices in UC Treatment*



Mild | Moderate (+/- steroid-dependent) | Severe (steroid-refractory)

Naïve
(mostly equipoised, patient preference important)

Moderate but milder/more time: Ozanimod/etrasimod (proctitis)
Vedolizumab
IL-23 inhibitors

Moderate/less time/more acute:
IL-23 inhibitors>ustekinumab
Infliximab
Vedolizumab>adalimumab

Infliximab
Upadacitinib
Cyclo

Biologic-exposed

Change mechanism if did not work

Some patients will benefit from combined biologics

JAKi (tofa, upadacitinib) if failed anti-TNFs

*my strategy
Tofa/upadacitinib (JAKi) and ustekinumab/mirikizumab/Risankizumab (IL-23) similar mechanisms.
Verdict out on S1P agonists and JAKi in pregnancy.
I generally do not choose vedolizumab if dealing with EIMs.

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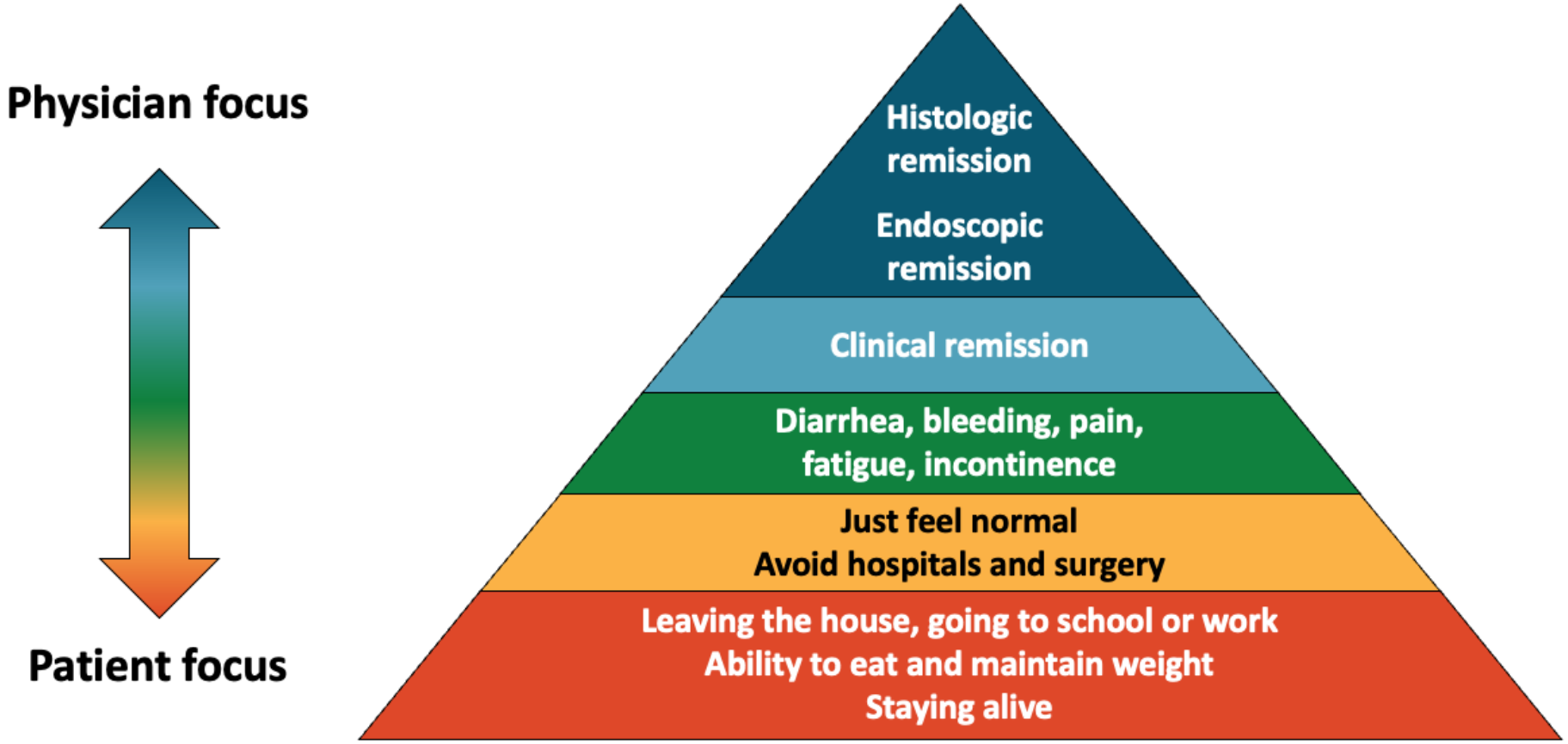
Hierarchy of Needs for the Patient With IBD



Siegel CA. *Am J Gastroenterol*. 2019;114:382-383; Rubin DT, et al. *Am J Gastroenterol*. 2019;114:384-413; Al Khoury A, et al. *Dig Dis Sci*. 2022;67:1956-1974.

Take Home Points

- ✓ **5 ASA-s reserved for mild UC**
- ✓ **Reassess early if response to 5-ASAs (starting advanced therapies early rather than later associated with best outcomes)**
- ✓ **Take into account the full picture of the patient:** disease severity, acuity, EIMs, age, pregnancy or child-bearing age, comorbidities and safety
- ✓ **Best sequence of advanced therapies:**
  - First line vs second line therapy differ in efficacy
  - Prior anti-TNF exposure associated with reduced efficacy for vedolizumab and ustekinumab
  - Exposure to other biologics may not impact efficacy of anti-TNF efficacy (more data needed)
  - Risankizumab (IL-23 inhibitors) and Upadacitinib with good efficacy after all biologic exposures

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How Healthcare Providers Can Be Better Advocates for their Patients

Aline Charabaty, MD
Associate Professor of Clinical Medicine
Assistant Clinical Director of the Division of Gastroenterology and Hepatology at Johns Hopkins School of Medicine, Baltimore, Maryland
Clinical Director of the IBD Center at Johns Hopkins Sibley Memorial Hospital, Washington, DC

Kimberly Orleck, PA-C
Senior Director of Advanced Practice Providers
Atlanta Gastroenterology Associates
United Digestive

Amber Tresca
Patient Activist
Founder of About IBD

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“Being an advocate requires that an individual believes he or she can effect change, is motivated to do so, and is able to envision what improvements are needed and how they can be instituted.”

Thomasson C. *Virtual Mentor*. 2014;16:753-757.

