Helicobacter Highlights

A Case-Based Review of the ACG Guidelines

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Patient Case

A 43-year-old man has been experiencing dyspepsia for 8 months, characterized by postprandial burning in the epigastrium, but without retrosternal burning or regurgitation. He reports no nausea, vomiting, unintended weight loss, or rectal bleeding. Labs do not show anemia, abnormal liver tests, or other biochemical abnormalities. Which of the following is the most appropriate next step?

A. Start 4-week trial of once-daily PPI therapy
B. Refer for upper endoscopy
C. Test for *H. pylori* and treat if positive
D. Start a tricyclic antidepressant
E. Start metoclopramide

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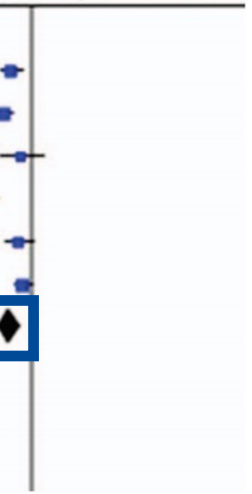
Meta-Analysis: *H. pylori* Test and Treat vs. Placebo

Study or Subgroup	PPI Events	PPI Total	Antacide/alginate Events	Antacide/alginate Total	Weight	Risk Ratio M-H, Random, 95% CI	Year	Risk Ratio M-H, Random, 95% CI
1.1.1 Global assessment of dyspepsia (primary outcome most stringent definition of Not symptom-free)								
Meineche-Schmidt 1997	136	273	173	266	17.4%	0.77 [0.66, 0.89]	1997	
Goves 1998	197	333	285	337	18.9%	0.70 [0.63, 0.77]	1998	
Rabeneck 2002	37	71	41	69	12.0%	0.88 [0.65, 1.18]	2002	
Meineche-Schmidt 2004	196	556	177	272	17.6%	0.54 [0.47, 0.62]	2004	
Veldhuyzen van Zanten 2005	75	135	87	133	15.7%	0.85 [0.70, 1.03]	2005	
Baysal 2015	102	132	114	132	18.5%	0.89 [0.80, 1.00]	2015	
Subtotal (95% CI)		**1500**		**1209**	**100.0%**	**0.75 [0.64, 0.88]**		
Total events	743		877					
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 34.83$, df = 5 ($P < 0.00001$); $I^2 = 86\%$								
Test for overall effect: Z = 3.49 (P = 0.0005)								



Moayyedi, et al. AJG 2017; 112: 988-1013

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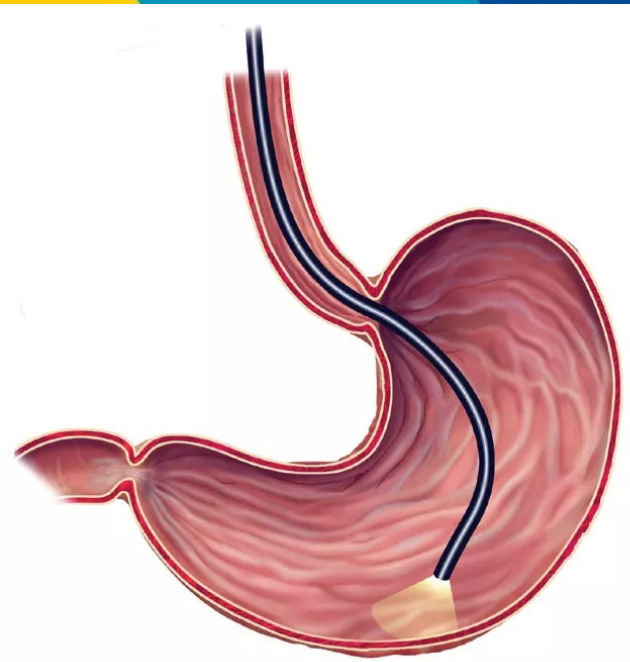
Why Not Perform an EGD?

- ACG dyspepsia guidelines recommend EGD only if ≥60-years-old or in the presence of alarm features
- When gastric cancer is cause of dyspepsia, it tends to already be stage IV
- Caveat: higher risk individuals (e.g., born in Southeast Asia, positive family history) may require earlier EGD



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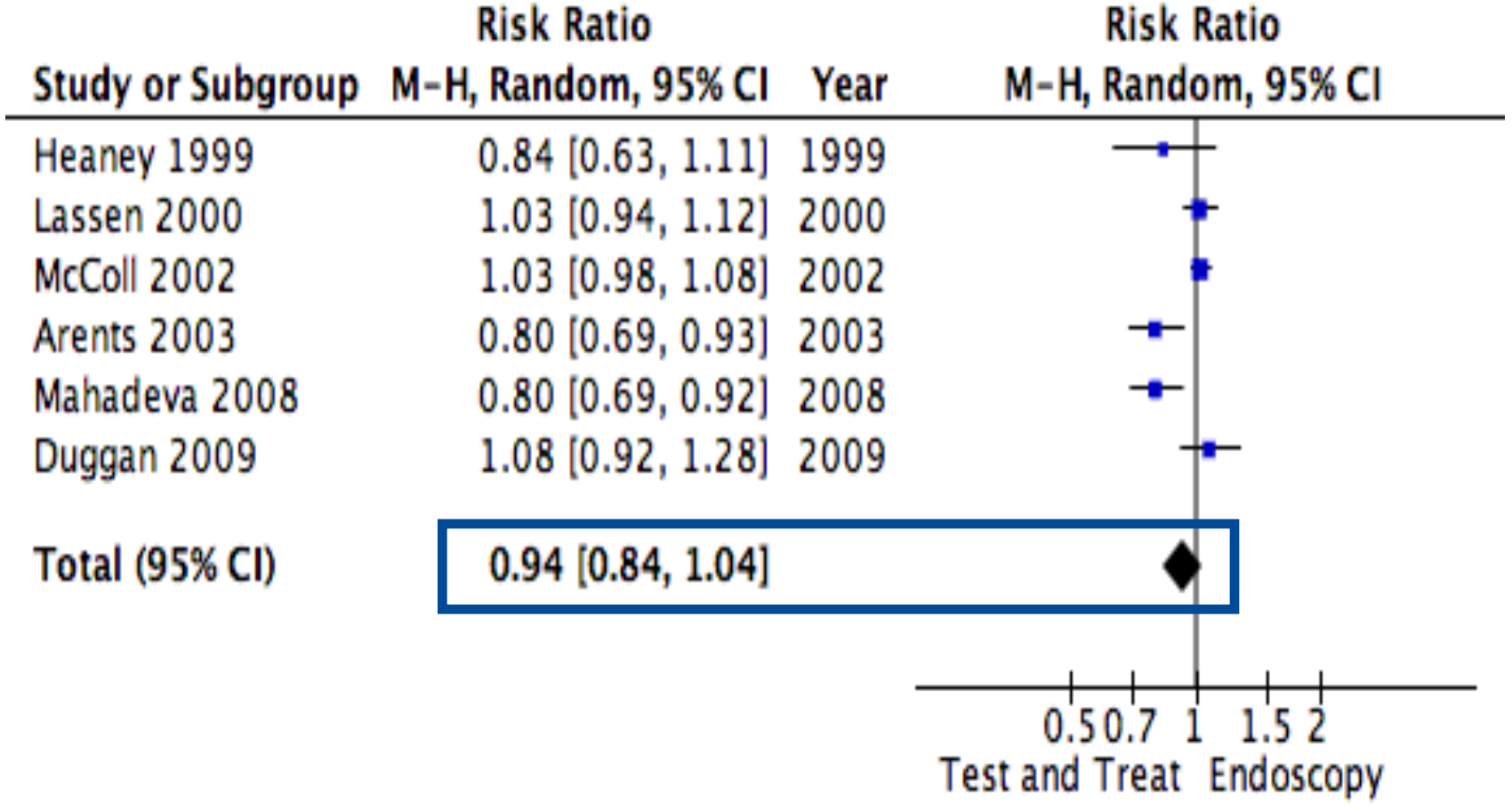
Meta-Analysis: *H. pylori* Test and Treat vs. Early Endoscopy



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Patient Case – Continued

A stool antigen test for *H. pylori* returns positive. The patient has never been previously tested or treated for *H. pylori*, has no recent antibiotic exposures, and is not allergic to penicillin. Which of the following do the 2024 ACG guidelines recommend as the most appropriate therapy?

A. Bismuth, metronidazole, doxycycline, omeprazole x 10 days
B. Bismuth, metronidazole, tetracycline, omeprazole x 10 days
C. Bismuth, metronidazole, doxycycline, omeprazole x 14 days
D. Bismuth, metronidazole, tetracycline, omeprazole x 14 days
E. Metronidazole, clarithromycin, omeprazole x 14 days
F. Rifabutin, Amoxicillin, omeprazole x 10 days

H. pylori Treatment Regimens

Key Points

- Bismuth-based quadruple therapy first line (87% eradication)
- Avoid doxycycline (higher efficacy with tetracycline)
- Always 14 days (not 10 days)
- Rifabutin triple is acceptable but lower quality of evidence
- Minimize use of macrolides and levofloxacin
- Potassium-competitive acid blocker (PCAB) can boost antibiotic efficacy

Patient Case – Continued

The patient receives BQT therapy for 14 days. The epigastric pain moderately improves during the treatment period, but then returns within a week of completing therapy.

→ Why did the symptoms improve and then worsen again?
→ Should you confirm HP cure? If so, how?

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Confirming Cure

- All patients receiving HP treatment should have cure confirmed
  (not just for MALT, or a bleeding peptic ulcer, but for everyone)
- Confirm cure with active test: stool antigen, urea breath test, gastric biopsy
- Wait 4 weeks after ending antibiotics and bismuth
- Discontinue PPIs for at least 2 weeks before testing
- Do not use serological studies

Patient Case – Continued

You check a stool antigen test with the patient off PPI therapy and discover that it's still positive. The patient also continues to report persistent meal-related epigastric pain.

→How should you proceed?

Patient Case – Continued

The patient received a second-round treatment with a rifabutin-based triple therapy for 14 days. The dyspepsia persists, and *H. pylori* stool antigen testing, off PPIs, reveals persistent positivity.

→Now what?

Take Home Points

- Start with BQT for 14 days; it’s an all-around good bet
- Always confirm cure
- Consider rifabutin-based triple therapy for second round
- Minimize use of macrolides or levofloxacin in absence of susceptibility testing
- If you do use a macrolide, consider using a PCAB instead of a PPI

Chey, et al. 2024 ACG Guidelines (in press)

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Test Approach

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

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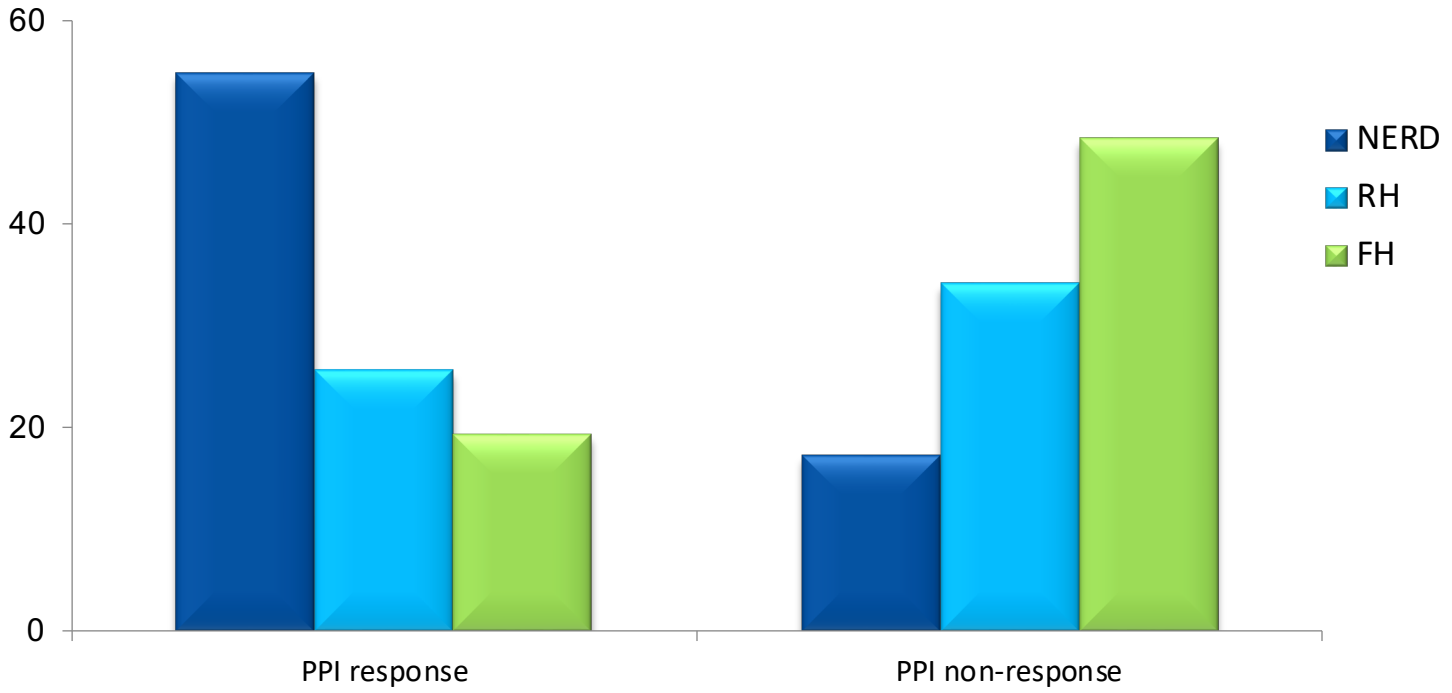
Typical Esophageal Symptoms: PPI Response

Current Standard: Empiric acid suppression

312 heartburn patients
endoscopy negative
PPI trial for 8 weeks
pH impedance testing off PPI

RH: reflux hypersensitivity
FH: functional heartburn



de Bortoli N, et al. *Neurogastroenterol Motil*. 2014;26:28-35.

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Response to Proton Pump Inhibitors

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

Gyawali CP, Fass R. *Gastroenterology*. 2018;154:302-318.

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Erosive esophagitis[3]	85.6	28.3	2.96 (2.14-4.11)	1.8

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Noncardiac chest pain, positive GERD testing[5]	42	20	4.3 (2.6-6.7)	4.5
Noncardiac chest pain, negative GERD testing[5]	11	24	0.44 (0.28-0.69)	7.7

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Noncardiac chest pain, negative GERD testing[5]	11	24	0.44 (0.28-0.69)	7.7
Chronic cough[6]	18.1	9.3	1.94 (0.87-4.34)	11.4
Laryngeal symptoms[7]	14.7	16	0.92 (0.41-2.05)	79.2

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Diagnostic Approach Based on Symptoms

Troublesome symptoms suspicious for GERD	Initial approach No alarm symptoms	Esophageal physiologic evaluation	Adjunctive approach
Typical: heartburn, regurgitation, esophageal chest pain	empiric trial of antisecretory therapy	endoscopy, wireless pH monitoring (preferred) or pH-impedance monitoring, HRM	postprandial HRIM, behavioral therapy for rumination
Atypical*: belching		endoscopy, pH-impedance monitoring, HRM	behavioral therapy for supragastric belching
Atypical*: chronic cough, asthma		endoscopy, pH-impedance or wireless pH monitoring, HRM	pulmonary evaluation***
Atypical**: hoarseness, globus, nausea, abdominal pain, dyspepsia		endoscopy, pH-impedance or wireless pH monitoring, HRM	laryngoscopy for throat symptoms***

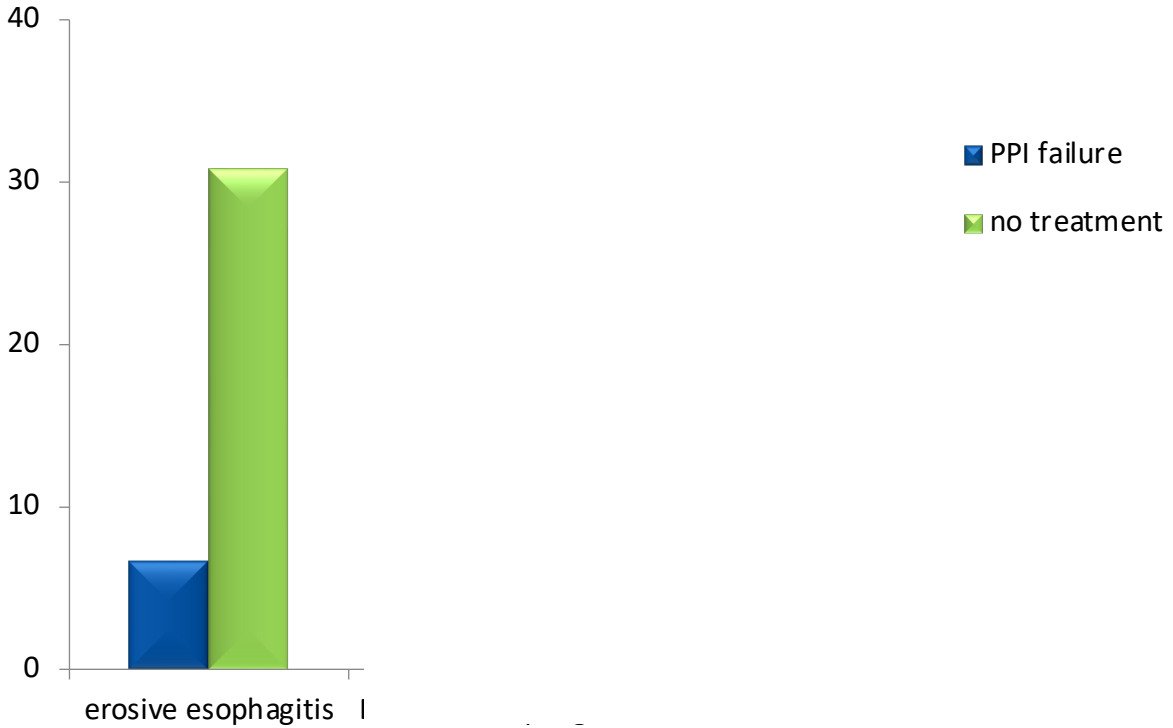
* likelihood of GERD is lower than with typical symptoms, testing is performed to identify or rule out a reflux basis for symptoms

** 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.

Value of Endoscopy



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

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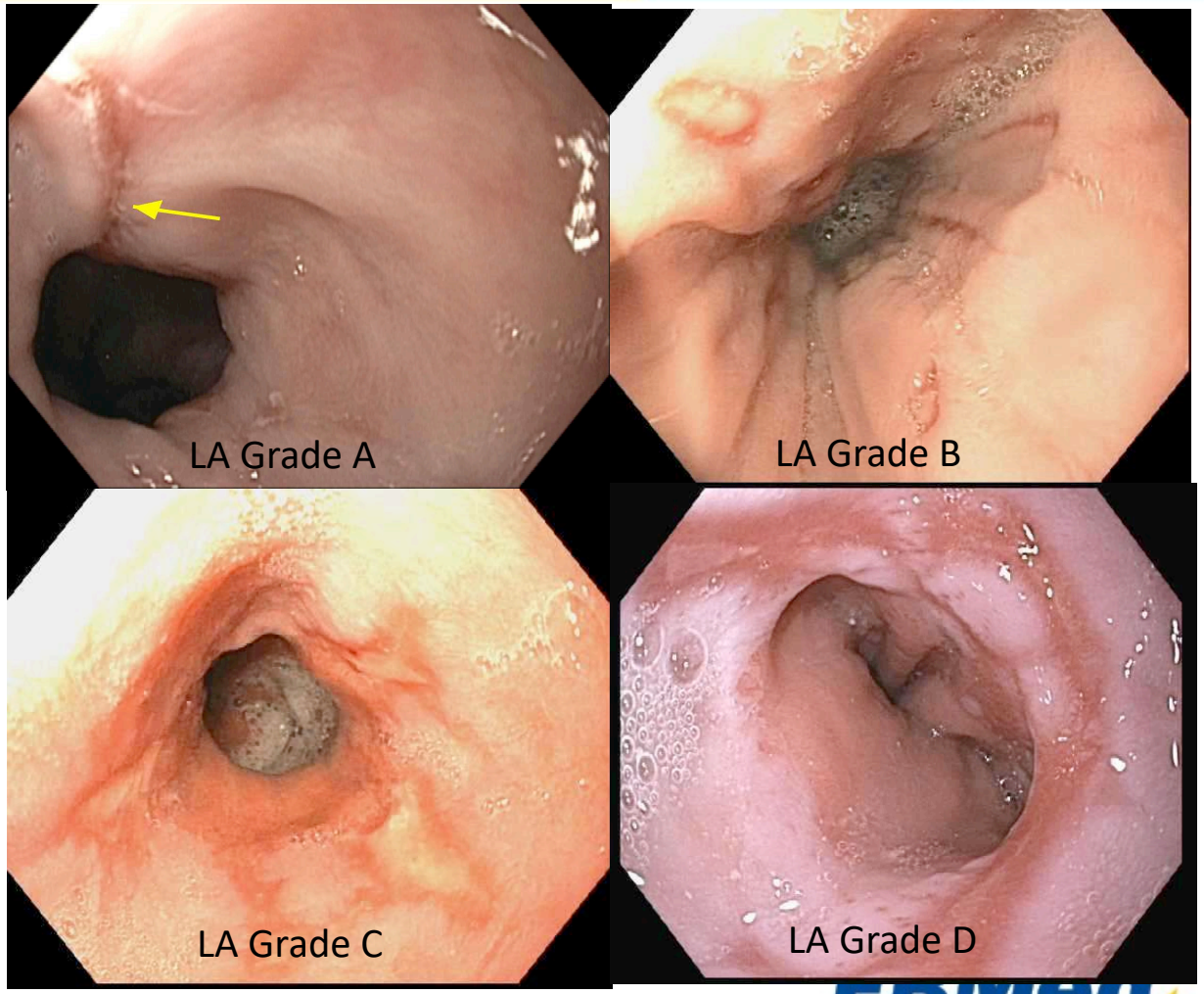

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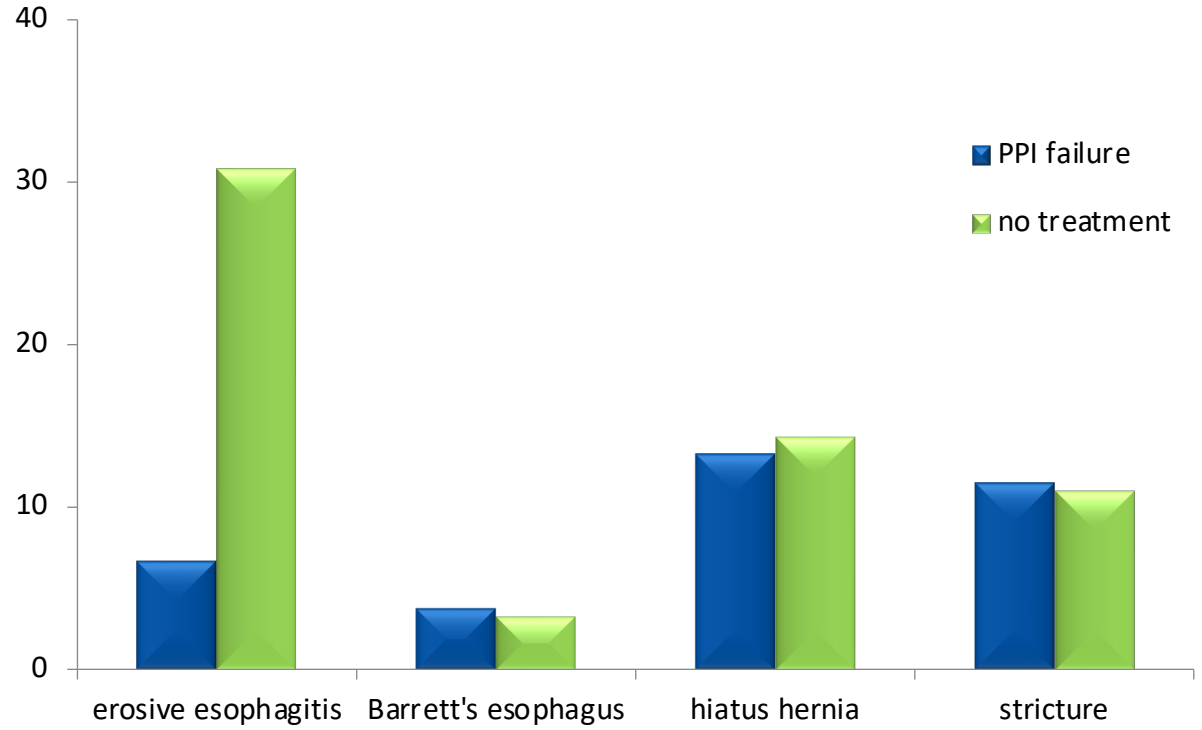

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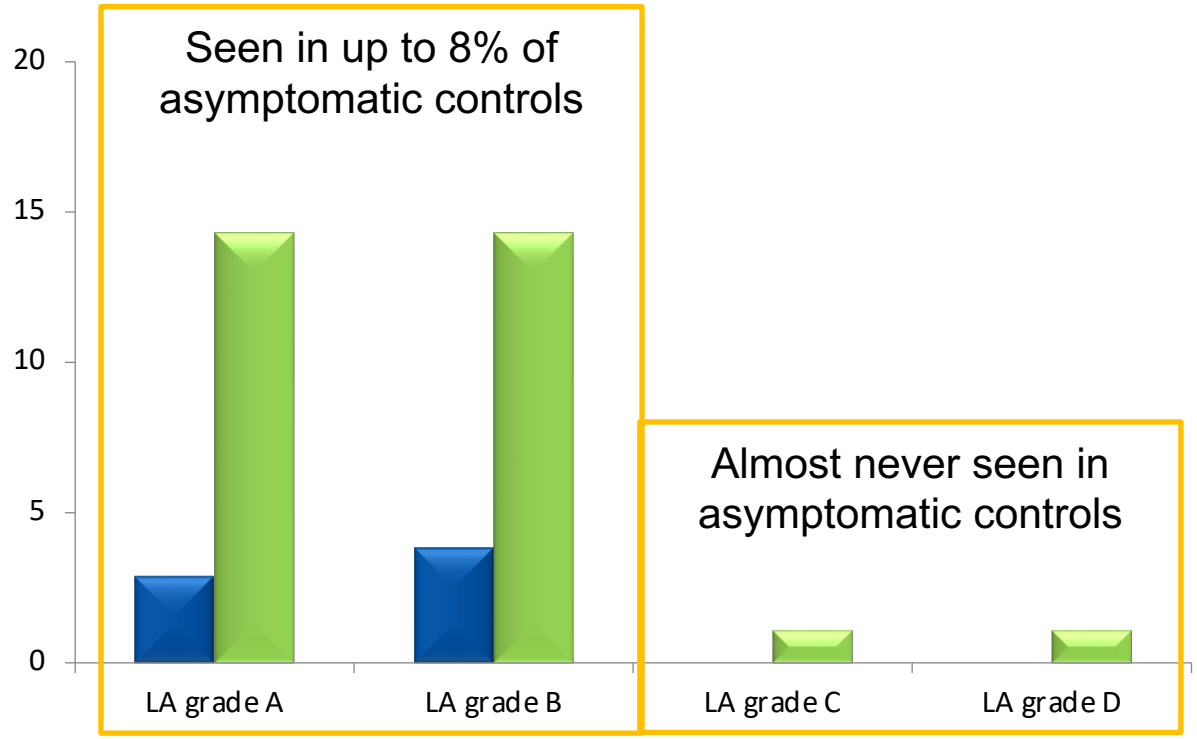

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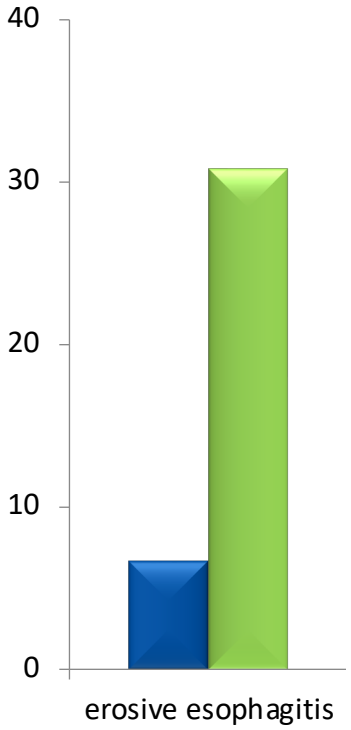

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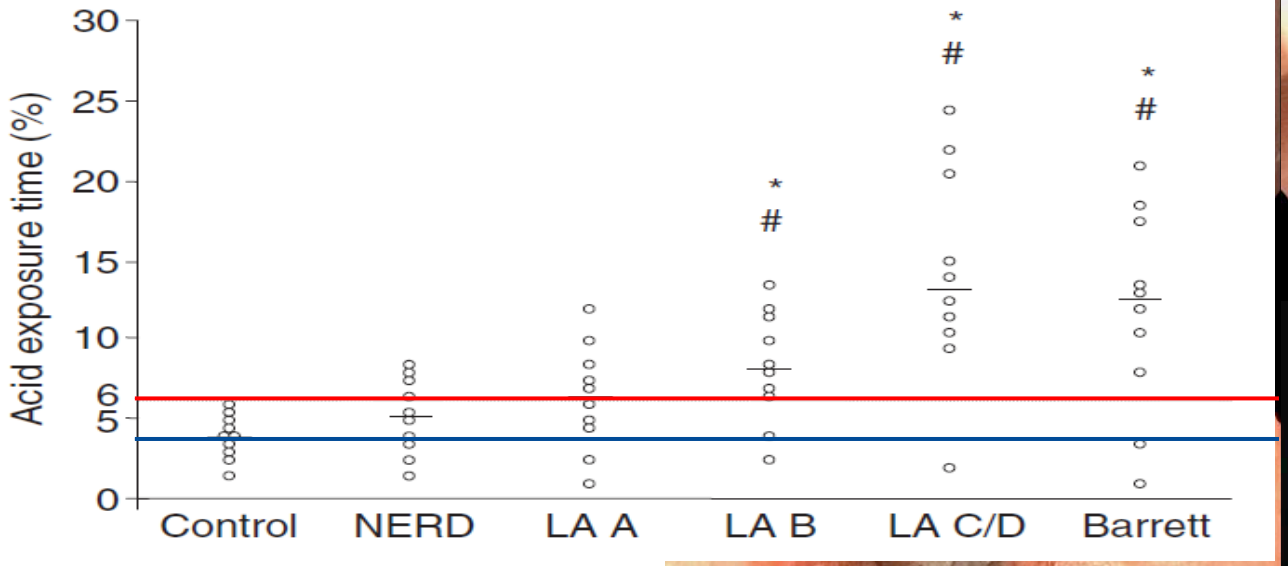

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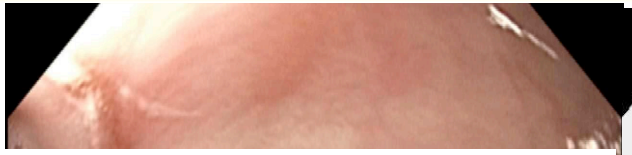

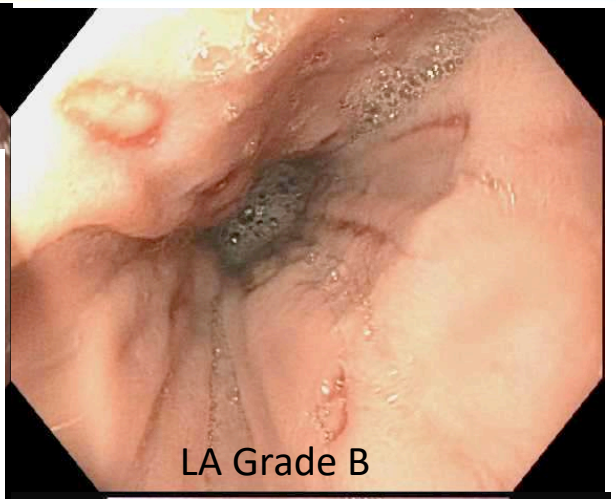

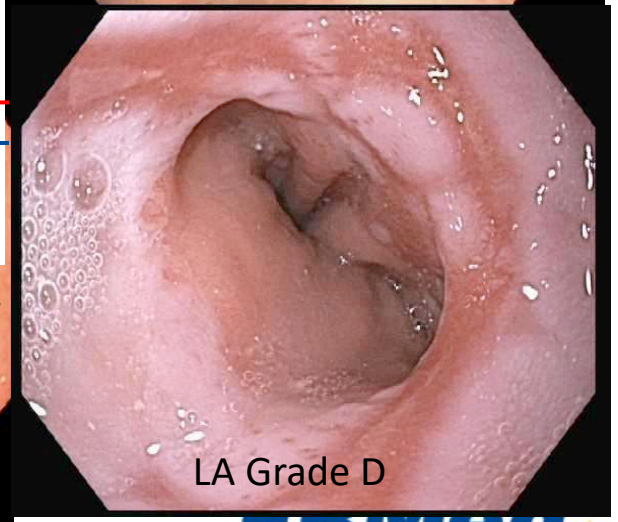

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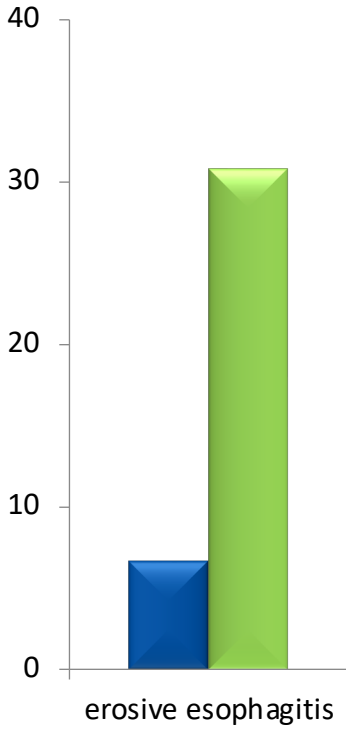

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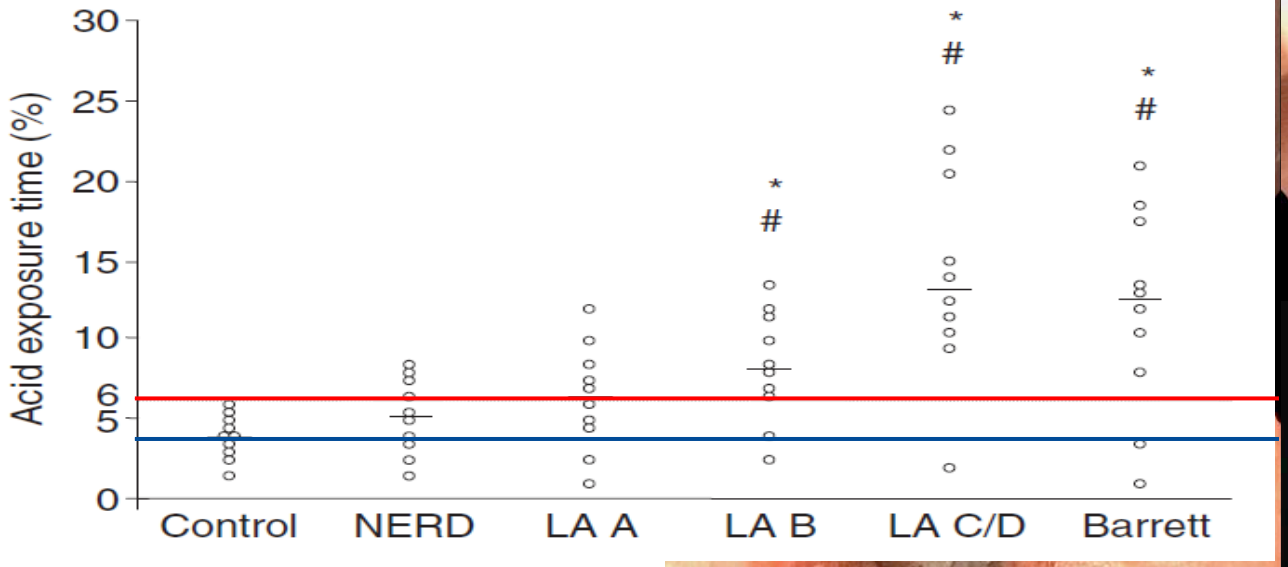

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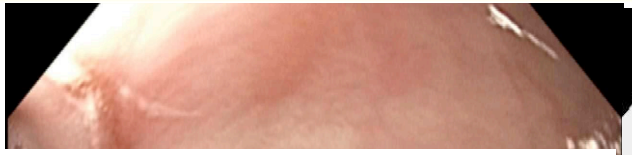
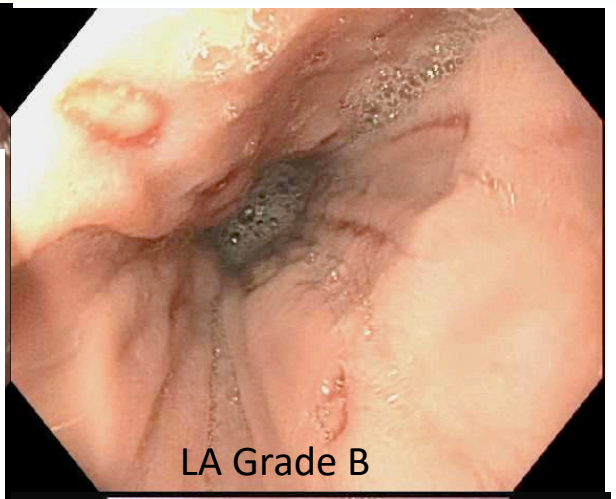
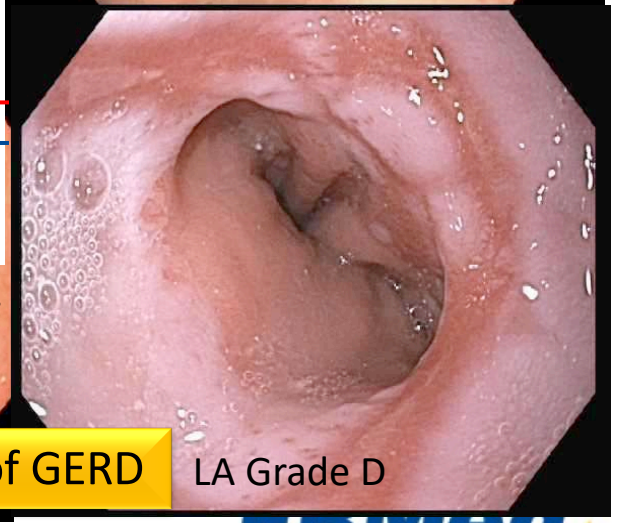