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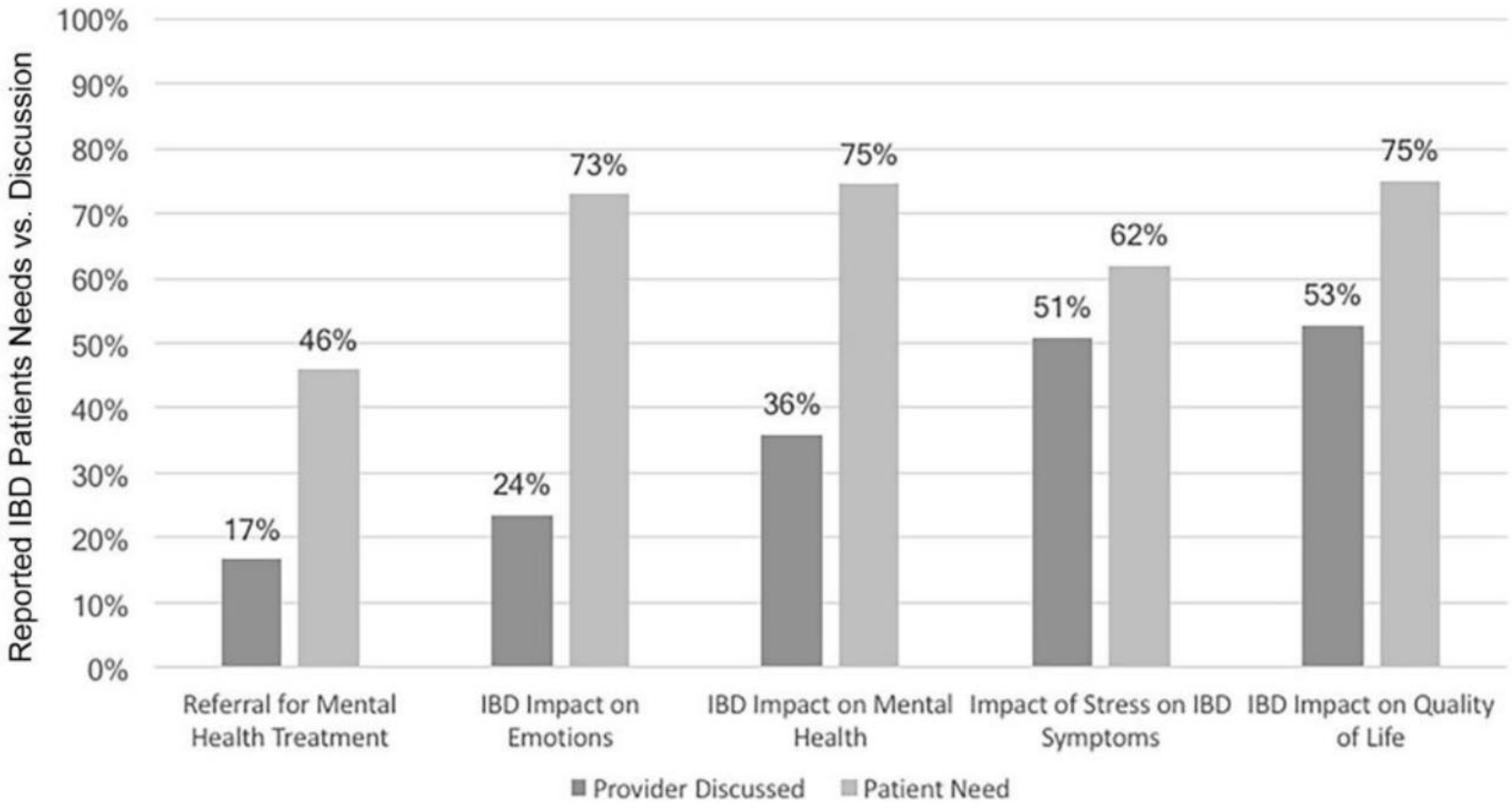
Active Listening

Question: How can clinicians effectively engage, connect, and establish trust with patients?

- Active asking and active listening
- Invite patients and families to explain their disease journey
- Encourage patients and care partners to ask the most important questions first
- Ask open-ended questions
- Let patients guide the conversation
- Ask how their health has affected QoL and ADLs
- Patients need to feel heard, with their concerns and needs being validated and addressed

Pollak KI, et al. *J Am Board Fam Med*. 2011;24:665-672.

The Scope of The Awareness Gap



Craven MR, et al. *J Clin Psychol Med Settings*. 2019;26:183-193.

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Closing the Awareness Gap

Question: Healthcare providers and patients often speak different languages. We are focused on specific treatment goals and objective measures of disease remission, which might not resonate with patients. How can clinicians and patients close the awareness gap?

- Patients and healthcare providers may be *talking* but not *connecting*
- Patients and care partners living with chronic illness often navigate adverse life experiences
- They are focused on improving their QoL and addressing how their disease is affecting them at the psychosocial and emotional level
- Guidance and support in practicing self-advocacy and self-efficacy from healthcare professionals is helpful in improving QoL

LaDonna KA, et al. *Med Educ*. 2021;55:486-495.

Aligning Clinician and Patient Goals to Avoid Incomplete and Fractionated IBD Care

Physician goals: Objective measures of remission

- Steroid-free remission
- Endoscopic remission
- Prevention of complications

- **Shared decision-making involves:**
  - **Shared goals**
  - **Objective + subjective measures**
  - **Patient preferences**

Patient goals: Psychosocial measures of remission

- Avoid bathroom accidents
- Ability to go to school/work
- Enjoy relationships and intimacy
- Enjoy social and leisure pursuits
- Improve emotional health
- Restful sleep
- Enjoy food
- Resolve anxiety, depression, fatigue
- Decrease financial burden
- Avoid medication SE

Slide courtesy A Charabaty.

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Patient Treatment Goals: Speaking the Same Language

Disease Activity and Severity, Patient's Health Literacy and Activation, and Patient's Social Determinants of Health Affect Each Component

Feel better as soon as possible (Induction of Clinical Response / Remission)	**QoL: Resume social / professional activities, avoid ER, hospital, surgery (Maintenance of Remission)**
Anxiety of medication SE (Balanced conversation of risks / benefits of meds vs risk of undertreating disease)	**Medication that does not interfere with life (Method of administration, need for monitoring, need for combo)**

Slide courtesy A Charabaty.

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Using Shared Decision-Making

Question: How can shared decision-making help in aligning goals between clinicians and patients?

- Activate the patient:
  - Patients understand they play an active role in making decisions
  - Educate patients about disease and therapies so they are empowered with the knowledge to make decisions
  - Frame the relationship as a partnership
  - Take patient preferences into account
  - Look for the therapies that are the best fit for patient disease activity and severity but also lifestyle, preferences, access, and coverage
  - Work together to find lifestyle changes that are effective but realistic and culturally aligned

Lofland JH, et al. *Patient Prefer Adherence*. 2017;11:947-958.

The Shared Decision-Making Model

	Paternalistic	Shared	Informed
Information exchanges	One way (largely) Healthcare provider → patient Medical Minimum legally required	Two way Healthcare provider ⟷ patient Medical and personal All relevant for decision-making	One way (largely) Healthcare provider → patient Medical All relevant for decision-making
Deliberation	Healthcare professional(s)	Healthcare professional(s) and patient	Patient
Deciding on treatment to implement	Healthcare professional(s)	Healthcare professional(s) and patient	Patient

Shared decision making is relevant when there is more than one reasonable option and the possible benefits and harms of each option affect patients differently

Slide courtesy A Charabaty.

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Social Determinants of Health

Question: How can clinicians address social determinants of health?

- Advocate for equitable access to healthcare services
- Promote diversity within the healthcare workforce
- Engage in creating solutions for systemic barriers to care

Mental Health Commission of Canada. Making the Case for Peer Support. Mental Health Commission of Canada Web site. July 2016. https://mentalhealthcommission.ca/resource/making-the-case-for-peer-support. Accessed Mar 27, 2024.

Patient Advocacy Groups and Community-Based Organizations

Question: Why should healthcare providers get involved in patient advocacy groups (PAGs)?

- Public trust for physicians[1] and physician assistants[2] is high
- Volunteering with PAGs can help lend them legitimacy and lead to funding support
- Working with schools, public health departments, and other local groups can support a wide variety of patient education initiatives

1. Earnest MA, et al. *Acad Med.* 2010;85:63-67; 2. American Academy of Physician Associates (AAPA). The Patient Experience: Perspectives on Today's Healthcare. Available at: https://www.aapa.org/download/113513/?tmstv=1684243672.