LA Grade B



LA Grade D

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

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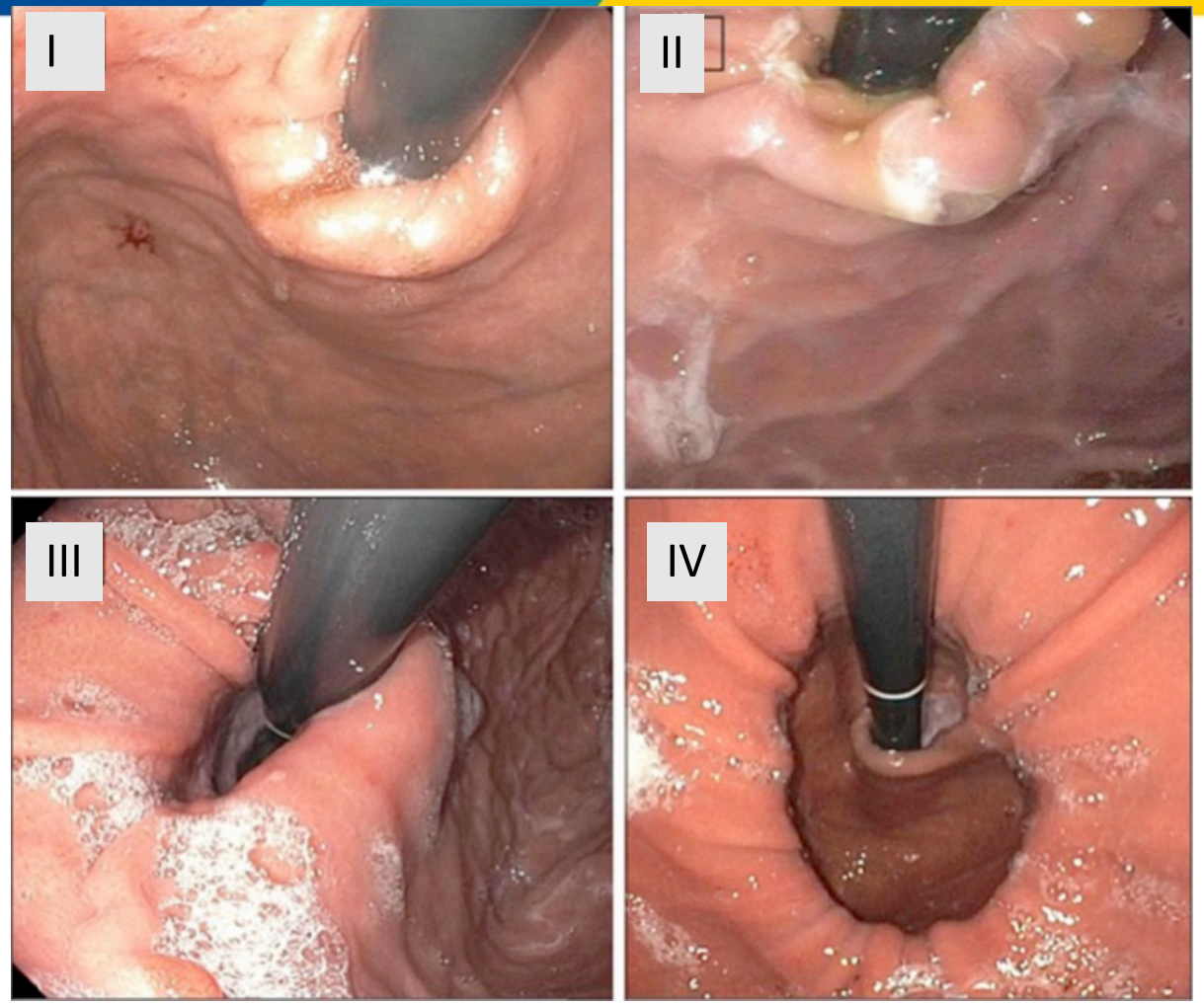
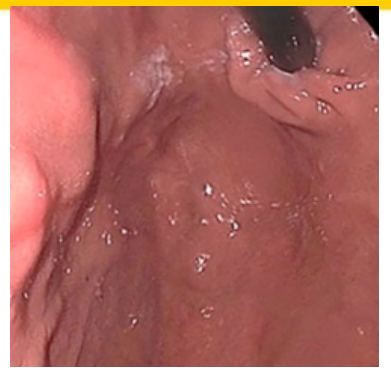
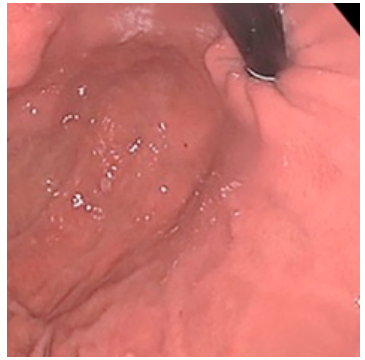
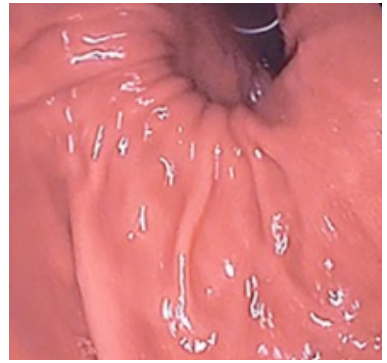


Hill grade of EGJ on retroflexion







Hill LD, et al. *Gastrointest Endosc*. 1996;44:541-547.

ASGE. GERD Guideline. 2024. In press.

Nguyen N, et al. *Foregut.* 2022;2:339-348.

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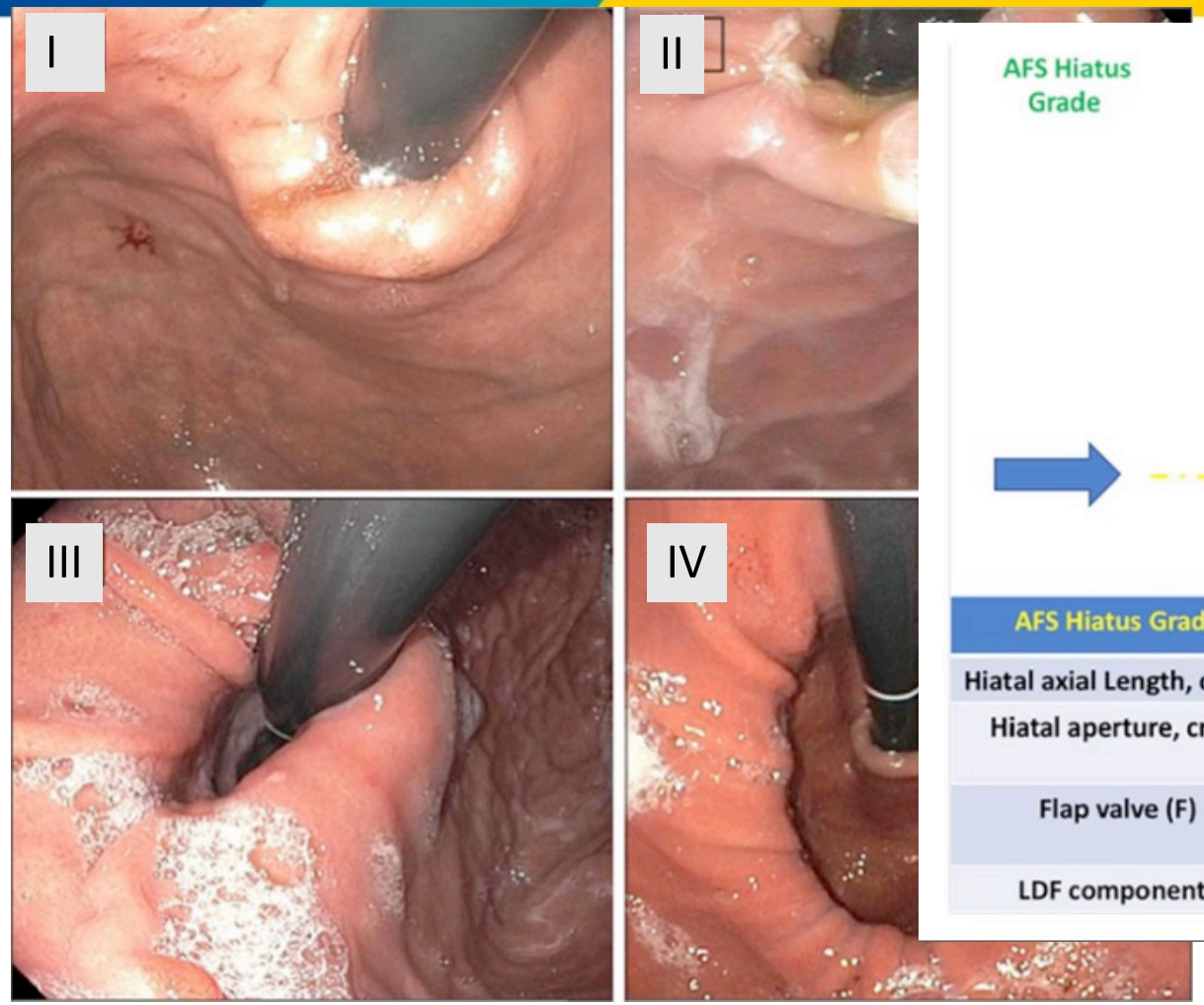
Value of Endoscopy



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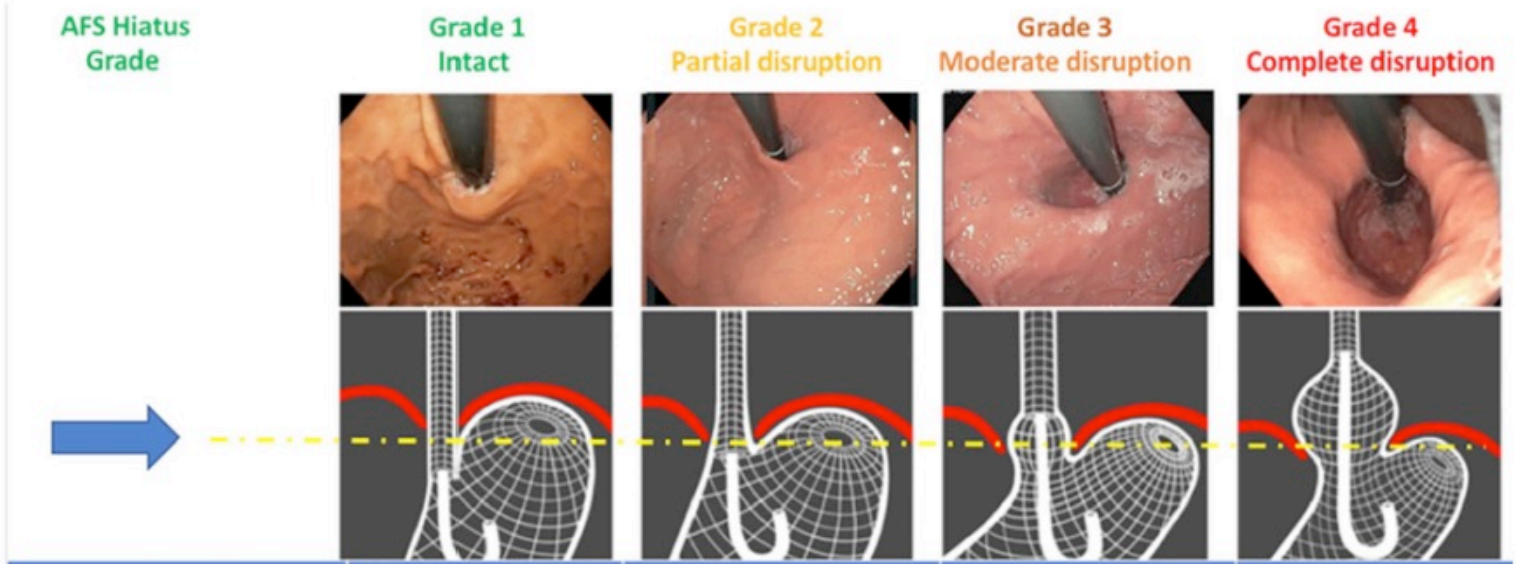

AFS Hiatus Grade	1	2	3	4
Hiatal axial Length, cm (L)	None (0 cm)	None (0 cm)	0-2 cm	>2 cm
Hiatal aperture, cm (D)	Snug to scope 1 cm	Loose 1-2 cm	Open 2-3 cm	Wide open >3 cm
Flap valve (F)	Present, full lip with Omega shape (F+)	Absent, thinning & flattening valve lip (F-)	Absent (F-)	Absent (F-)
LDF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

Hill LD, et al. *Gastrointest Endosc*. 1996;44:541-547.

ASGE. GERD Guideline. 2024. In press.

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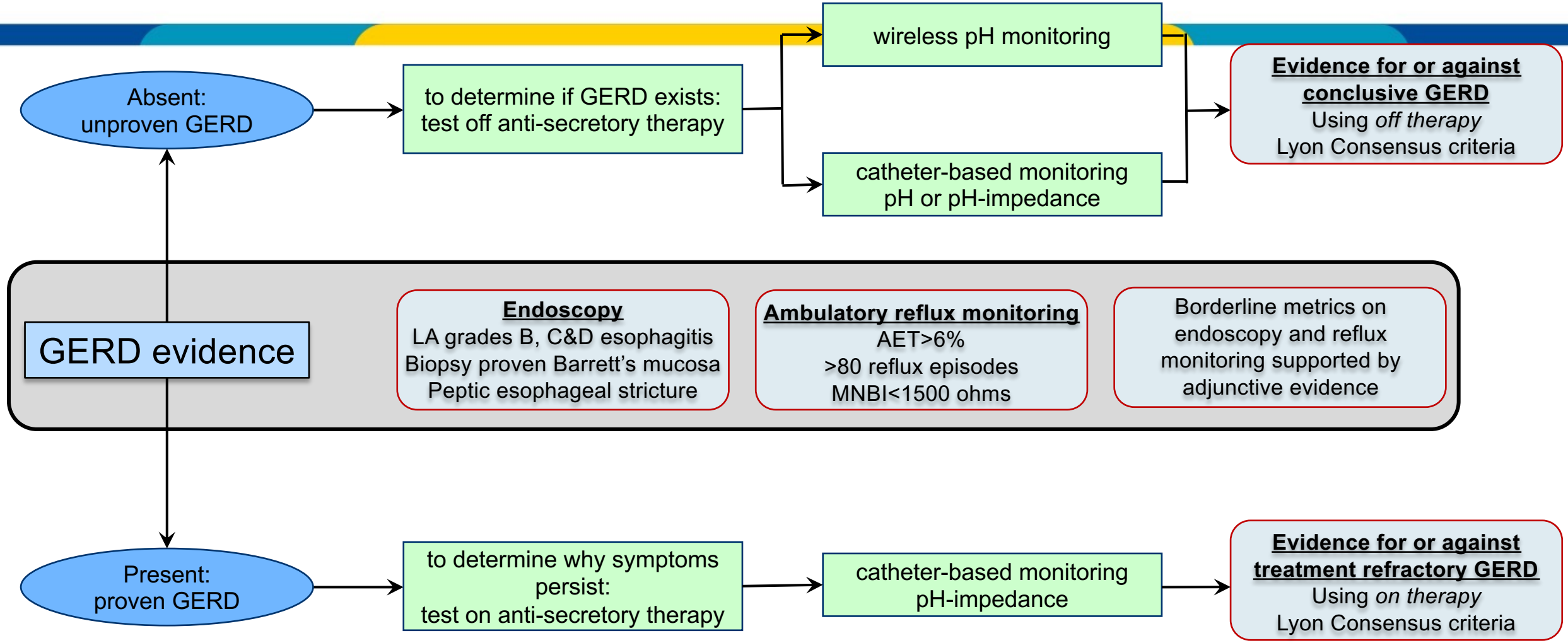
Value of Ambulatory Reflux Monitoring



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

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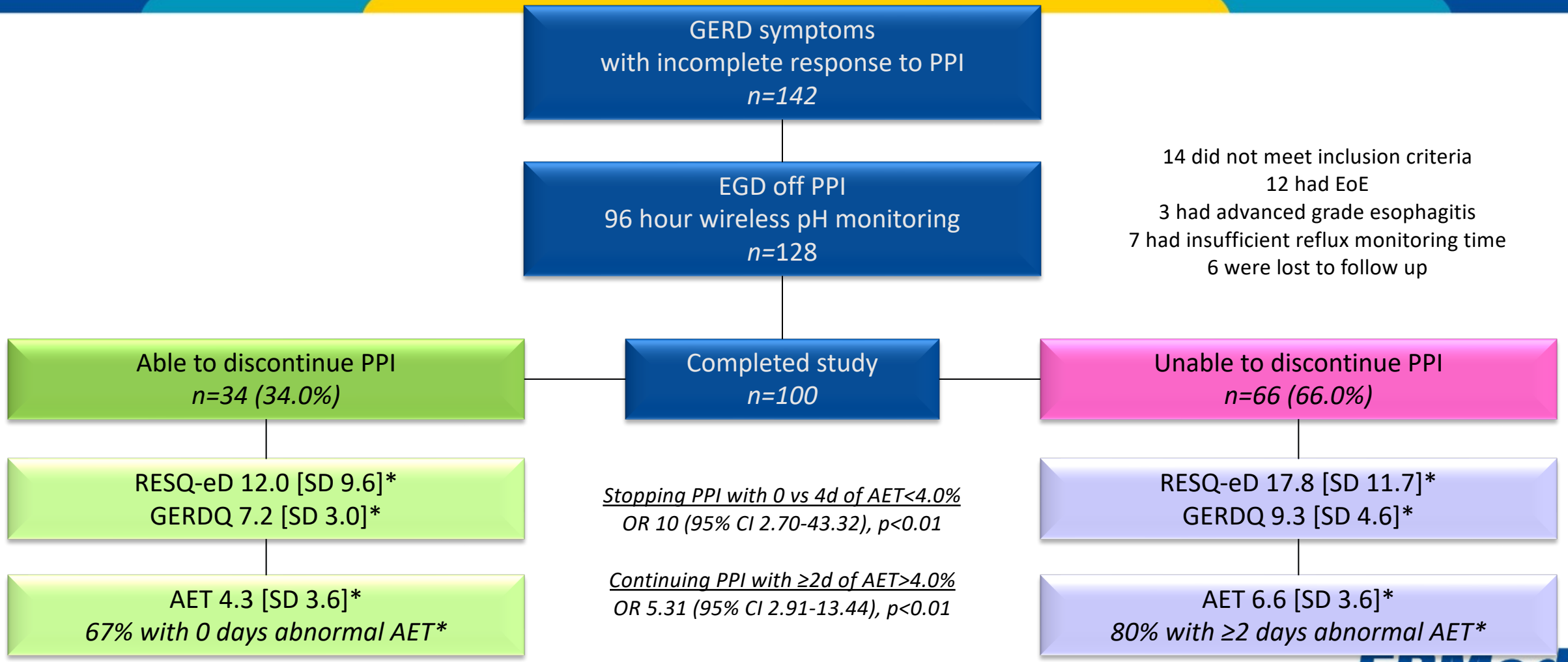
Value of Prolonged pH Monitoring



*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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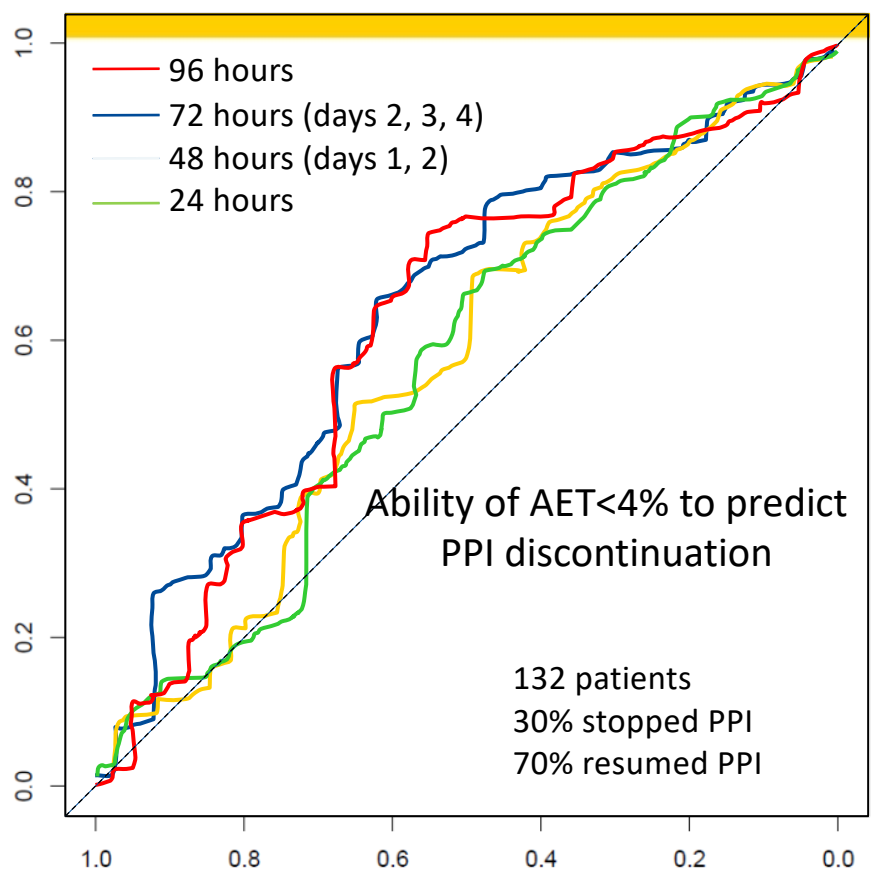
Value of Prolonged pH Monitoring



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%)

RESQ-eD 12.0 [SD 9.6]*
GERDQ 7.2 [SD 3.0]*

AET 4.3 [SD 3.6]*
*67% with 0 days abnormal AET**

Unable to discontinue PPI
n=66 (66.0%)

RESQ-eD 17.8 [SD 11.7]*
GERDQ 9.3 [SD 4.6]*

AET 6.6 [SD 3.6]*
*80% with ≥2 days abnormal AET**

Continuing PPI with ≥2d of AET>4.0%
OR 5.31 (95% CI 2.91-13.44), p<0.01

**p<0.05*

Yadlapati R, et al. *Am J Gastroenterol*. 2022;117:1573-1582;
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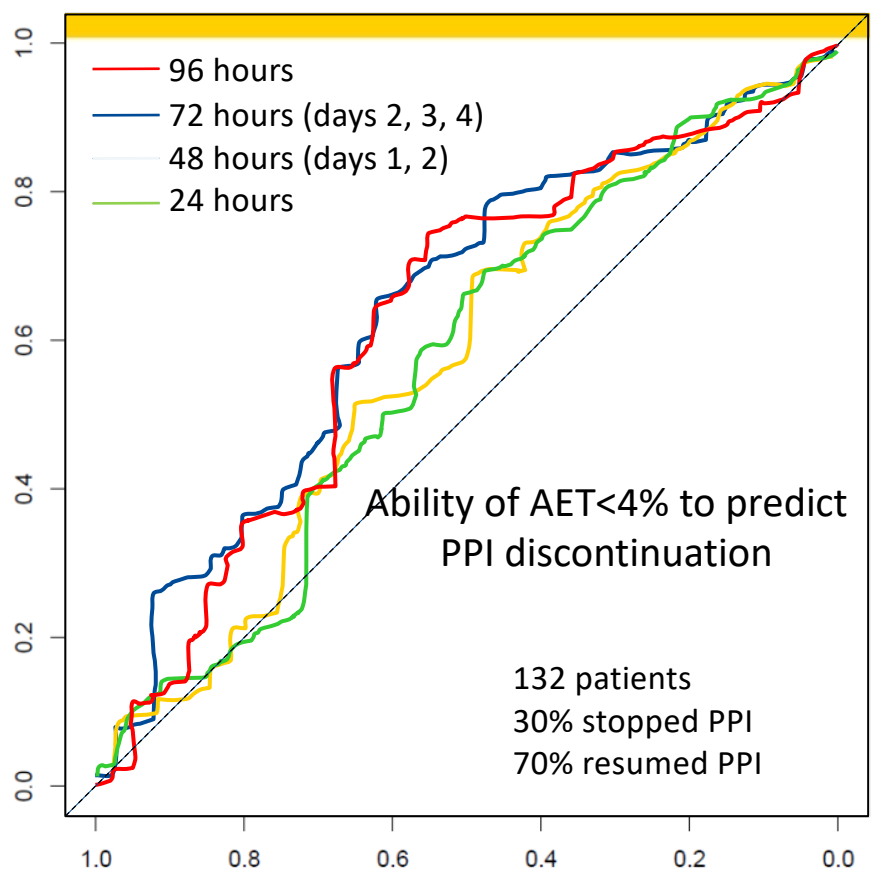
Value of Prolonged pH Monitoring



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Unable to discontinue PPI
n=66 (66.0%)

RESQ-eD 17.8 [SD 11.7]*
GERDQ 9.3 [SD 4.6]*

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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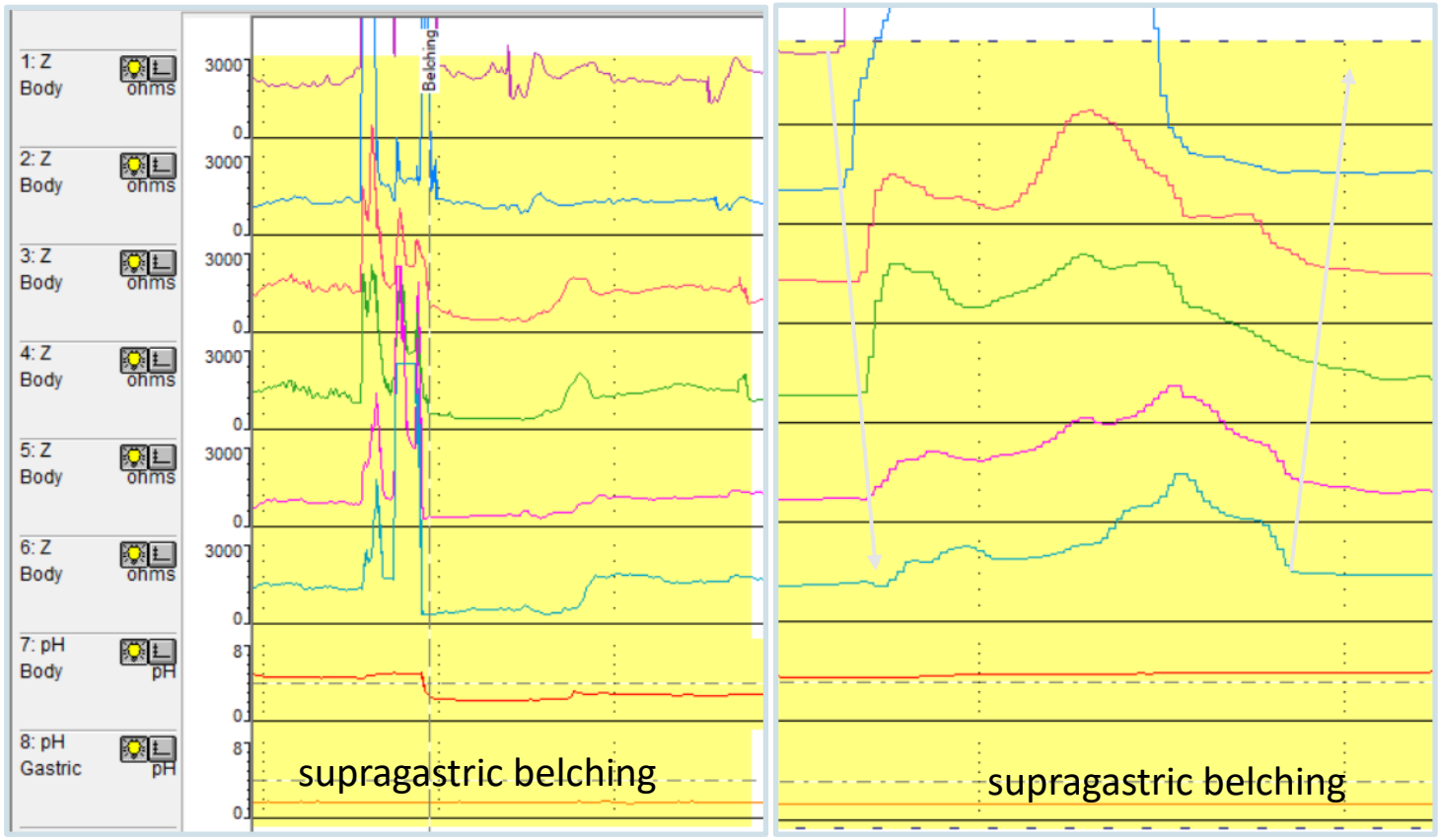
pH Impedance Monitoring: Behavioral Syndromes



Yadlapati R, et al. *Clin Gastroenterol Hepatol*. 2018;16:211-218.e1;
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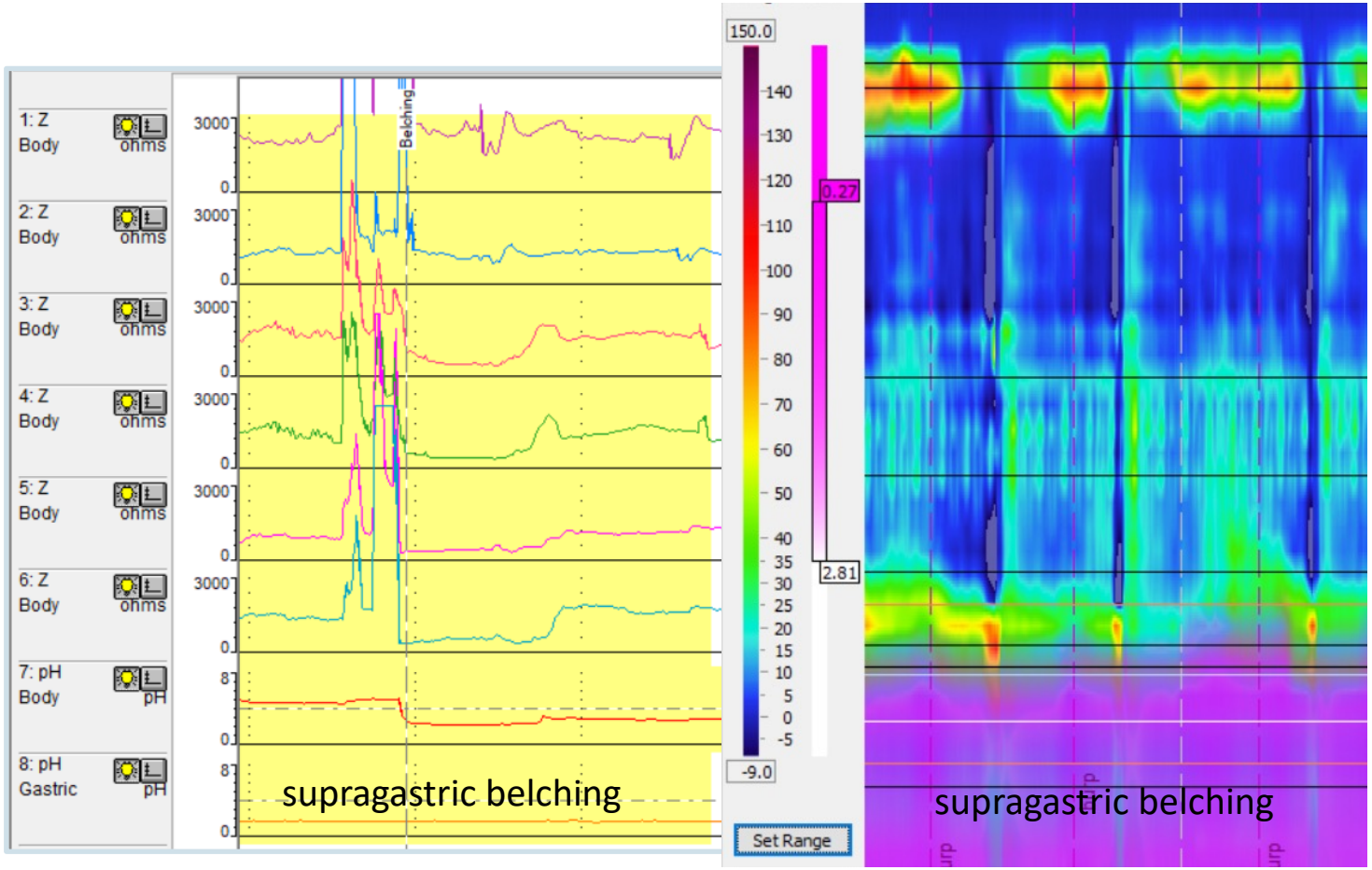

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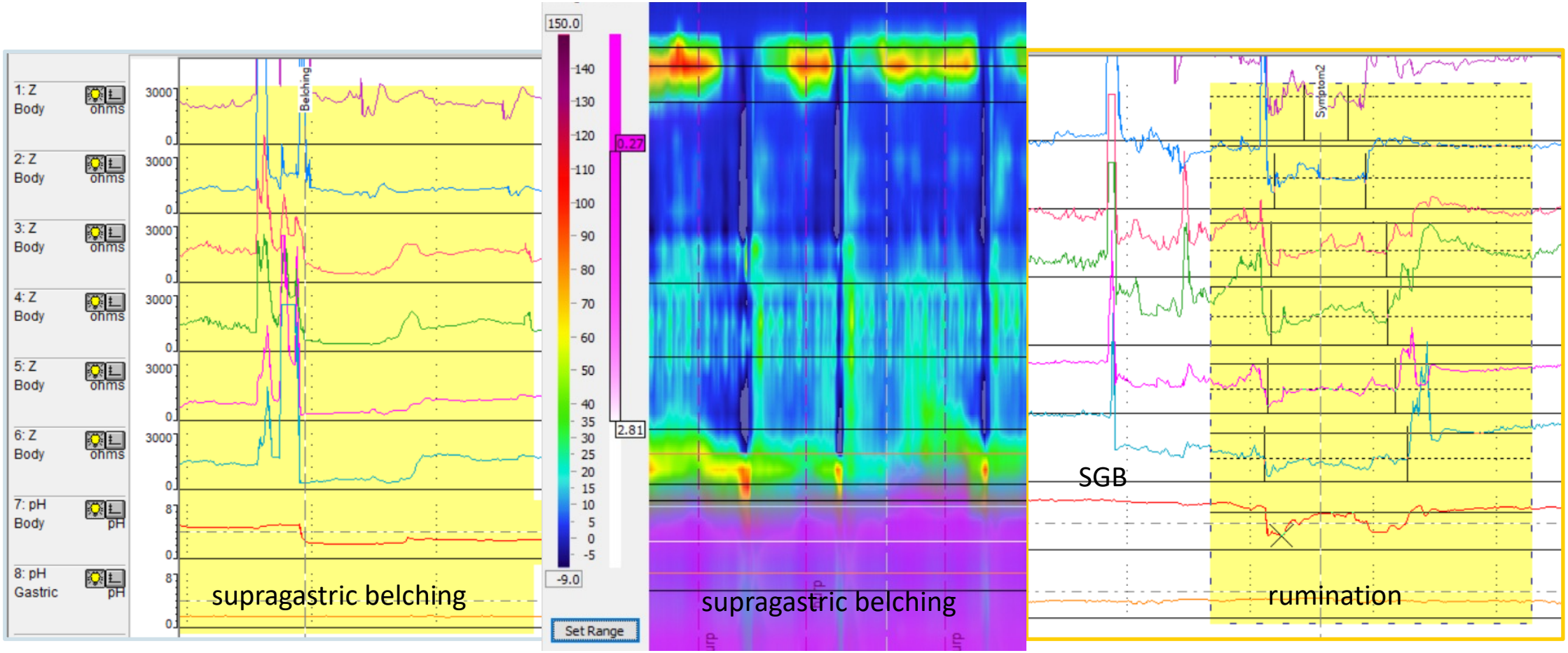

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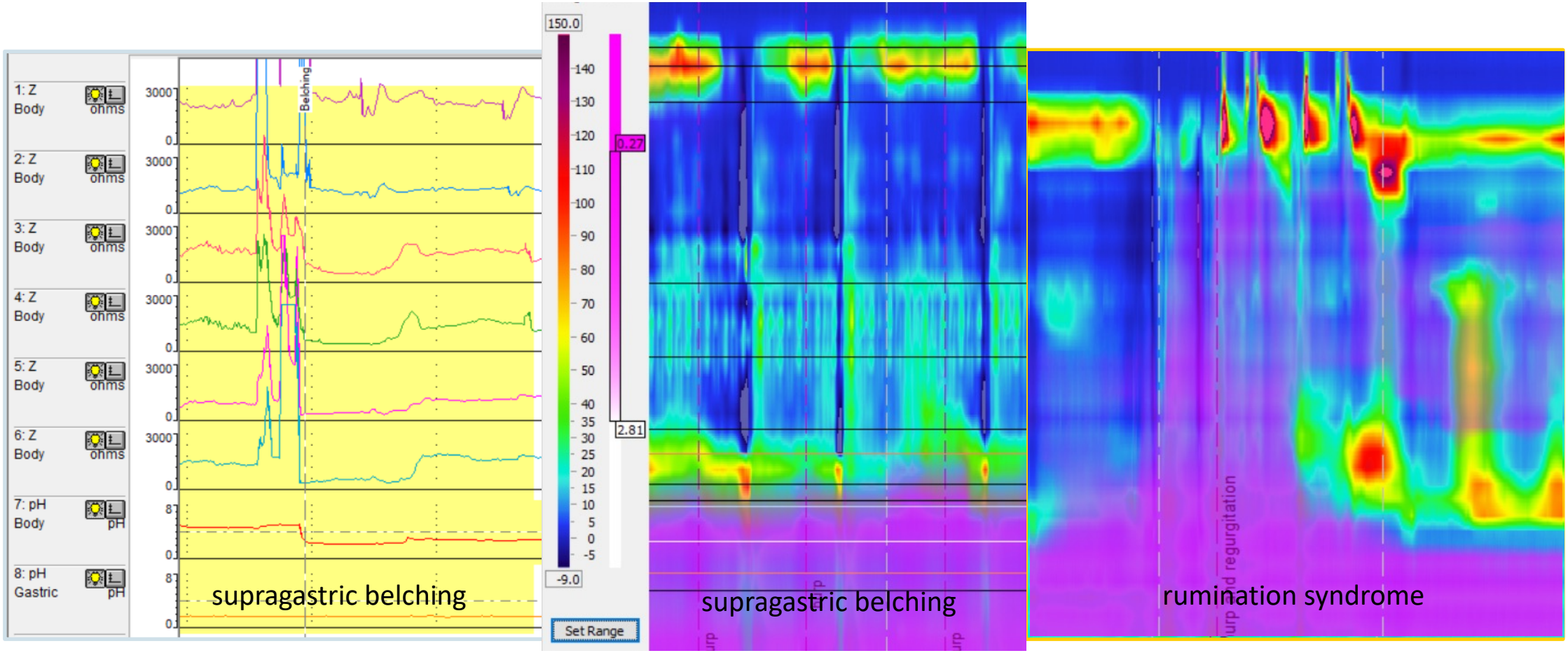