Summary

- Patients and clinicians different views of how chronic illness affects everyday life
- Active listening can help in discovering patient goals and challenges
- Activating/educating patients and using a common language helps align goals and reach a shared decision for a treatment plan
- This process actually improves:
  - Follow-up
  - Patient compliance with a treatment plan
  - Patient outcomes

Case Studies in IBD

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S1P Modulators in Ulcerative Colitis

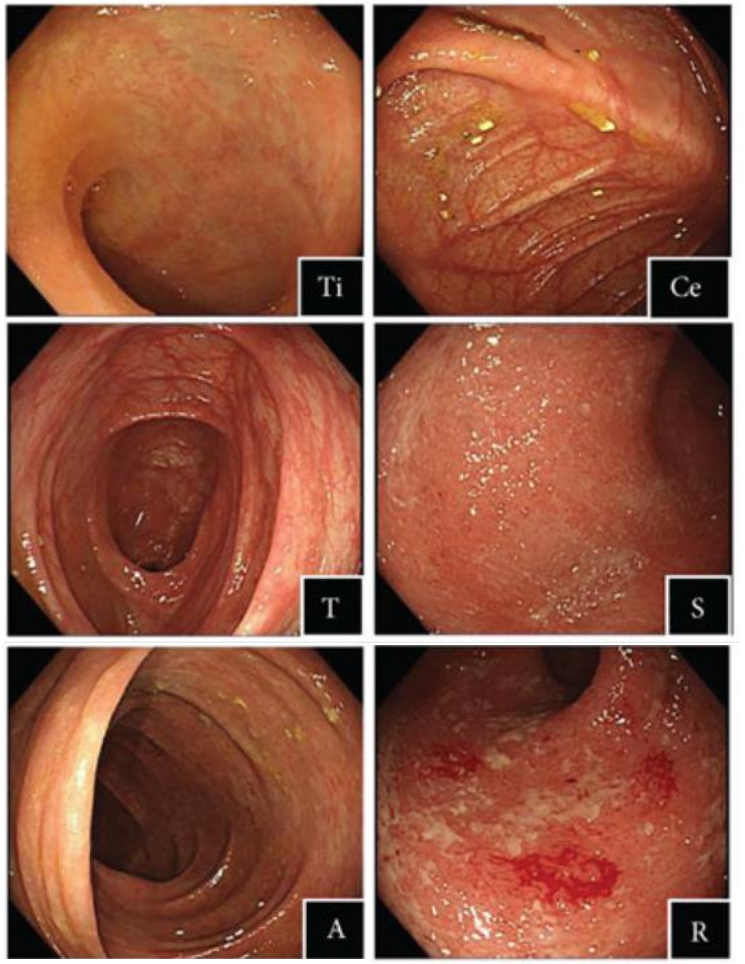
Joseph Sleiman, MD – IBD fellow at Cleveland Clinic, Cleveland, OH

Meet John

- **32-year-old obese male with a new onset of bloody diarrhea, abdominal pain, and tenesmus for the past three months.**
- Initially experienced loose stools (~5-6 per day) with occasional blood, but progressively worse despite dietary modifications.
- **Past Medical History:** No prior gastrointestinal disease. BMI 34.
- **Family History:** No family history of inflammatory bowel disease (IBD). Mother with diabetes.
- **Social History:** Smoker, occasional alcohol use, no recent travel or infections.

Diagnostic Workup

- **Colonoscopy Findings:** Diffuse erythema, friability, and superficial ulcerations extending from the rectum to the mid-descending colon.
- **Biopsy Results:** Crypt abscesses, crypt architectural distortion, and mucosal inflammation consistent with **chronic moderately severe inflammation.**
- **Fecal Calprotectin:** Elevated 5,756 µg/g
- **C-reactive Protein (CRP):** 6.2 mg/L
- **Hemoglobin:** 11 g/dL, MCV 70
- **Stool Cultures:** Negative for infectious causes.



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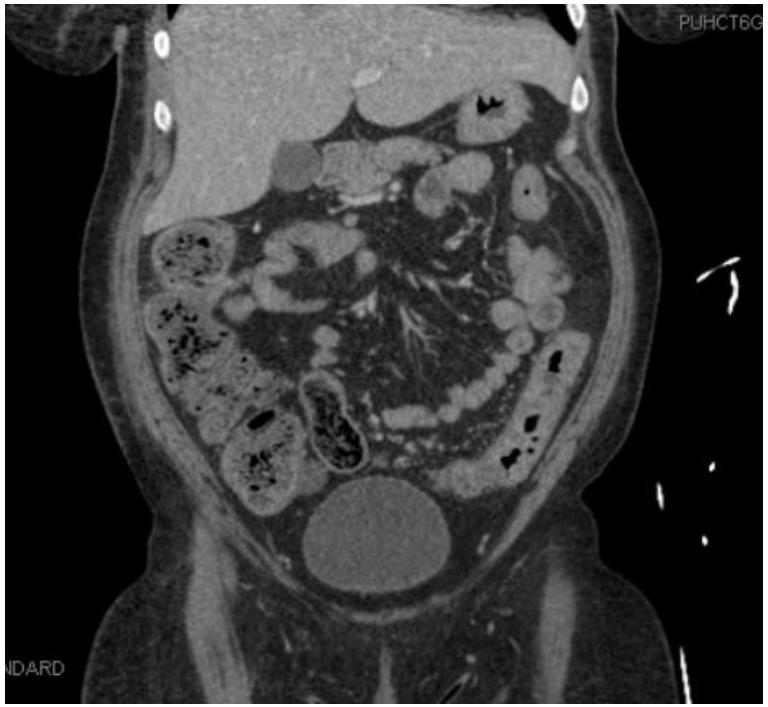
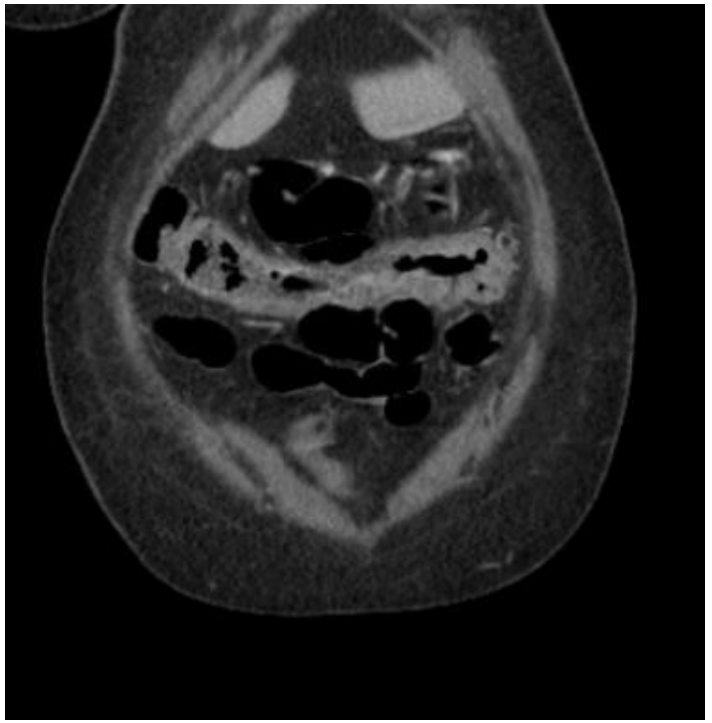
CT Scan





Evidence of thickening in his sigmoid and transverse colon, but not right colon

Question

John expresses wishes for a safe and effective oral therapy, given his busy life schedule. He heard about etrasimod and is wondering if it is a good option.

- How do you counsel patients when considering etrasimod? Is this an appropriate therapy for this patient?
- What other past medical history do you care to know for this particular agent?

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THE LANCET

Etrasimod as induction and maintenance therapy for ulcerative colitis (ELEVATE): two randomised, double-blind, placebo-controlled, phase 3 studies

William J Sandborn, Séverine Vermeire*, Laurent Peyrin-Biroulet, Marla C Dubinsky, Julian Panes, Andres Yarur, Timothy Ritter, Filip Baert, Stefan Schreiber, Sheldon Sloan, Fabio Cataldi, Kevin Shan, Christopher J Rabbat, Michael Chiorean, Douglas C Wolf, Bruce E Sands, Geert D'Haens, Silvio Danese, Martina Goetsch, Brian G Feagan*

Lancet 2023; 401: 1159-71.