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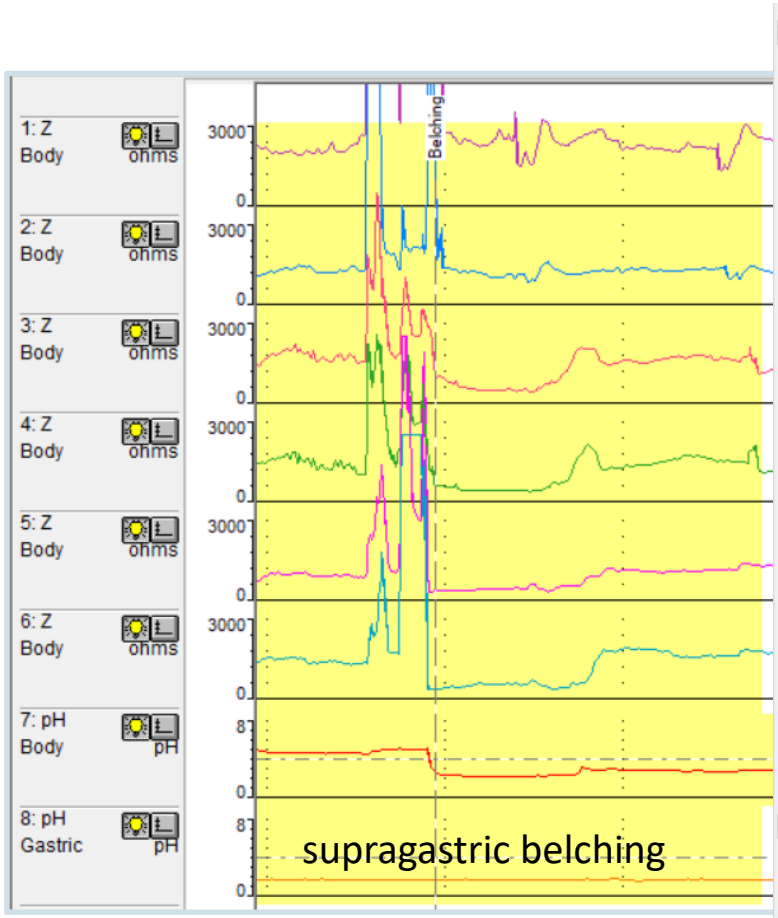
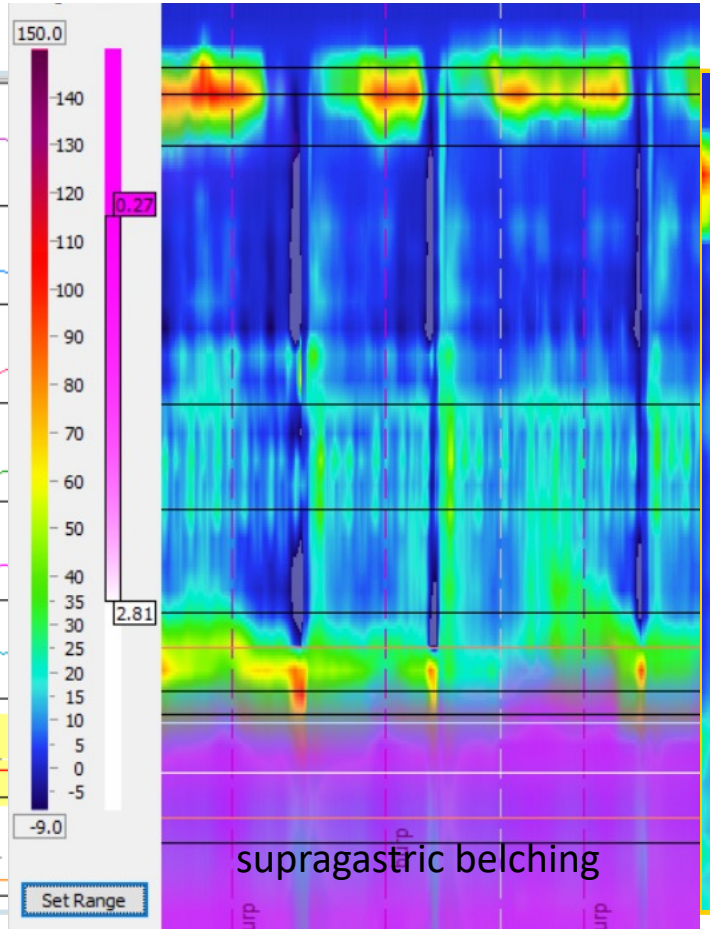
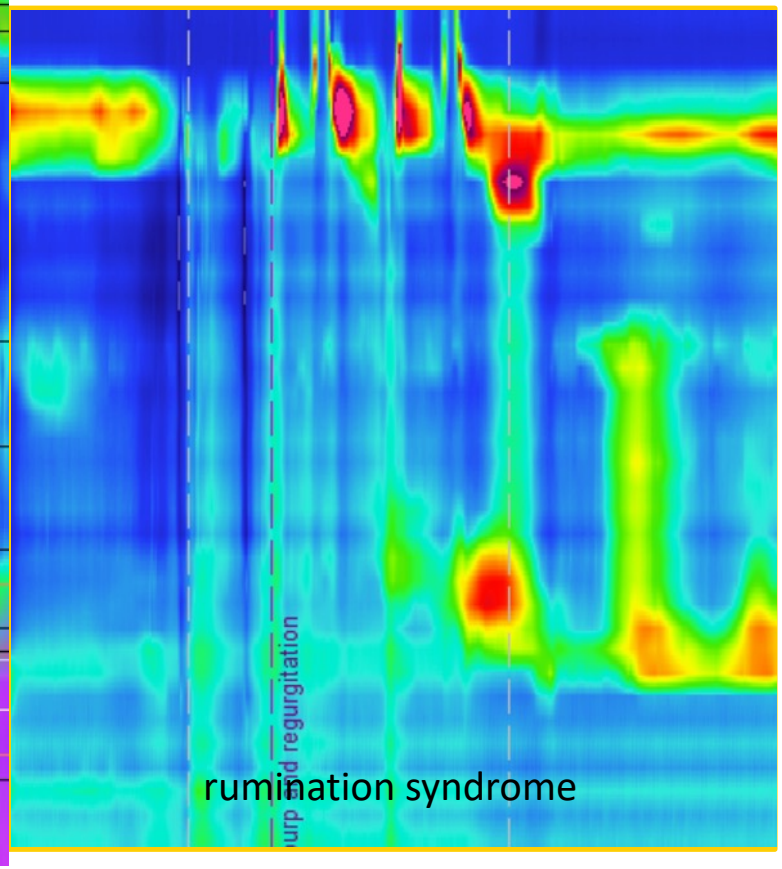


supragastric belching



supragastric belching


rumination syndrome

Yadlapati R, et al. *Clin Gastroenterol Hepatol*. 2018;16:211-218.e1;
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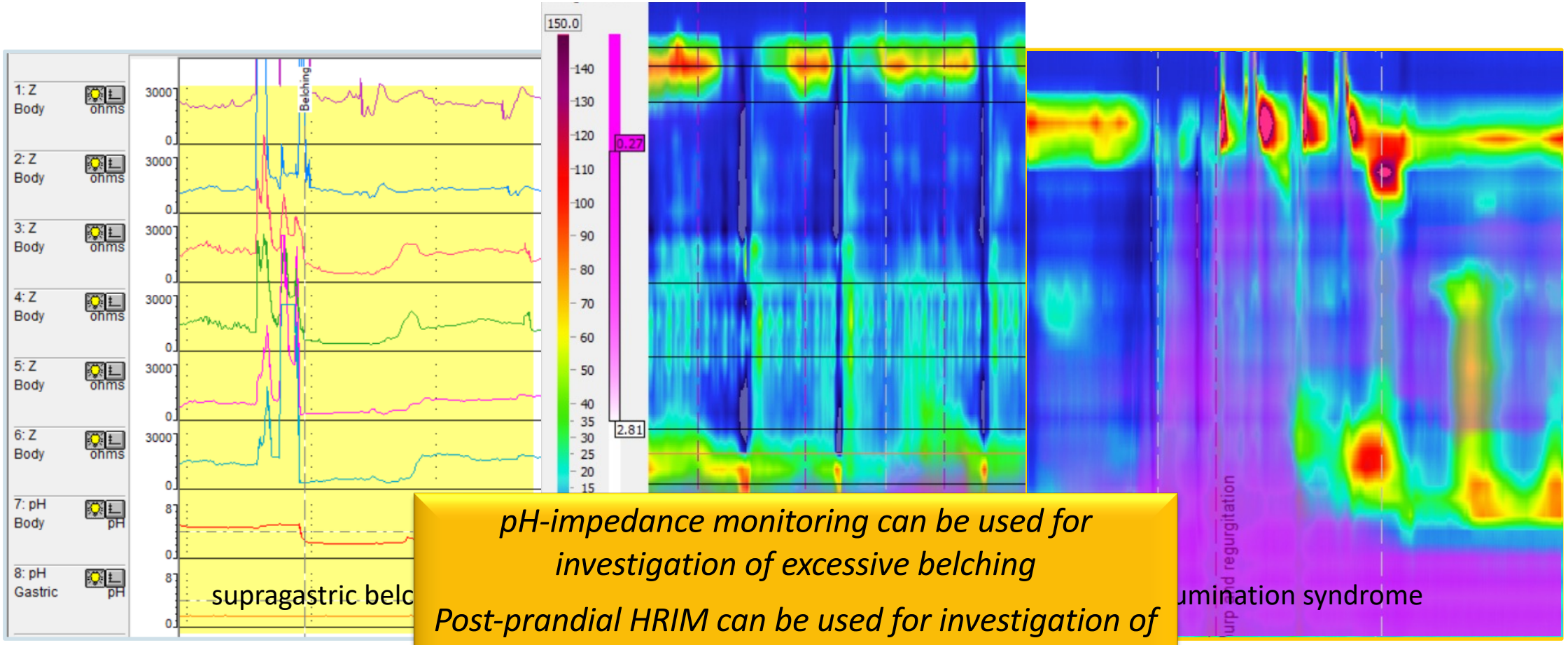
pH Impedance Monitoring: Behavioral Syndromes



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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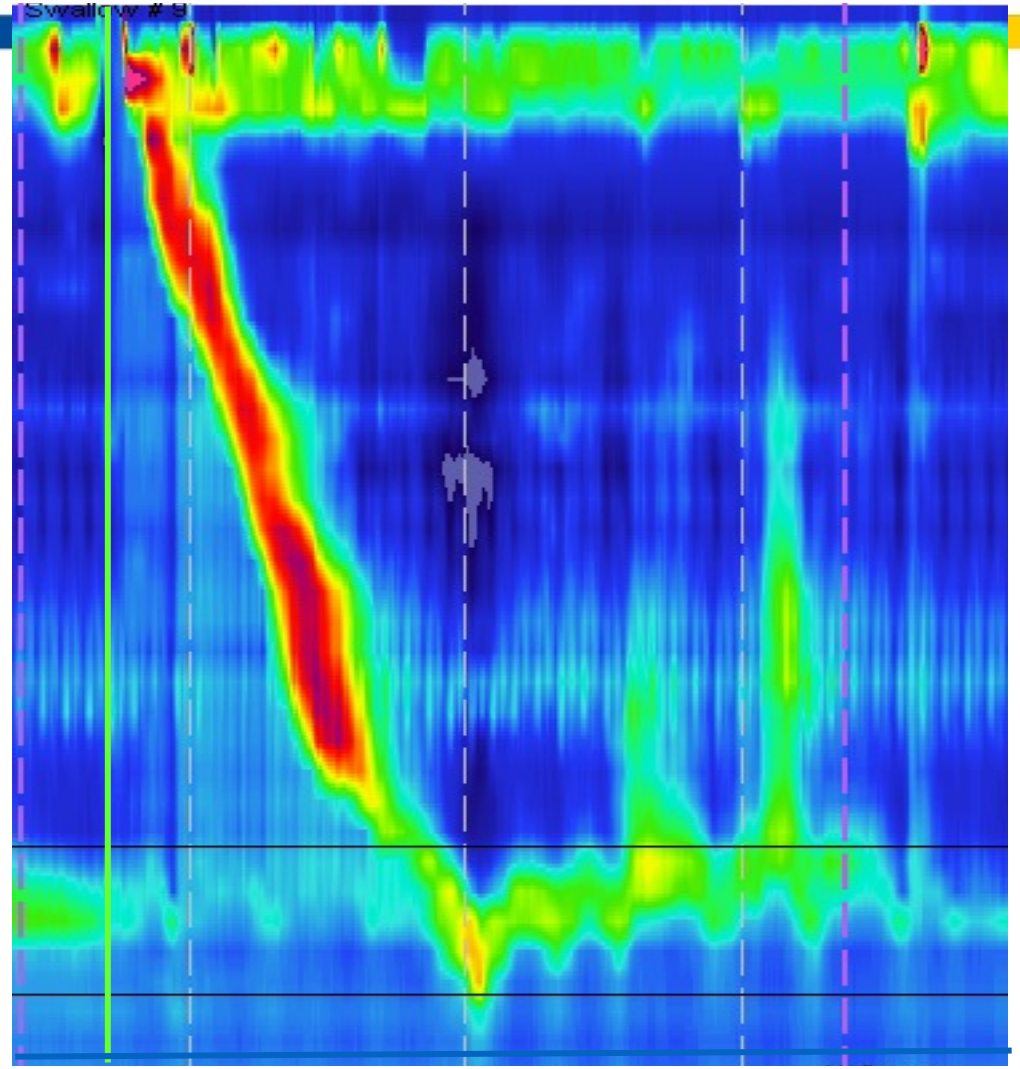
Value of High Resolution Manometry



Gyawali CP, et al. *Neurogastroenterol Motil*. 2013;25:99-133; Kahrilas PJ, et al. *Neurogastroenterol Motil*. 2015;27:160-174.

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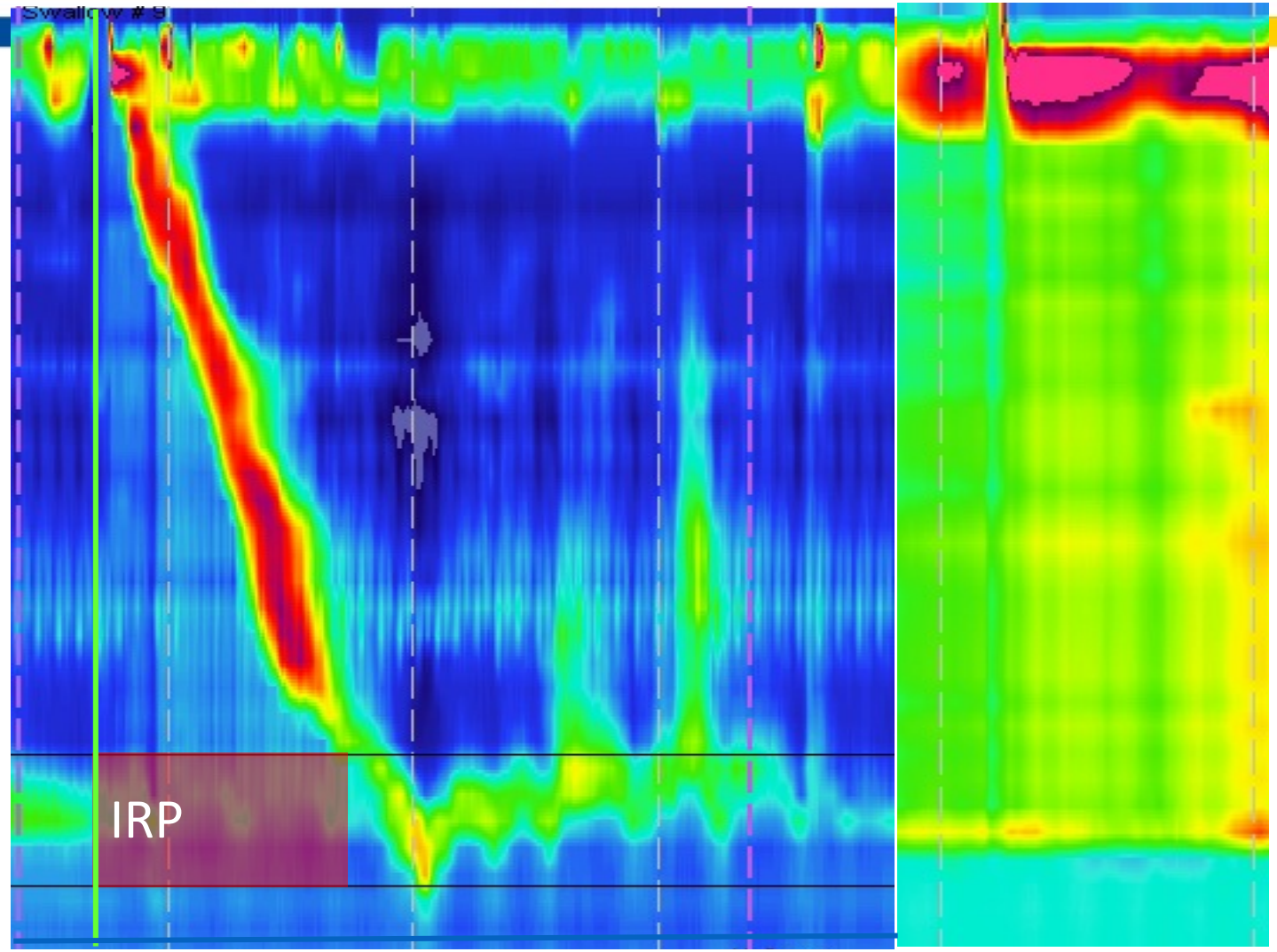