New Therapy: Etrasimod

- **Title**:
  - Estrasimod (2mg daily) as Induction and Maintenance Therapy for UC (ELEVATE UC 12 and 52)
- **Mechanism of action:**
  - Sphingosine-1-phosphate receptor molecule (S1P): partially and reversibly blocks the trafficking of lymphocytes from lymphoid organs to the peripheral blood and appears to minimize lymphocyte mobilization to inflammatory sites.
- **Route of administration:**
  - Oral, with no dose escalation protocol needed (compared to ozanimod)
- **Key takeaway:**
  - Etrasimod can be used to treat patients with moderate to severe UC

Sandborn, et al. *Lancet*. 2023

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Etrasimod: Study Design

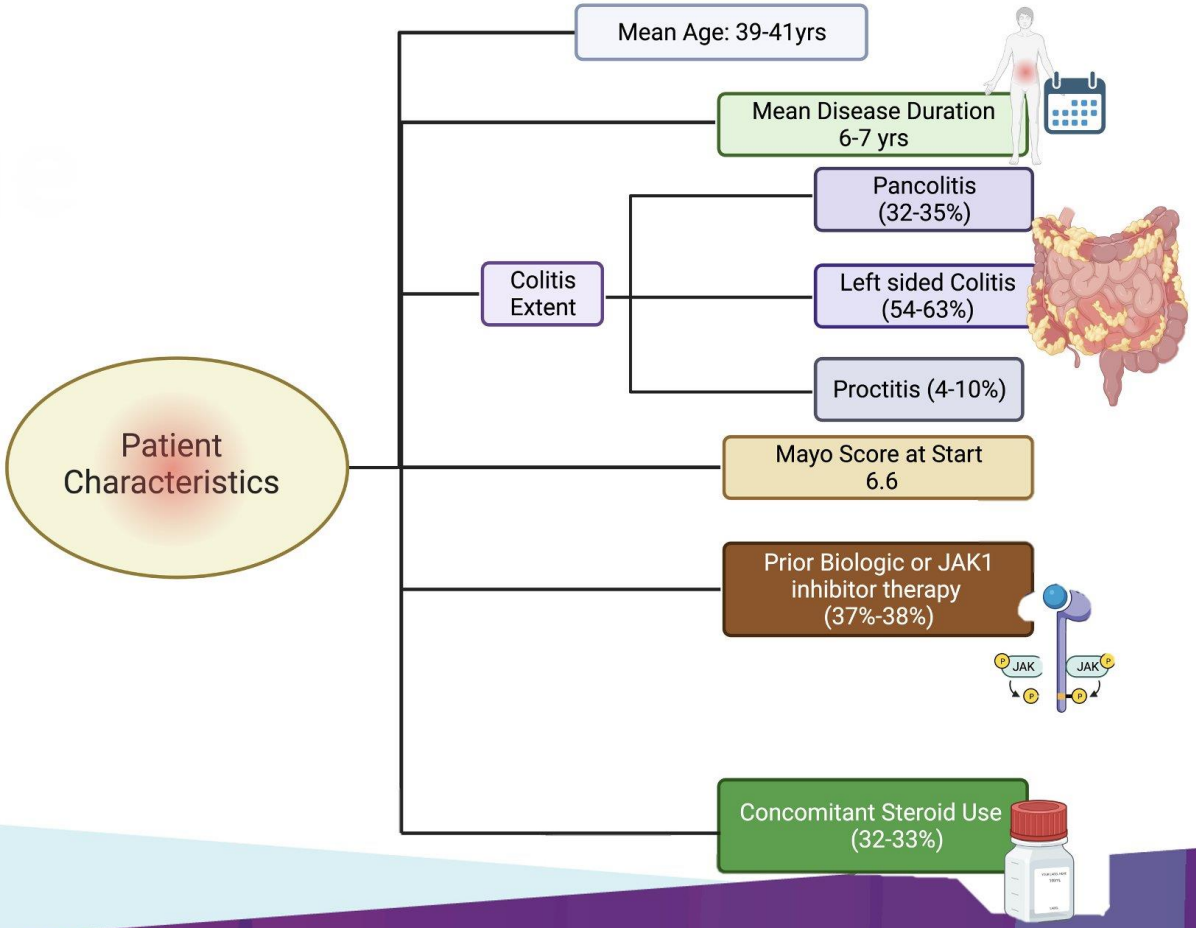
- **Study type:** randomized, double-blind placebo-controlled
- **Population**: moderate to severely active UC (modified Mayo Score of 4-9 with endoscopic subscore of >2, rectal bleeding subscore >1)
  - Refractory to at least one **(but not ≥3)** UC therapy (biologic or JAK inhibitor)
  - Patients with isolated proctitis (<10 cm of rectal involvement) were also enrolled.
- **Intervention**:
  - UC-12 induction study: **Treat through design***, assigned 2:1 therapy vs placebo
    - 238 estrasimod, 116 placebo
  - UC-52 maintenance study: **Treat through design**, assigned 2:1 therapy vs placebo
    - 289 etrasimod, 144 placebo
- **Outcomes**:
  - Primary: clinical remission at weeks 12 and 52
  - Secondary: symptomatic remission, endoscopic improvement, HEMI, sustained clinical remission, corticosteroid-free clinical remission

*patients were not re-randomized to etrasimod or placebo based on clinical response/remission after 12 weeks

EVIDENCE-BASED GI
AN ACG PUBLICATION
Clinical take-aways and evidence-based summaries of articles in GI, Hepatology & Endoscopy

Etrasimod, a Sphingosine 1-Phosphate Receptor Modulator, for Moderate-Severe Ulcerative Colitis: New Options for Oral Therapy.

Summary of: Sandborn WJ, Vermeire S, Peyrin-Biroulet L, et al. Lancet 2023; 401: 1159-71.