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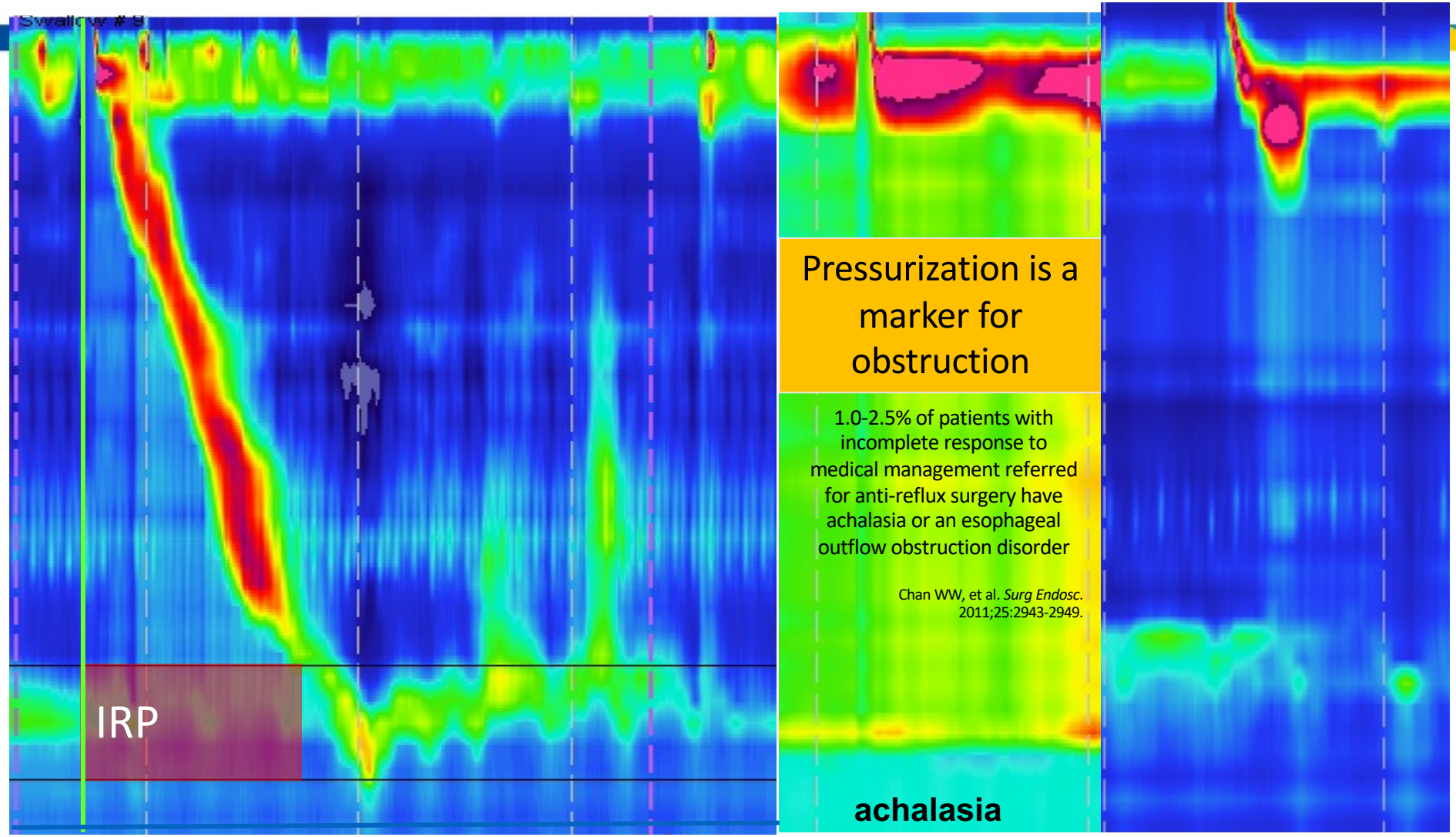

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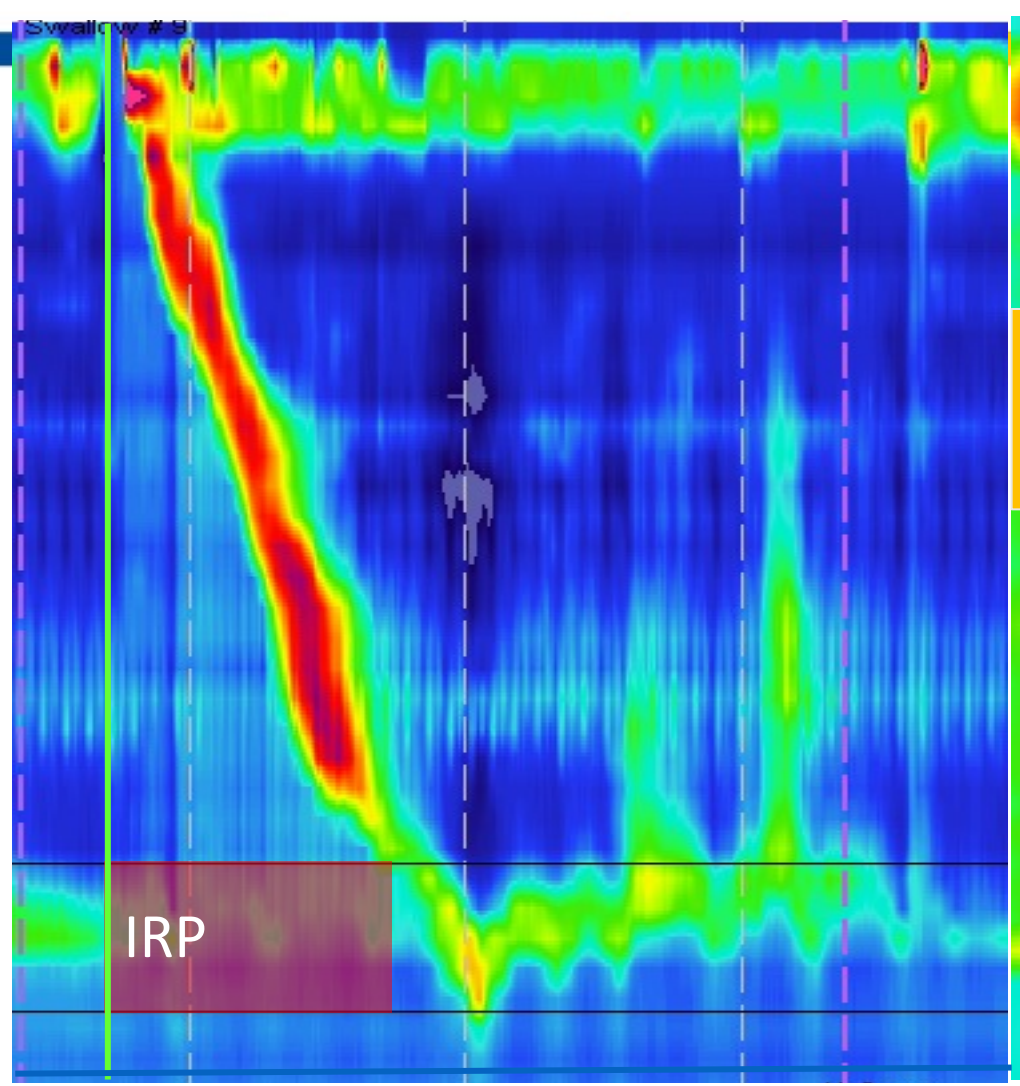

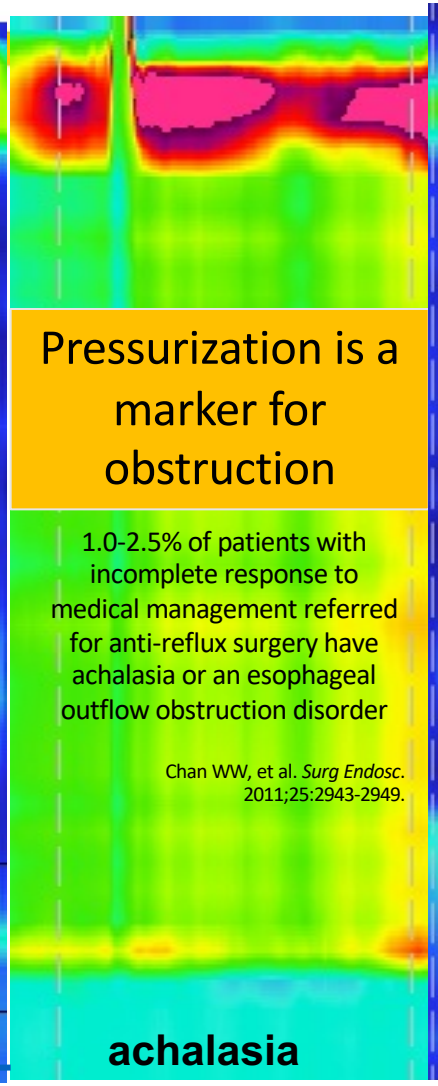

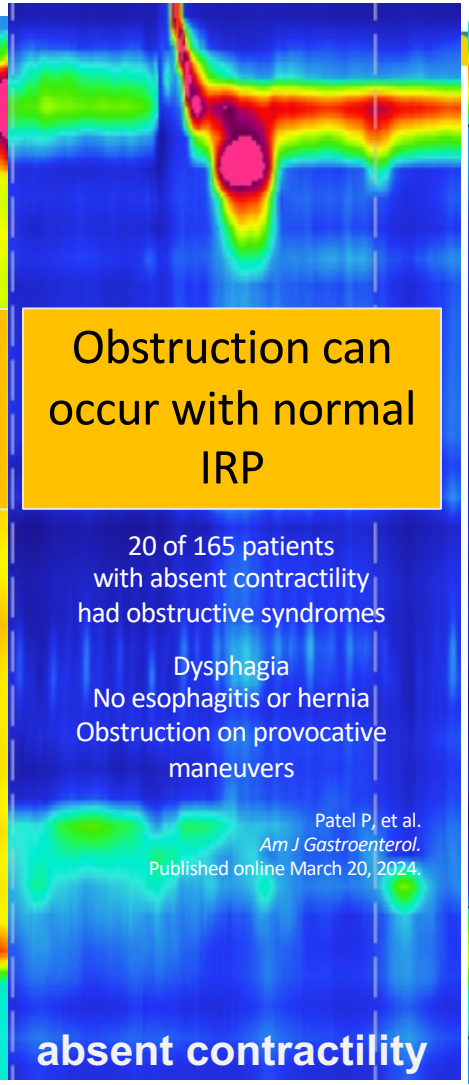

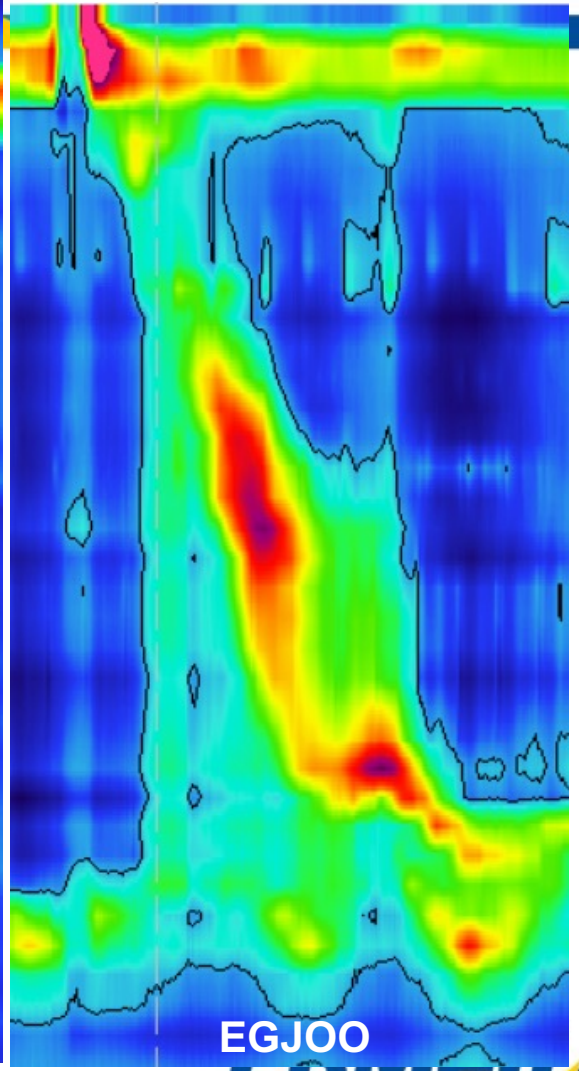

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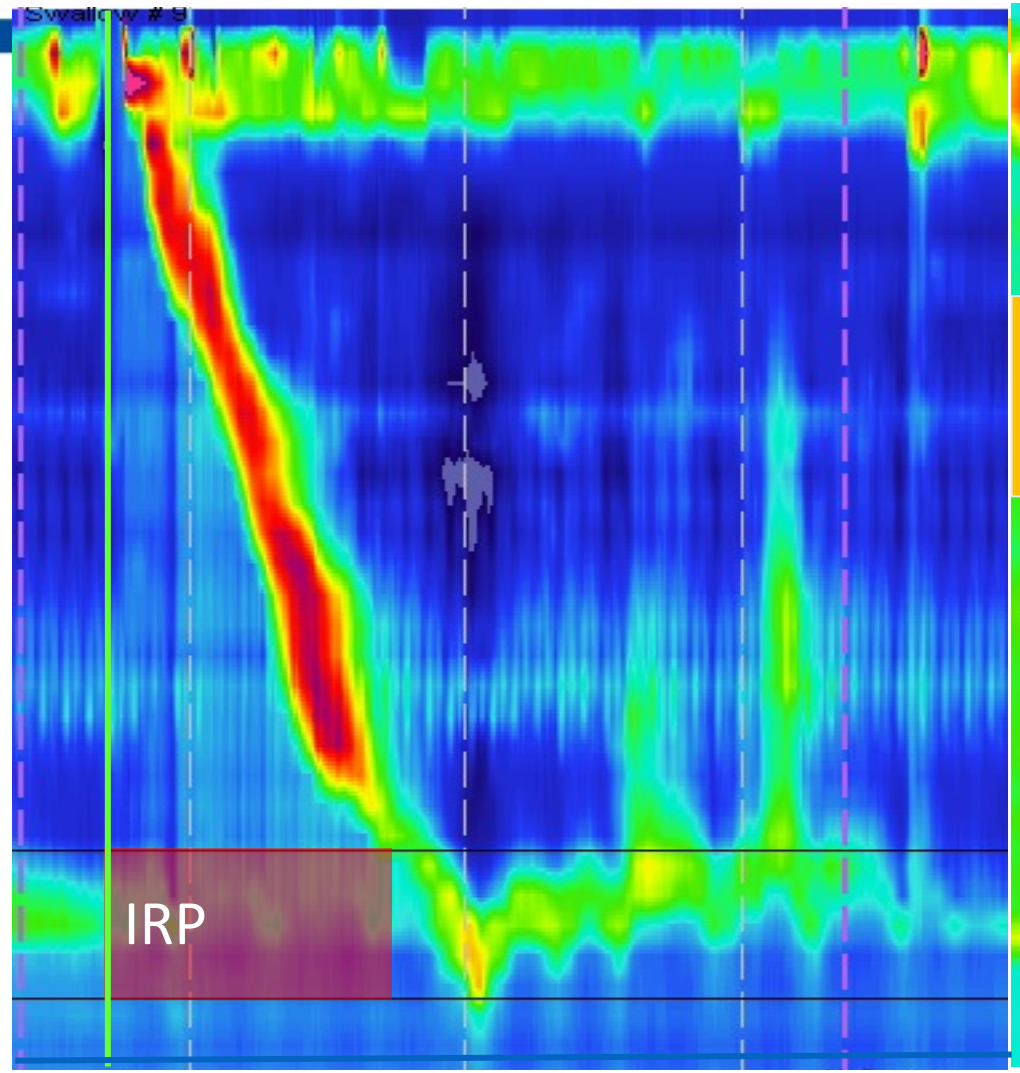
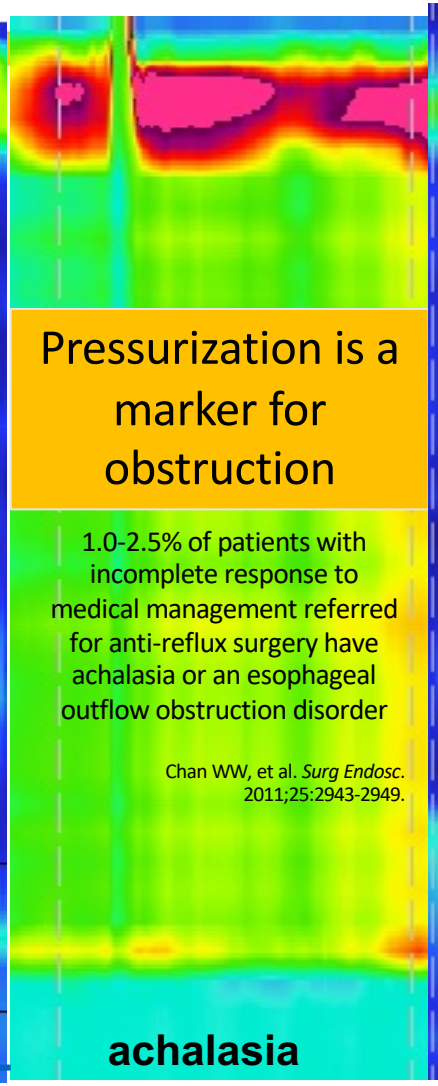


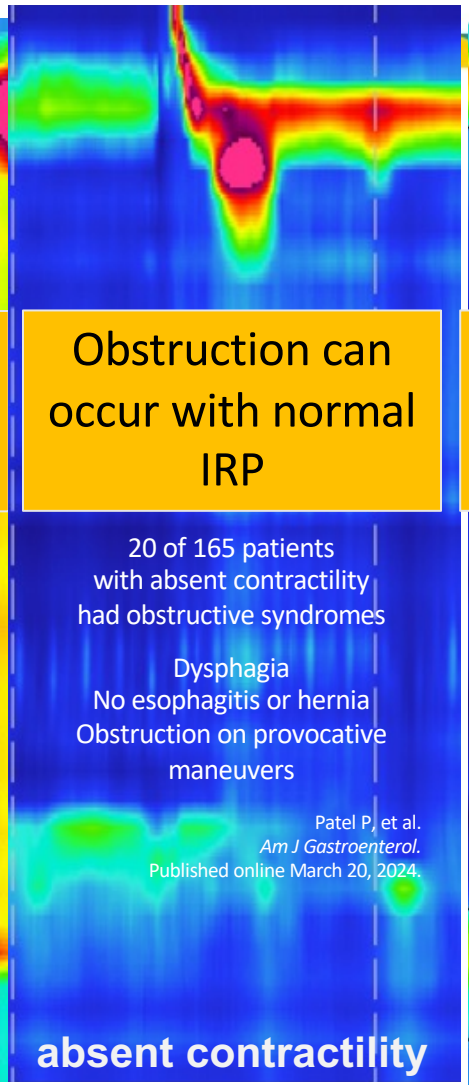


Pressurization is a marker for obstruction

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;25:2943-2949.

achalasia



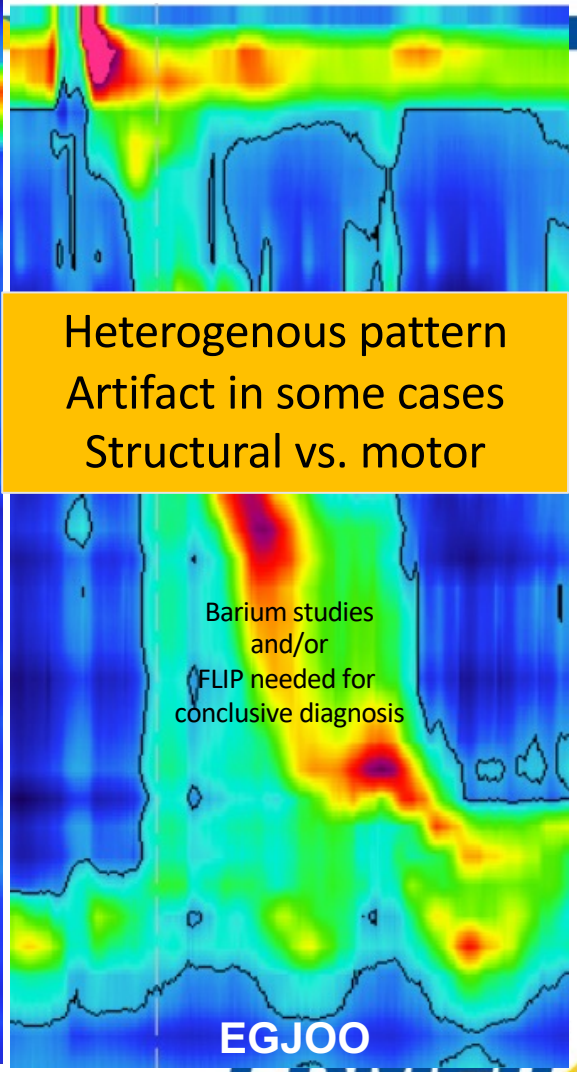
Obstruction can occur with normal IRP

20 of 165 patients with absent contractility had obstructive syndromes

Dysphagia
No esophagitis or hernia
Obstruction on provocative maneuvers

Patel P, et al. *Am J Gastroenterol*. Published online March 20, 2024.