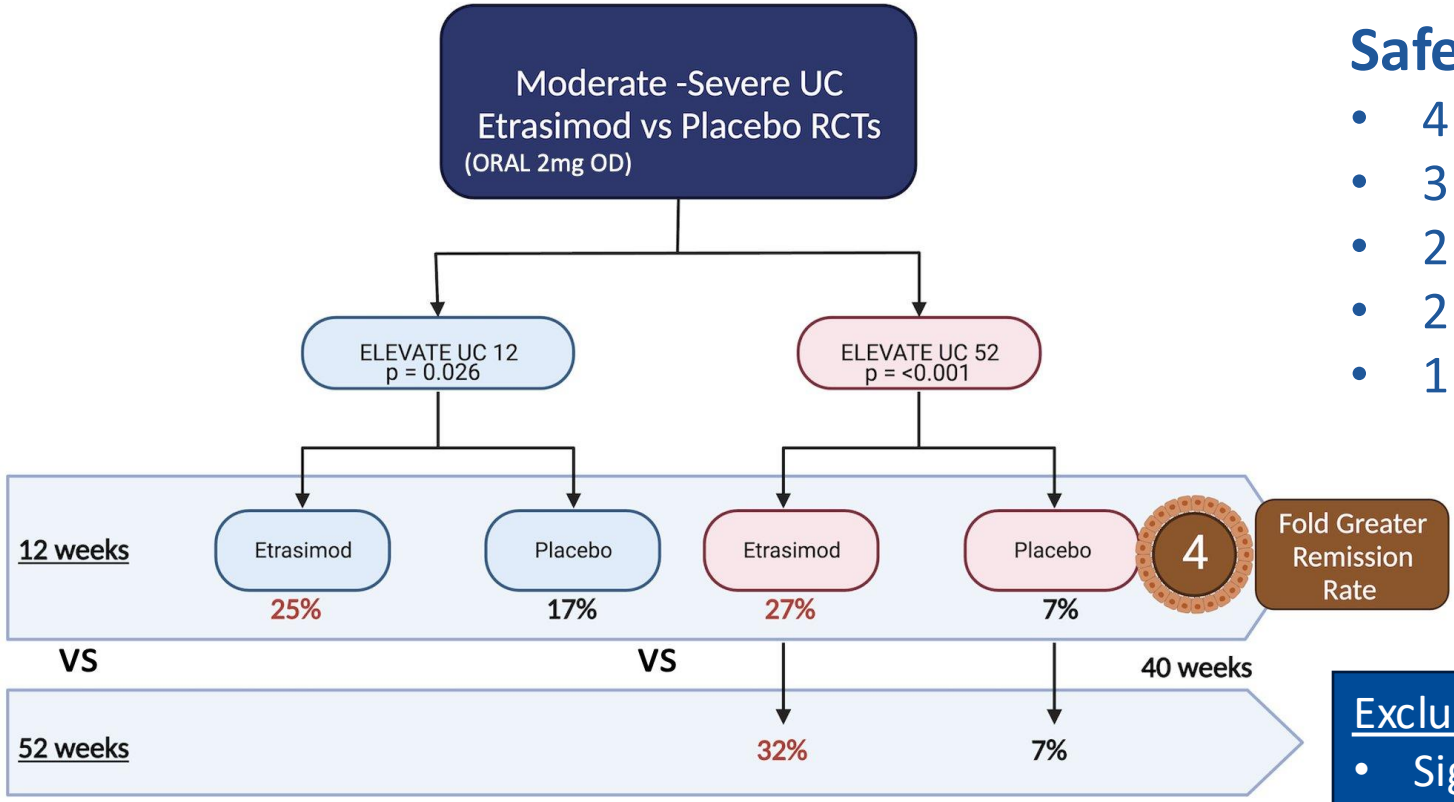


Patient Characteristics

EVIDENCE-BASED GI
AN ACG PUBLICATION
Clinical take-aways and evidence-based summaries of articles in GI, Hepatology & Endoscopy

Etrasimod, a Sphingosine 1-Phosphate Receptor Modulator, for Moderate-Severe Ulcerative Colitis: New Options for Oral Therapy.

Summary of: Sandborn WJ, Vermeire S, Peyrin-Biroulet L, et al. Lancet 2023; 401: 1159-71.



Safety Profile (N=527):

- 4 bradycardia
- 3 serious infections
- 2 arrhythmias
- 2 herpes zoster infections
- 1 macular edema

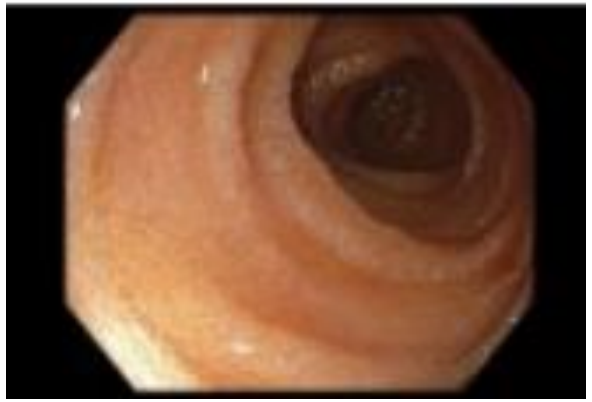
Key secondary endpoints also met (e.g. improvements in endoscopic outcomes, corticosteroid-free remission)

Exclusion criteria:

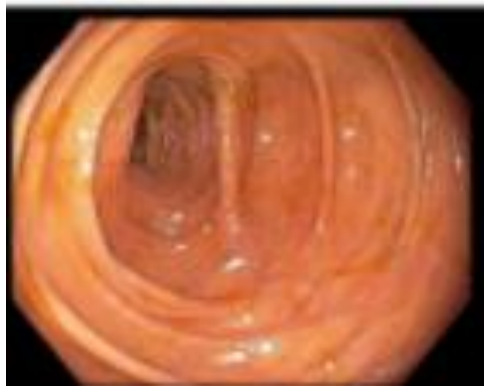
- Significant CV condition (e.g., MI, stroke, 2nd/3rd degree AV block)
- H/o opportunistic infections
- H/o macular edema
- Pregnancy or lactation

Case Continues

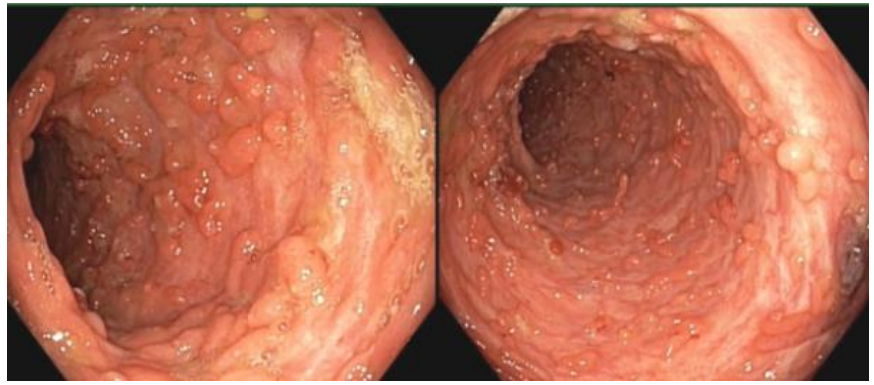
Patient with complete resolution of symptoms at week 16. **Fecal calprotectin 300**. Thoughts?



Ileum



ascending colon



descending colon

sigmoid

- No active disease in the entire colon and ileum.
- Pseudopolyps at the hepatic flexure and sigmoid.

Overcoming Barriers to Care: Step-Edits, Prior Authorizations, and Prescription Coverage

Joseph Sleiman, MD – IBD fellow at Cleveland Clinic, Cleveland, OH

Meet Cassandra

- 36-year-old male with **moderate ulcerative colitis**, steroid-dependent but reluctant to start injectable biologics due to needle phobia.
- **Treatment History:** The patient had non-response to corticosteroids, immunomodulators (azathioprine) and ozanimod. We discussed trial of tofacitinib.

Insurance Obstacles:

1. **"Experimental" Labeling:** The insurance company argued that **tofacitinib was not a first-line treatment** despite its FDA approval for moderate-severe UC.
2. **Formulary Exclusion:** tofacitinib was **not covered under the patient's plan**, and the insurance recommended mesalamine or a TNF inhibitor instead.
3. **Cost Barrier:** The out-of-pocket cost was **$8,000 per month** without insurance coverage.

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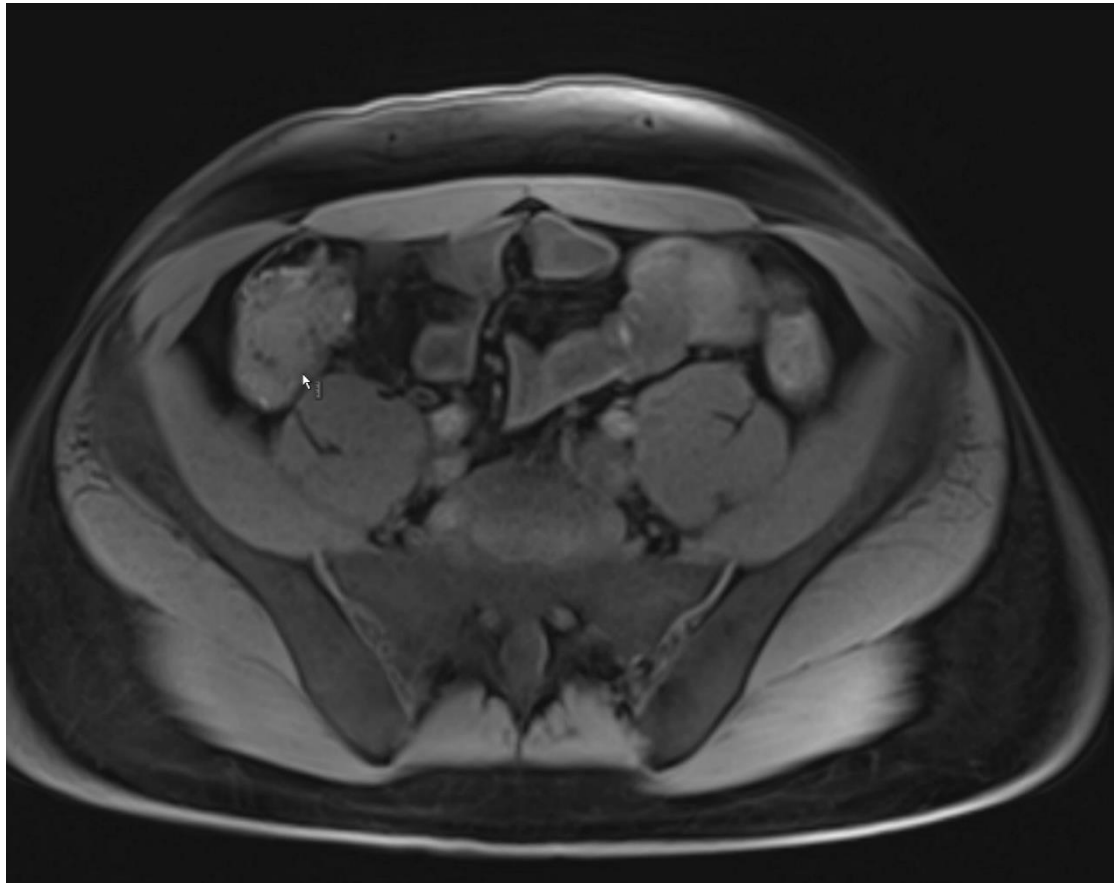
Resolution