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.

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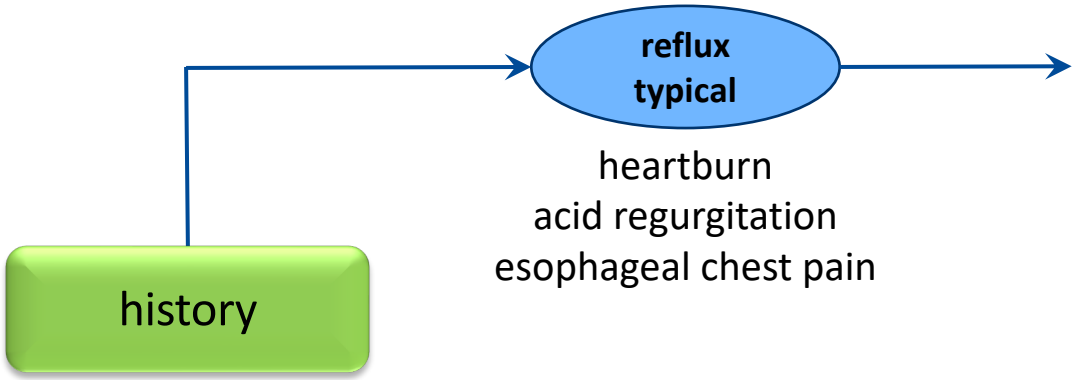

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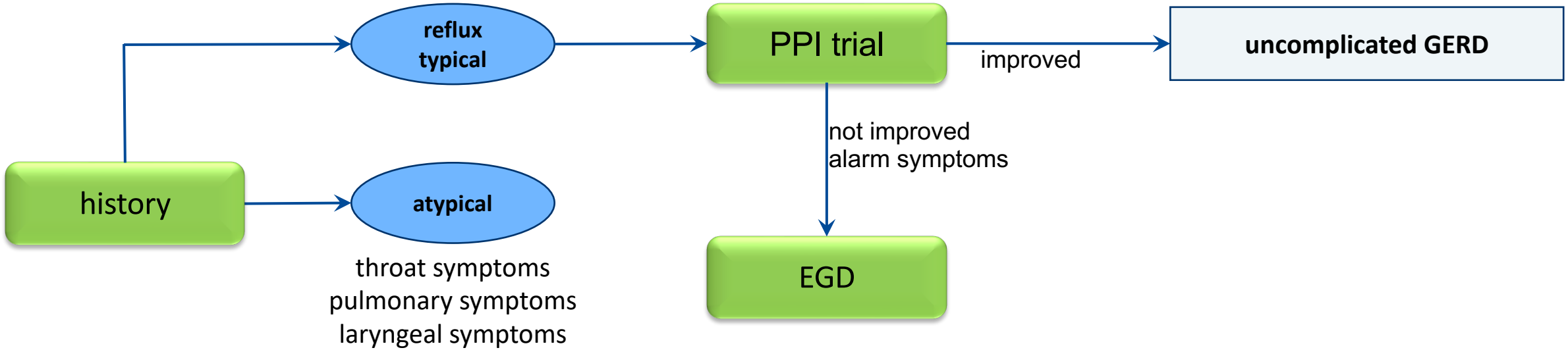

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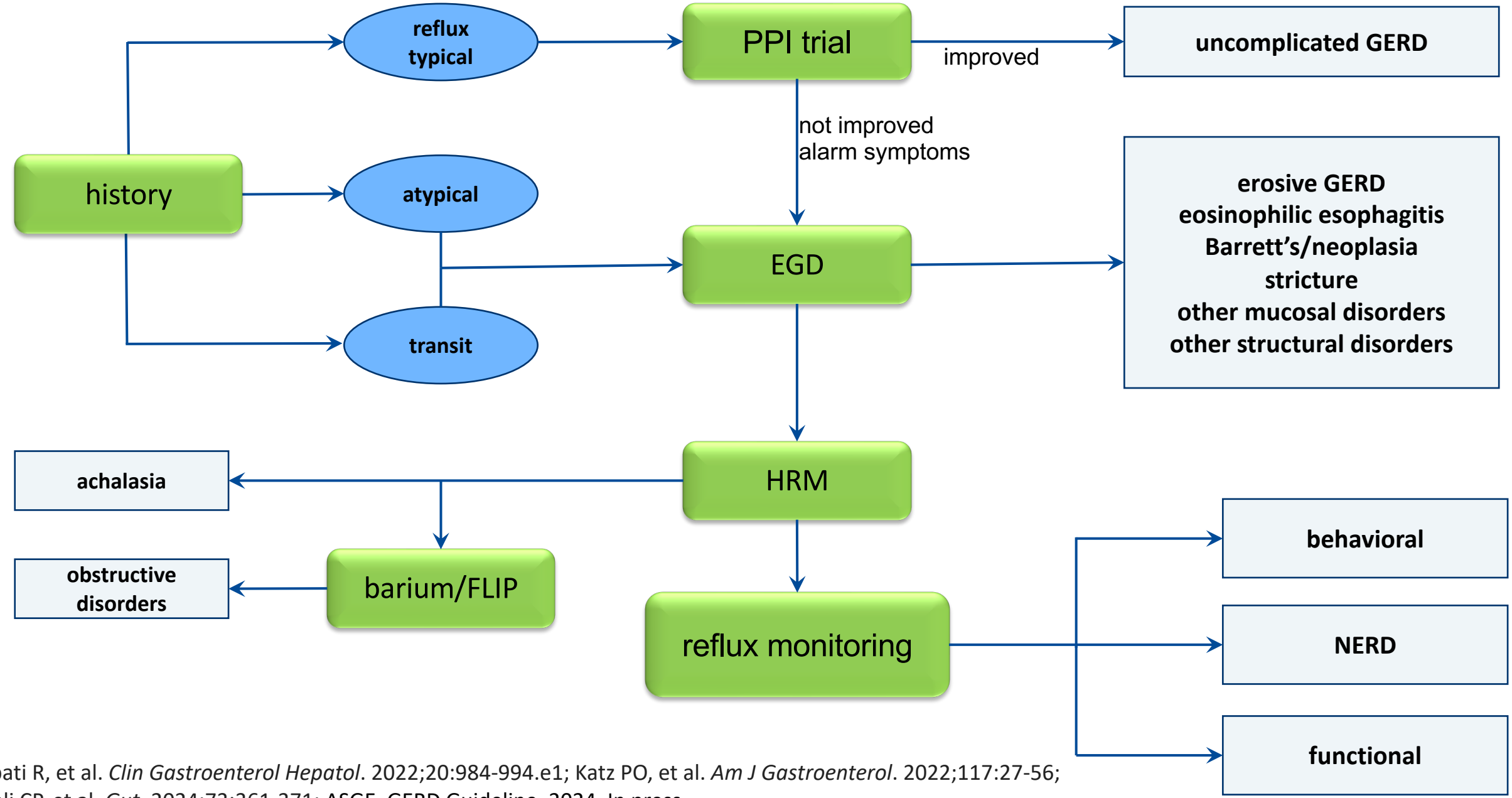

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Division of Gastroenterology

Washington University in St.Louis
School of Medicine

Birthplace of High Resolution Manometry
St. Louis, Missouri, USA

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TREAT the Patient...Please

Felice Schnoll-Sussman, MD, MSc
Professor Clinical Medicine
Weill Cornell Medicine
New York, NY
President AFS

Disclosures: Ethicon (consulting), Sebela/Braintree (Consulting)

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Why Do I TREAT Rather Than Test?

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What Do We *REALLY* Need to Know About Our Patient?

What Do We *REALLY* Need To Know About Our Patient?

1. Does my patient *REALLY* have GERD? (Dr. Gyawali)
2. What does my patient *REALLY* want? (Dr. Schnoll-Sussman)

But there is one more question we need to ask, before answering these questions…

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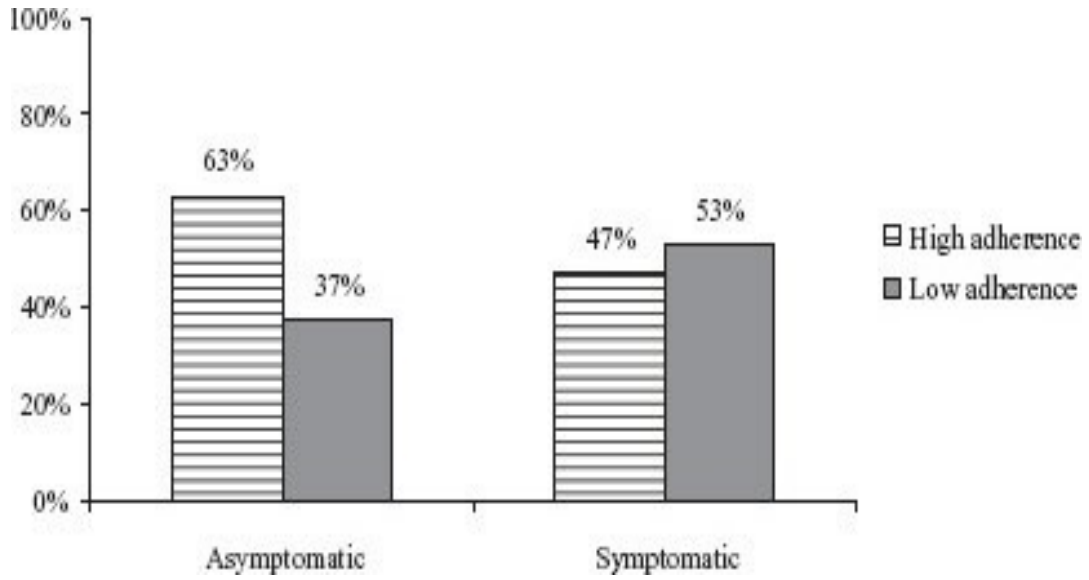
Low levels of adherence with proton pump inhibitor therapy contribute to therapeutic failure in gastroesophageal reflux disease FREE

K. Dal-Paz, J. P. Moraes-Filho, T. Navarro-Rodriguez, J. N. Eisig, R. Barbuti, E. M. M. Quigley Author Notes

- Cross-sectional, 240 patients diagnosed with GERD, on standard/double dose omeprazole
- Classified as NERD vs. EE vs. Barrett's esophagus
- Questionnaire for adherence
- 60.8% did not know the name of the disease treated
- 47.5% reported low levels of adherence to Omeprazole
- 34.6% did not take PPI in correct manner (fasting, 30 mins before meals)



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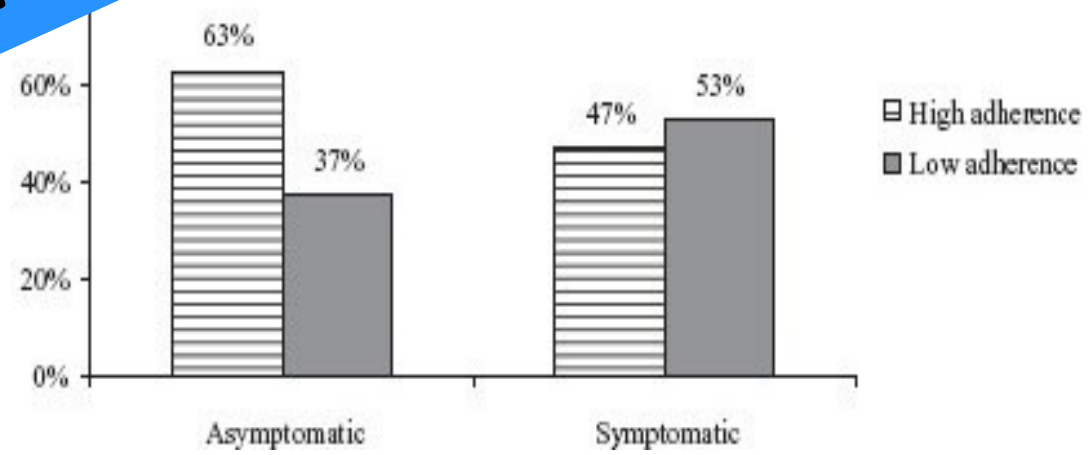
Is Your Patient Compliant With Their Medications? If not… Don't test…TREAT



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What Is the Big Rush? What Are You Nervous About?

1. The patient has had an EGD and does not have cancer, obstruction, EoE, Barrett's, obvious gastroparesis, large para/hiatal hernia, peptic stricture, etc...what's the big rush to do more testing?
2. Dr. Gyawali's argument is that upfront pH testing is going to save money and time *but is that really true*? What are the hidden costs?
3. In real-world practice how available/practical is reflux testing?

What Additional Information Is Gleaned by pH Monitoring After a Normal EGD?

1. Degree of acid exposure – can help determine frequency and duration of acid reflux episodes…

Who cares…patient just wants to feel better

2. Reflux patterns – whether it happens certain times of day (e.g. nighttime, postprandial)...

Just ask the patient when do they get heartburn

3. Symptom association – helps determine if GERD symptoms are indeed related to acid reflux...

Just treat the symptoms and see if they get better

4. Differentiating acid and Non-Acid Reflux …

Who cares if the treatment works

5. Evaluation of surgical candidacy …

If you get them better, they won't need surgery

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Hidden Costs of TESTING?

What are the average costs for a patient to visit a medical practice?

1. Lost wages – EGD with wireless pH monitoring requires at a minimum 1 day
2. Transportation costs – Train/bus…taxi/uber/lyft…personal car
3. Childcare
4. Escort home
5. Pain and suffering

Rates to park a car at the ambulatory center in NYC

Rates

30 Min	$16.90
1 Hour	$20.27
2 Hours	$27.03
4 Hours	$29.57
8 Hours	$32.10
24 Hours	$35.48
Oversize Add'l	$8.45
Tax Not Included	18.375%

Amex, Bills, Coins, Debit card, Discover, MC/Visa

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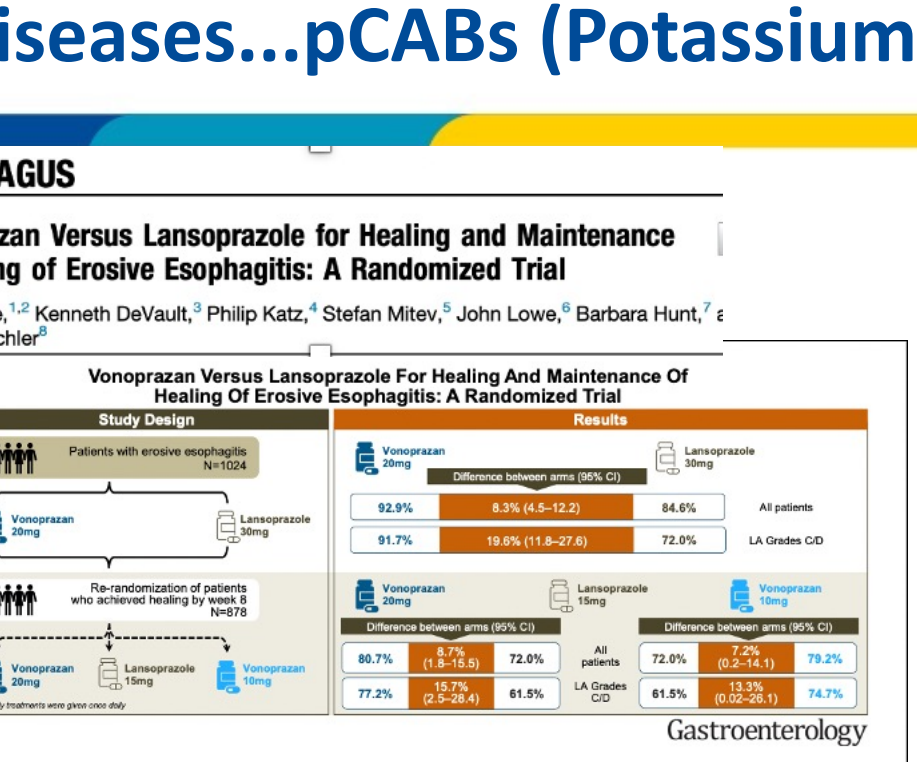
We Have Entered a New Era for the Treatment of Acid-Related Diseases...pCABs (Potassium-Competitive Acid Blockers)



ESOPHAGUS

Vonoprazan Versus Lansoprazole for Healing and Maintenance of Healing of Erosive Esophagitis: A Randomized Trial

Loren Laine,[1,2] Kenneth DeVault,[3] Philip Katz,[4] Stefan Mitev,[5] John Lowe,[6] Barbara Hunt,[7] a
Stuart Spechler[8]

Vonoprazan Versus Lansoprazole For Healing And Maintenance Of Healing Of Erosive Esophagitis: A Randomized Trial

Study Design

Patients with erosive esophagitis N=1024

Healing Phase (8 weeks)

Vonoprazan 20mg

Lansoprazole 30mg

Re-randomization of patients who achieved healing by week 8 N=878

Maintenance Phase (24 weeks)

Vonoprazan 20mg

Lansoprazole 15mg

Vonoprazan 10mg

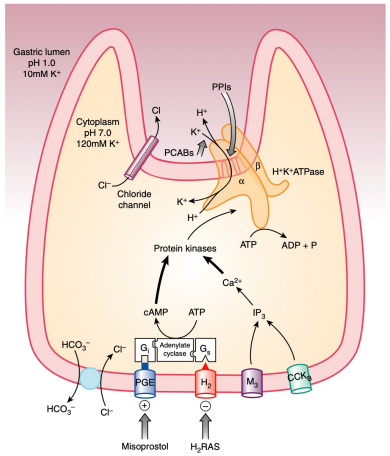
All study treatments were given once daily

Results

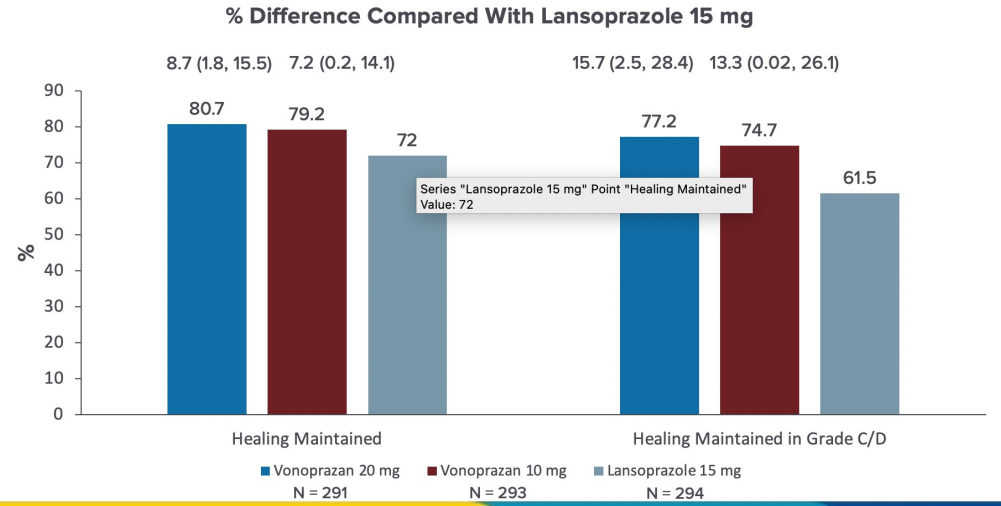
	Vonoprazan 20mg	Difference between arms (95% CI)	Lansoprazole 30mg	
Healing	92.9%	8.3% (4.5–12.2)	84.6%	All patients
Healing	91.7%	19.6% (11.8–27.6)	72.0%	LA Grades C/D