- **File formal appeal** citing American College of Gastroenterology guidelines and the patient's severe needle phobia, which made biologics impractical.
- First appeal was denied → initiated a **compassionate-use request** through the drug manufacturer's assistance program.
- After five weeks, the insurance finally approved tofacitinib under a **tier exception** after the demonstration that mesalamine had failed and that an oral advanced therapy was the best alternative.

Outcome:
The patient started tofacitinib but **suffered prolonged steroid exposure** while waiting, leading to side effects like insomnia, weight gain, and hypertension.

Case 3: Georges

- Dx w/ small bowel Crohn's disease at 25 (2020).
- Was on Adalimumab from 2021 to 2023, discontinued due to secondary loss of response (recurrent frequent flares, generally requiring prednisone).
- **MRI 11/2022**: A long segment of inflammatory bowel in the proximal ileum. A short segment of chronic inflammatory bowel disease with signs of active inflammation in the distal ileum with attendant stricture and pre-stenotic dilatation.
- **Colonoscopy 1/2023:** patchy aphthous ulcerations and erythema in the terminal ileum.
- Decision to switch to risankizumab in May 2023 with symptomatic improvement.
- **Colonoscopy 5/2024:** mild active ileitis.
- **Moved to OHIO state**



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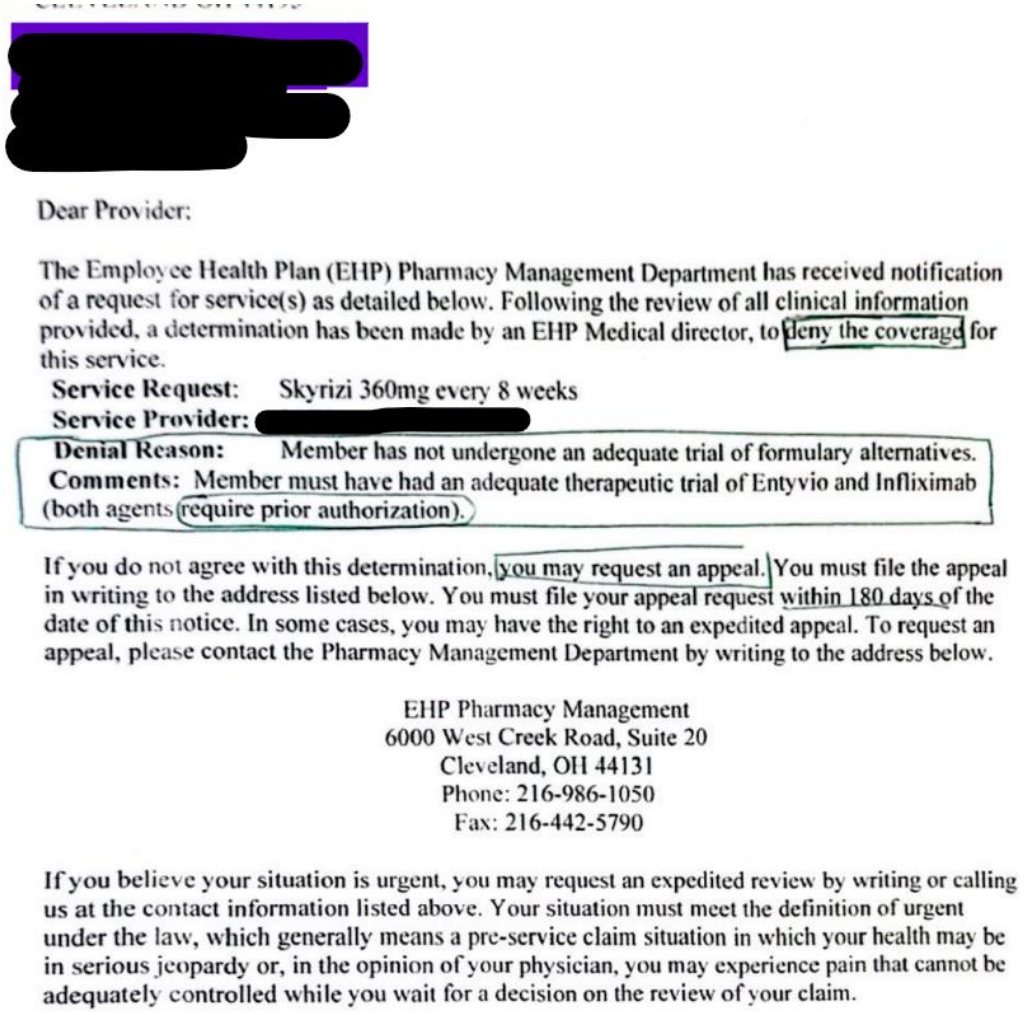
Insurance Denial



[redacted]

Dear Provider:

The Employee Health Plan (EHP) Pharmacy Management Department has received notification of a request for service(s) as detailed below. Following the review of all clinical information provided, a determination has been made by an EHP Medical director, to deny the coverage for this service.

Service Request: Skyrizi 360mg every 8 weeks
Service Provider: [redacted]
Denial Reason: Member has not undergone an adequate trial of formulary alternatives.
Comments: Member must have had an adequate therapeutic trial of Entyvio and Infliximab (both agents require prior authorization).

If you do not agree with this determination, you may request an appeal. You must file the appeal in writing to the address listed below. You must file your appeal request within 180 days of the date of this notice. In some cases, you may have the right to an expedited appeal. To request an appeal, please contact the Pharmacy Management Department by writing to the address below.

EHP Pharmacy Management
6000 West Creek Road, Suite 20
Cleveland, OH 44131
Phone: 216-986-1050
Fax: 216-442-5790

If you believe your situation is urgent, you may request an expedited review by writing or calling us at the contact information listed above. Your situation must meet the definition of urgent under the law, which generally means a pre-service claim situation in which your health may be in serious jeopardy or, in the opinion of your physician, you may experience pain that cannot be adequately controlled while you wait for a decision on the review of your claim.

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Appeal

URGENT APPEAL & REQUEST FOR EXPEDITED REVIEW

To whom this may concern:

On behalf of this patient [redacted] who is under the care of Dr [redacted], I am writing this letter to document the medical necessity of administering Skyrizi subcutaneous on-body injector at the dose of 360 mg every 4 weeks. Nicholaus is being treated for inflammatory bowel disease, specifically stricturing ileal Crohn's disease in the [redacted]

[redacted] has already been receiving Skyrizi treatment under a previous insurance plan. This therapy was started in May of 2023. He has been receiving his injections on an 8-week basis and has had positive clinical response to these infusions and tolerated them without side effects. He has done well with complete symptom control. Unfortunately, his most recent colonoscopy (5/2024) did indicate that he has developed new, mild disease activity. In addition to this, several previous MRe scans show evidence of a stricture in the distal/terminal ileum. This has remained stable and unchanged since initial discovery in 2021. Given that he has otherwise done very well on his current Skyrizi therapy up to this point, we would like to keep him on a medication that we know has improved his disease (Skyrizi) but increase the frequency to keep his current mild ileitis and existing TI stricture from worsening.

As stated in the denial, you are requesting him to attempt therapy with Entyvio and Infliximab prior to starting Skyrizi. Under his previous care provider, patient was on Humira from 2021-2023, but had to change therapy d/t medication intolerance and inadequate disease control which required frequent use of steroids. It was at that time that he switched to Skyrizi. We would like to avoid attempting Infliximab at this time, as he has already tried and failed a medication within the same drug class, giving us reason to question a similar drug's efficacy on his disease. We would prefer to avoid stopping his current Skyrizi therapy and switching to Entyvio, as we know that thus far, Skyrizi has been beneficial for him. We feel we should continue to use Skyrizi for as long as we see good response and symptom control in patient. If his disease were to continue to worsen with the increased Skyrizi dosage frequency (Q4 weeks instead of Q8 weeks), we would then consider Entyvio and/or Infliximab as a complete change in his medication therapy. However, at this time, we feel strongly that we should continue to use the treatment that has thus far proven to be effective for his disease for the last 18+ months.

[redacted]

1/2

I am requesting you overturn this denial with a request for expedited review so he does not experience a delay in treatment and risk loss of response to the medication. Breaks in therapy or cessation of effective therapy does place patient at an increased risk of worsening disease, hospital admission, or necessity of surgical intervention.

Skyrizi has proven efficacy for moderate-severe refractory Crohn's disease, & long-term treatment with above maintenance dosing has been well tolerated by patients (Ferrante et al., 2021). Furthermore, Skyrizi has been shown to be more effective in inducing disease remission after a failed anti-TNF medication when compared to Entyvio (Singh, 2021). I am confident that you will agree and approve the requested medical therapy which is in the best interest of this patient. Please do not hesitate to contact me if I can provide additional information.

Sincerely,

[redacted]

(Signed electronically to expedite care)

References:

Ferrante M, Feagan BG, Panés J, Baert F, Louis E, Dewit O, Kaser A, Duan WR, Pang Y, Lee WJ, Gustafson D, Liao X, Wallace K, Kalabic J, D'Haens GR. Long-term safety and efficacy of risankizumab treatment in patients with Crohn's Disease: Results from the phase 2 open-label extension study. *J Crohns Colitis*. 2021 Dec 18; 15(12): 2001-2010. doi: 10.1093/ecco-jcc/jjab093. PMID: 34077509; PMCID: PMC8684487.

Singh S, Murad MH, Fumery M, Sedano R, Jairath V, Panaccione R, Sandborn WJ, Ma C. Comparative efficacy and safety of biologic therapies for moderate-to-severe Crohn's disease: A systematic review and network meta-analysis. *Lancet Gastroenterol Hepatol*. 2021 Dec; 6(12): 1002-1014. doi: 10.1016/S2468-1253(21)00312-5. Epub 2021 Oct 22. PMID: 34688373; PMCID: PMC8933137.

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APPEAL denied again

What are your next steps from here?

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Hot Topics in IBD Management: Avoiding Pitfalls

Stephen B. Hanauer, MD

Professor of Medicine

Medical Director, Digestive Health Center

Northwestern University Feinberg School of Medicine

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Relevant Conflicts

- Abbvie
- BMS
- Johnson & Johnson (Janssen)
- Lilly
- Merck
- Celltrion
- Pfizer
- Takeda

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Moderate-Severe Disease Can be Diagnosed at Presentation

Ulcerative Colitis

Risk for Colectomy

Extensive colitis

Deep ulcers

Age <40

High CRP and ESR

Steroid-requiring disease

History of hospitalization

Clostridium difficile infection

CMV infection

Crohn's Disease

Risk for Progression

Age at dx <30 yrs

Extensive anatomic involvement

Ileal/Ileocolonic involvement

Perianal/severe rectal disease

Deep ulcers

Previous surgical resection

Stricturing/penetrating behavior

Moderate-Severe Disease can be Diagnosed at Presentation!

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Adapted from Dassopoulos T, et al. *Gastroenterology*. 2015;149:238-245; Sandborn WJ. *Gastroenterology*. 2014;147:702-705.

The FDA regulates marketing of drugs, not clinical practice. Practice is monitored by Standards of Care.

- The FDA *does not regulate the practice of medicine*, medical services, the price or availability of medical products and whether they are reimbursed by health insurance or Medicare

- **"Generally accepted standards of medical practice"** means: Standards based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community. Physician and Health Care Provider Specialty Society recommendations.

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Network Meta-analyses and Post-hoc analyses are hypotheses, not the “truth”

- Maintenance Azathioprine
- Combination therapy (IFX + AZA)
- Mesalamine after advanced agents in UC

Management of ASUC is Evolving

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Evolution of “Oxford Protocol”

- 3-5 Days of IV steroids whether or not failing oral steroids
- 3-5 Days of IFX or CYS
  - Mostly IFX due to limited experience and monitoring
  - Accelerate dosing for patients with Albumin <3

- If inadequate response to IFX consider high dose JAK
  - Tofa 15mg bid or UPA 30mg bid

Patients Hospitalized Already on TNFi

- Consider higher dose JAK on Admission

- Hyperbaric Oxygen trial available at Lake Forest via Northwestern NIH protocol (contact Parambir Dulai, parambir.dulia@northwestern.edu)

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Surgery is NOT a Failure or "Last Resort" in Crohn's Disease

- Short-resections restore QOL
- Don't Start Biologics for/with Stricturing Disease
  - Consider Resection for 1^0 or 2^0 Non-Response before 2^{nd} Biologic

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2 Evolving Scenarios

- Patient with disease not responding to 1 or 2 Advanced Agents
  - Likelihood of remitting after 2nd or 3rd advanced agent <50%
  - Likelihood of preventing recurrence after resection 80% (with post-op monitoring)

2nd Scenario Newly diagnosed with short-segment ileal disease

- **Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease**
- LIR!C study is a multicentre, randomised controlled, open-label, parallel group trial done at 29 teaching hospitals and tertiary care centres in the Netherlands and the UK
- 143 patients (47 [33%] male) with a median age of 27 years (IQR 22–40) were enrolled and randomly assigned to either infliximab (n=70) or resection (n=73)

Ponsioen CY, et al. *Lancet Gastroenterol Hepatol*. 2017;2:785-792.

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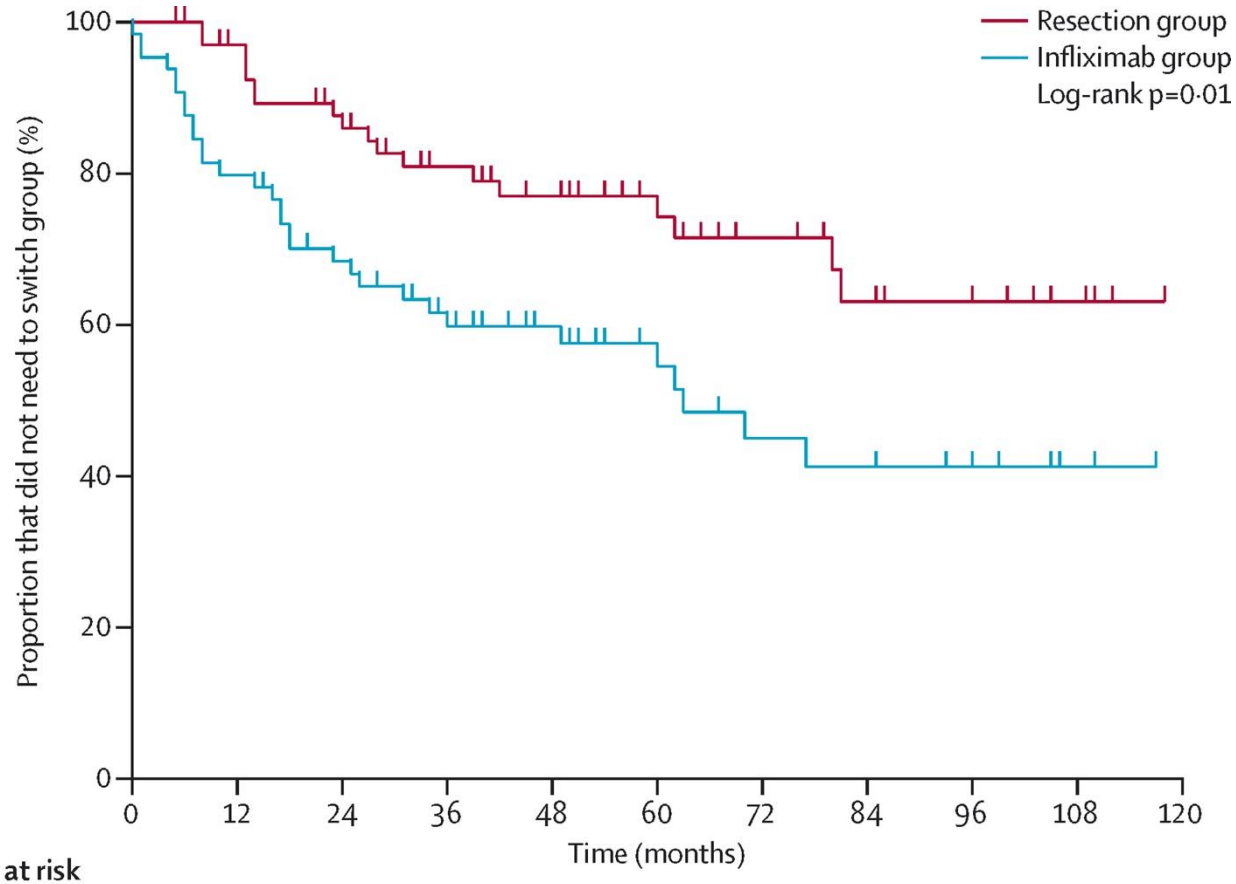
LIR!C study:
Early ileocecal resection vs. infliximab in Crohn's disease



Number at risk (number censored)											
Resection group	69 (0)	63 (4)	54 (7)	43 (14)	37 (18)	28 (27)	20 (33)	14 (37)	12 (39)	6 (45)	0 (51)
Infliximab group	65 (0)	50 (2)	41 (4)	34 (7)	27 (13)	19 (20)	12 (23)	11 (23)	9 (25)	6 (31)	0 (34)

Ponsioen CY, et al. *Lancet Gastroenterol Hepatol*. 2017;2:785-792.

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Selecting drugs for moderate-severe disease is less evidence driven than selections based on gender/age/co-morbidities

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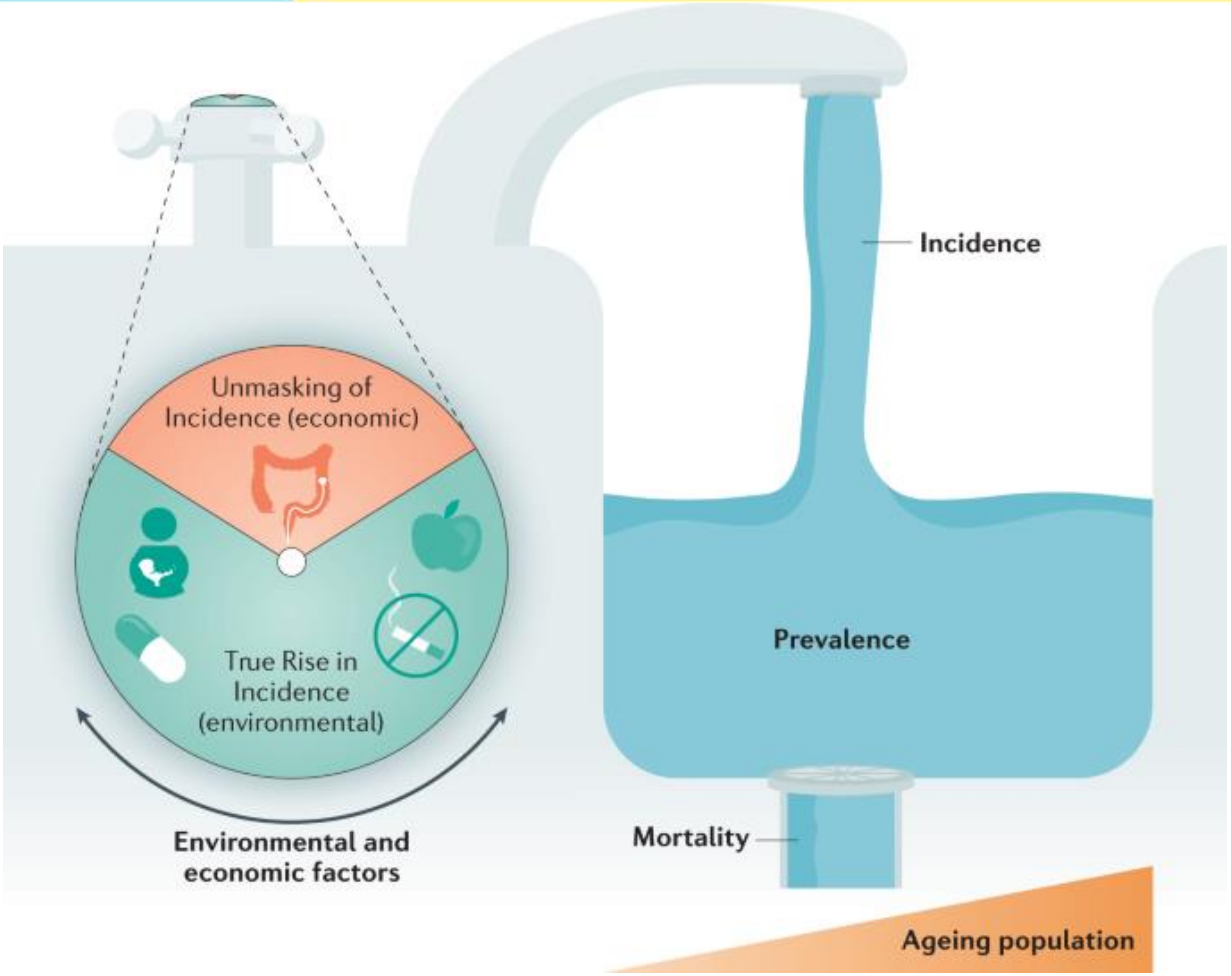
The interplay and determinants of IBD incidence, prevalence and mortality



Aging Population= Co-Morbidities !

Kaplan GG, Windsor JW. *Nat Rev Gastroenterol Hepatol*. 2021;18:56-66.

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Chronic disease activity is greater risk for cardiovascular disease than any IBD therapy

Jaiswal V, et al. *Medicine (Baltimore)*. 2023;102(6):e32775; Willerson JT, Ridker PM. *Circulation*. 2004;109(21 Suppl 1):II2-II10.

A Few Other Comments

- Recognize when perfect is the enemy of good (TTT can go too far)
- Continue biologics in pregnancy — “Healthy Mom = Healthy Baby”
- Don’t move to maintenance before achieving induction!
- Positioning advanced therapies for EIMs — “JAKs for joints, ILs for skin”
- Try vancomycin for ulcerative colitis (and pouchitis) with PSC
- TNFi + thiopurine combination for high-risk Crohn's ds, e.g. fistula, upper GI tract
- TDM only for TNFis?
- What me worry? Biosimilars now include Ustekinumab

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Questions & Answers

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Wrap-Up and Thank You

Philip Schoenfeld, MD

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EBMed's Great GI Debates: See You Next Year!

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