	Vonoprazan 20mg	Difference between arms (95% CI)	Lansoprazole 15mg		Vonoprazan 10mg	Difference between arms (95% CI)	
Maintenance	80.7%	8.7% (1.8–15.5)	72.0%	All patients	72.0%	7.2% (0.2–14.1)	79.2%
Maintenance	77.2%	15.7% (2.5–28.4)	61.5%	LA Grades C/D	61.5%	13.3% (0.02–26.1)	74.7%

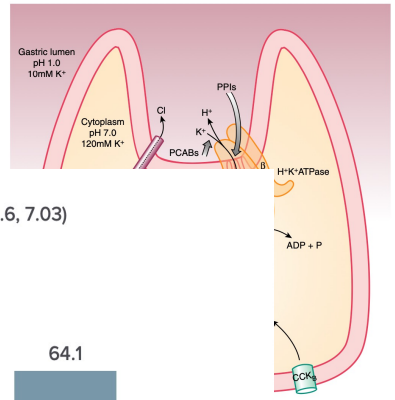
Gastroenterology

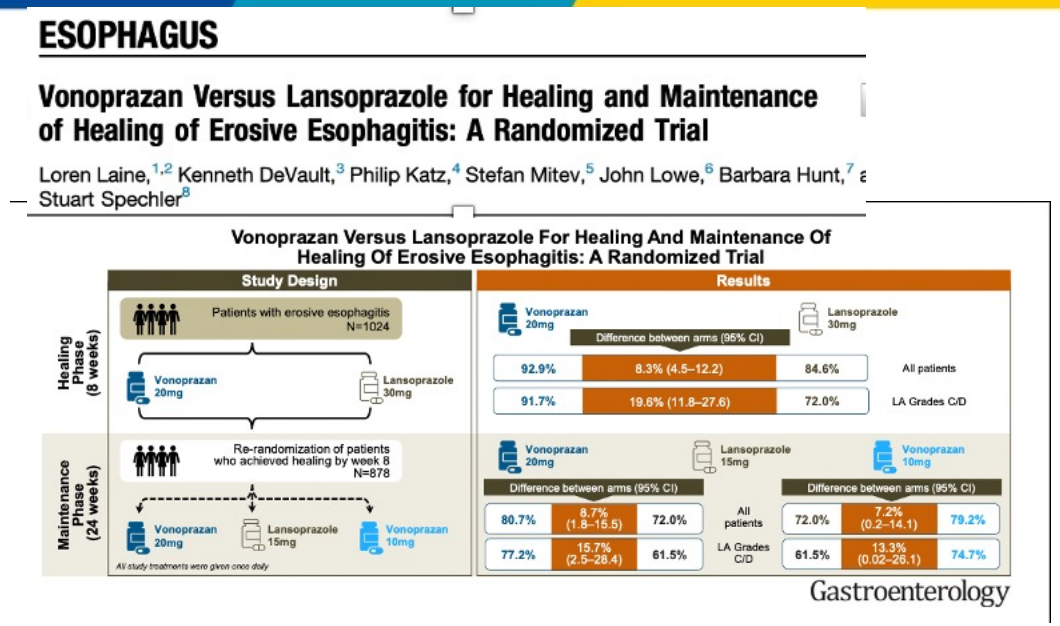


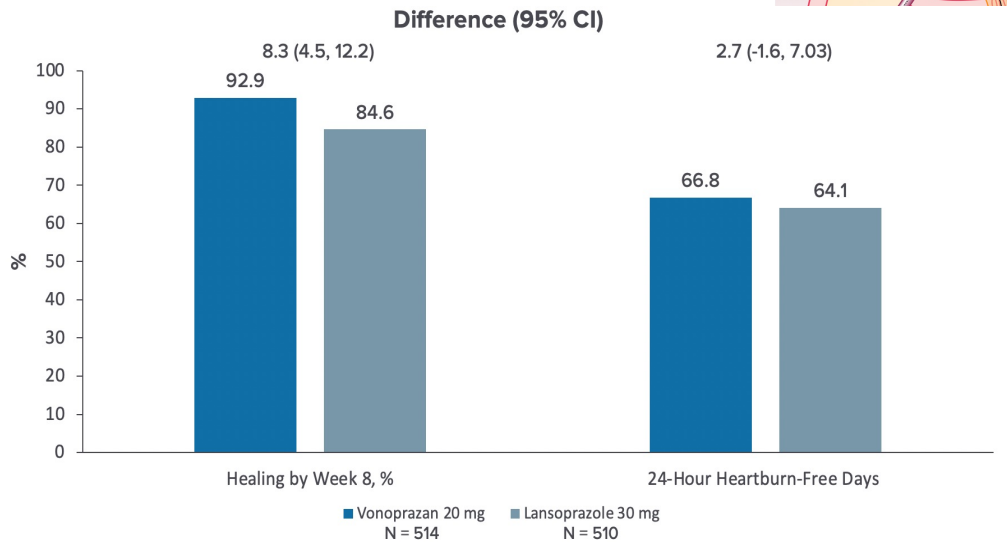
- Randomized, double blind, phase 3 multicenter trial (healing and maintenance phase)
- Vonoprazan was non-inferior to lansoprazole overall in esophagitis healing by 8 weeks and 24-hour heartburn-free days
- Vonoprazan was superior to lansoprazole in LA C/D esophagitis healing at 2 weeks and 8 weeks
- Vonoprazan 10 mg & 20 mg maintained healing at 6 months



We Have Entered a New Era for the Treatment of Acid-Related Diseases...pCABs (Potassium-Competitive Acid Blockers)







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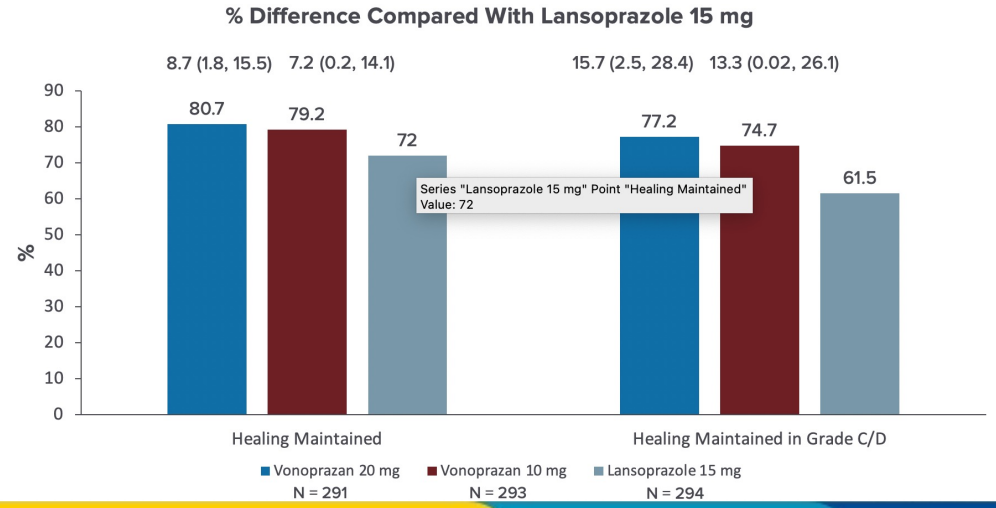
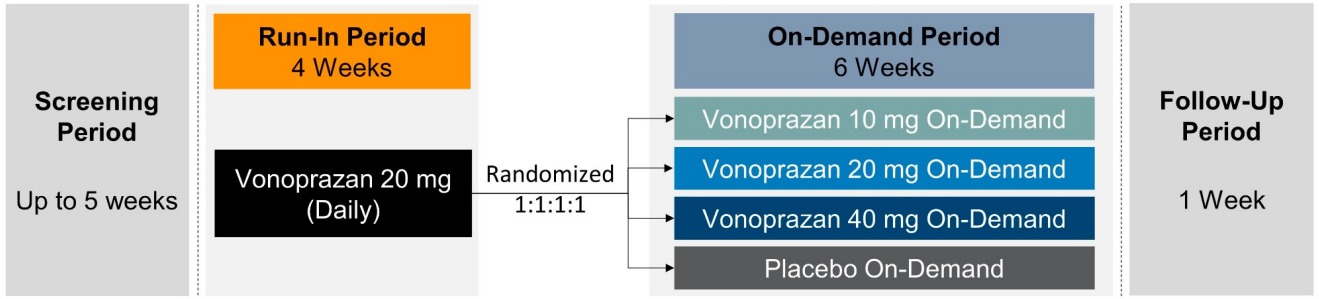
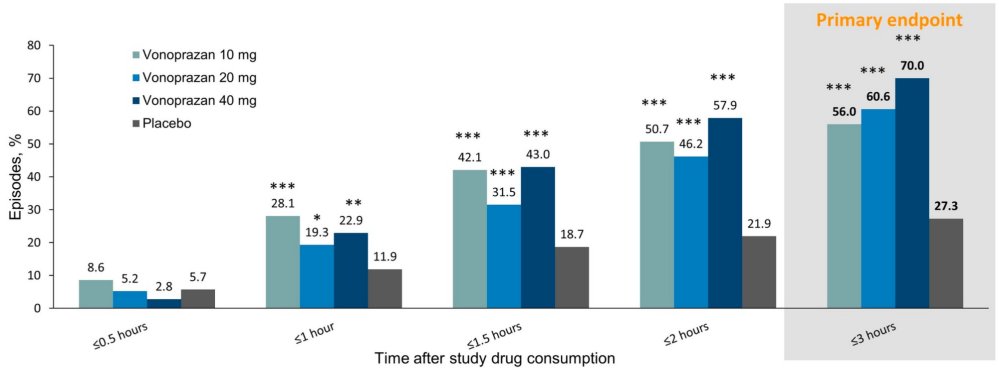


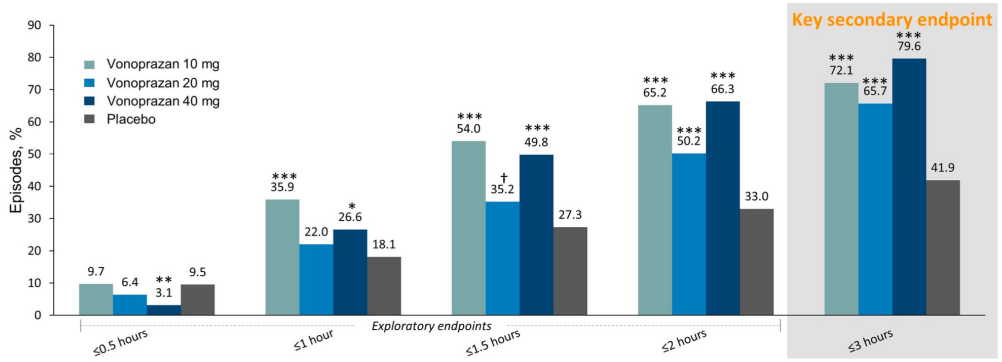
pCABs for Symptomatic Endoscopy Negative Classic GERD Symptoms



- NERD is a chronic, episodic condition
- On demand (as-needed) treatment that rapidly relieves symptoms is an attractive alternative to daily maintenance therapy

- Phase 2, double-blind, placebo-controlled trial Vonprazan vs placebo for as-needed treatment of symptomatic NERD
  - Rate of heartburn relief two times greater than placebo
  - Heartburn relief within 3 hour of on-demand use
  - Sustained relief for 24 hours





Fass R. APT 2023;58:1016-1027

Also…Some Other History That Dr. Christie 'Forgot' to Include:

1. Dr. Christie is such a wonderful clinician and noticed her patient is not wearing any jewelry. She asks her about that and is told "every time that her husband buys her cheap jewelry she breaks out in hives".
   - You must assume our patient has a nickel allergy
2. There is no time to do formal allergy testing and your institution/practice does not provide ambulatory reflux monitoring that is nickel-free
3. Patient absolutely refuses to have ANYTHING put down her nose (says that only little boys put things in their noses)

Therefore, you have **no other practical choice** than to first try her on a medication that has been proven to have enhanced acid suppressive effects

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Things to Remember if YOU Also ❤️ Your Patients

- PCABs provide significantly higher symptom response compared to placebo, especially with moderate to severe symptoms
- PCABs can be taken any time of day and only needed once a day
- Early heartburn relief is higher with PCABs than with placebo in adult NERD patients, observed as early as day #1 of treatment
- Early heartburn relief with PCABs allows consideration of on-demand therapy for adult NERD patients
- PCABs may provide relief of heartburn in NERD patients who failed PPI treatment

Plug for: Loren Laine's DDW plenary session presentation of NERD-301 on Monday afternoon

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Dr. Gyawali if you also ❤️ your patients….

TREAT FIRST…TEST LATER *IF* NEEDED

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How I Do It: Chronic Constipation and IBS

Satish SC Rao, MD, PhD, FRCP (Lon), FACG, AGAF

J. Harold Harrison, MD, Distinguished University Chair in Gastroenterology, Professor of Medicine

Director, Neurogastroenterology & Motility

Director, Digestive Health Clinical Research Center

Medical College of Georgia, Augusta, GA

AUGUSTA UNIVERSITY

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Disclosures

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

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Objectives

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

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Types of Constipation

1. Occasional Constipation
2. Chronic Constipation
   - *Primary*
     - *Slow transit constipation*
     - *Dyssynergic Defecation*
     - *IBS-C*
     - *Rectal Hyposensitivity/Hypersensitivity*
   - *Secondary*
   - *Opioid induced constipation*

Rao SS, et al. *Nat Rev Gastroenterol Hepatol*. 2016;13:295-305; Rao SS. *Gastroenterol Clin North Am*. 2007;36:687-711; Bharucha AE, et al. *Gastroenterology*. 2006;130:1510-1518.

Key Lesson

- Lumping all constipation as a one symptom disorder is wrong
  - Constipation is a polysymptomatic heterogeneous disorder
  - Patient's recall of symptoms is poor
  - Hence prospective symptom evaluation is key
  - Use Rome IV Criteria

Curtin B, et al. *J Neurogastroenterol Motil*. 2020;26:423-436.

OTC Therapies for Constipation-2022

OTC Products	Ramkumar/Rao, 1966-2004		Current Review, 2004-2020	
	Level of Evidence	Recommend. Grade	Level of Evidence	Recommend. Grade
Osmotic Laxatives				
PEG	I	A	I	A
Stimulants				
Senna	III	C	I	A
Bisacodyl	III	C	I	B
Sodium picosulfate	III	C	I	B
Magnesium				
Magnesium hydroxide	III	C	NA	NA
Magnesium-rich water	NA	NA	I	B
Magnesium oxide	NA	NA	I	B
Fruit-Based Laxatives and Foods with Prebiotics				
Kiwi	NA	NA	I	B
Mango	NA	NA	II	B
Ficus	NA	NA	II	B
Prunes	NA	NA	II	B
Rye bread with yogurt	NA	NA	III	C
Yogurt+galacto+ prunes + linseed oil	NA	NA	II	B

Rao SSC, Brenner DM. *Am J Gastroenterol*. 2021;116:1156-1181.

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OTC Therapies for Constipation-2022

OTC Products	Ramkumar/Rao, 1966-2004		Current Review, 2004-2020	
	Level of Evidence	Recommend. Grade	Level of Evidence	Recommend. Grade
Fiber-Containing Products				
Psyllium	II	B	II	B
Polydextrose	NA	NA	I	Insufficient
Inulin	NA	NA	I	Insufficient
Bran, methylcellulose	III	C	NA	NA
SupraFiber®	NA	NA	II	B
Miscellaneous				
Flaxseed oil	NA	NA	II	C
Fructo-oligosaccharide	NA	NA	III	Insufficient
Surfactants				
Docusate	III	C	NA	NA

Rao SSC, Brenner DM. *Am J Gastroenterol*. 2021;116:1156-1181.

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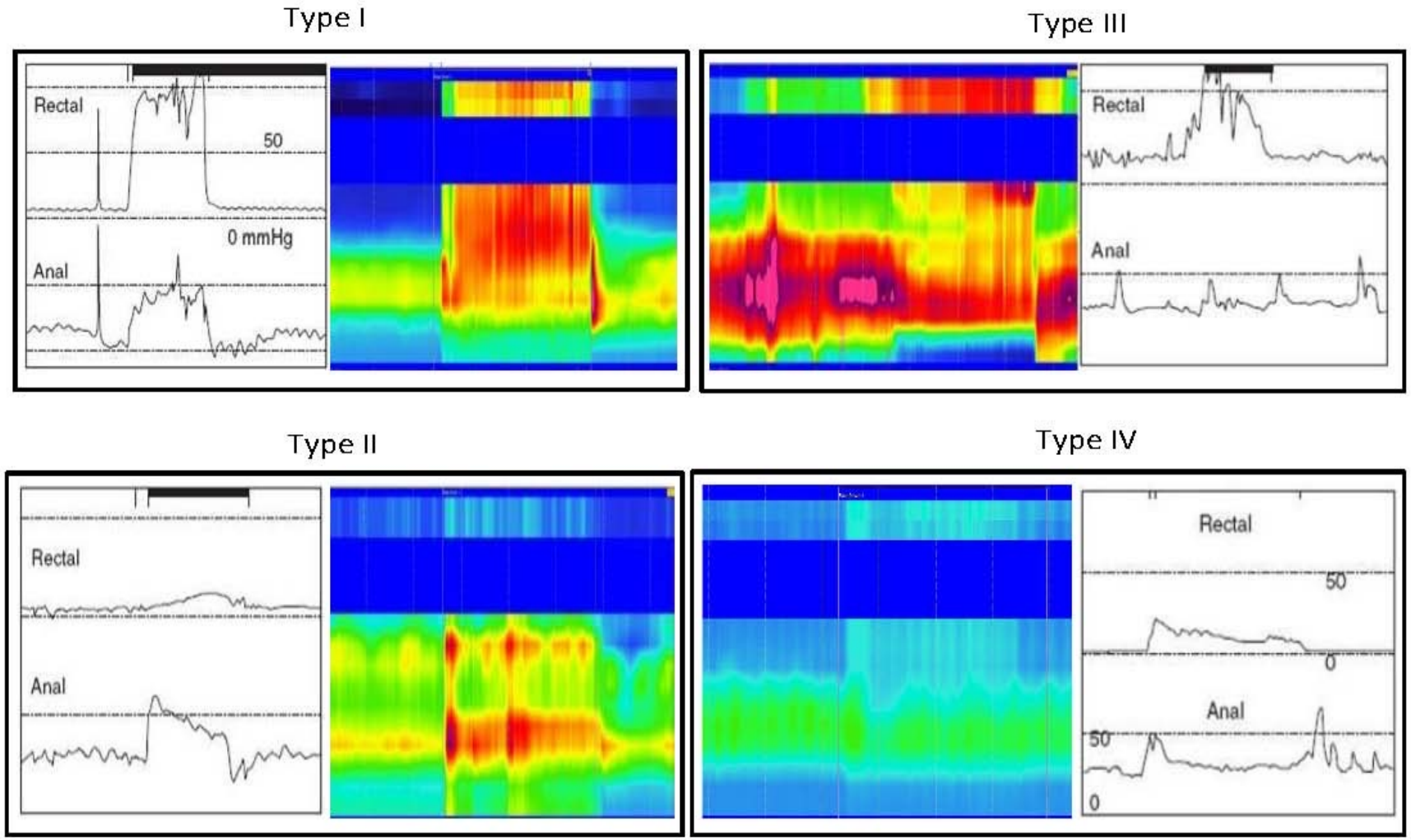
Case Study: 42-yr-old School Teacher

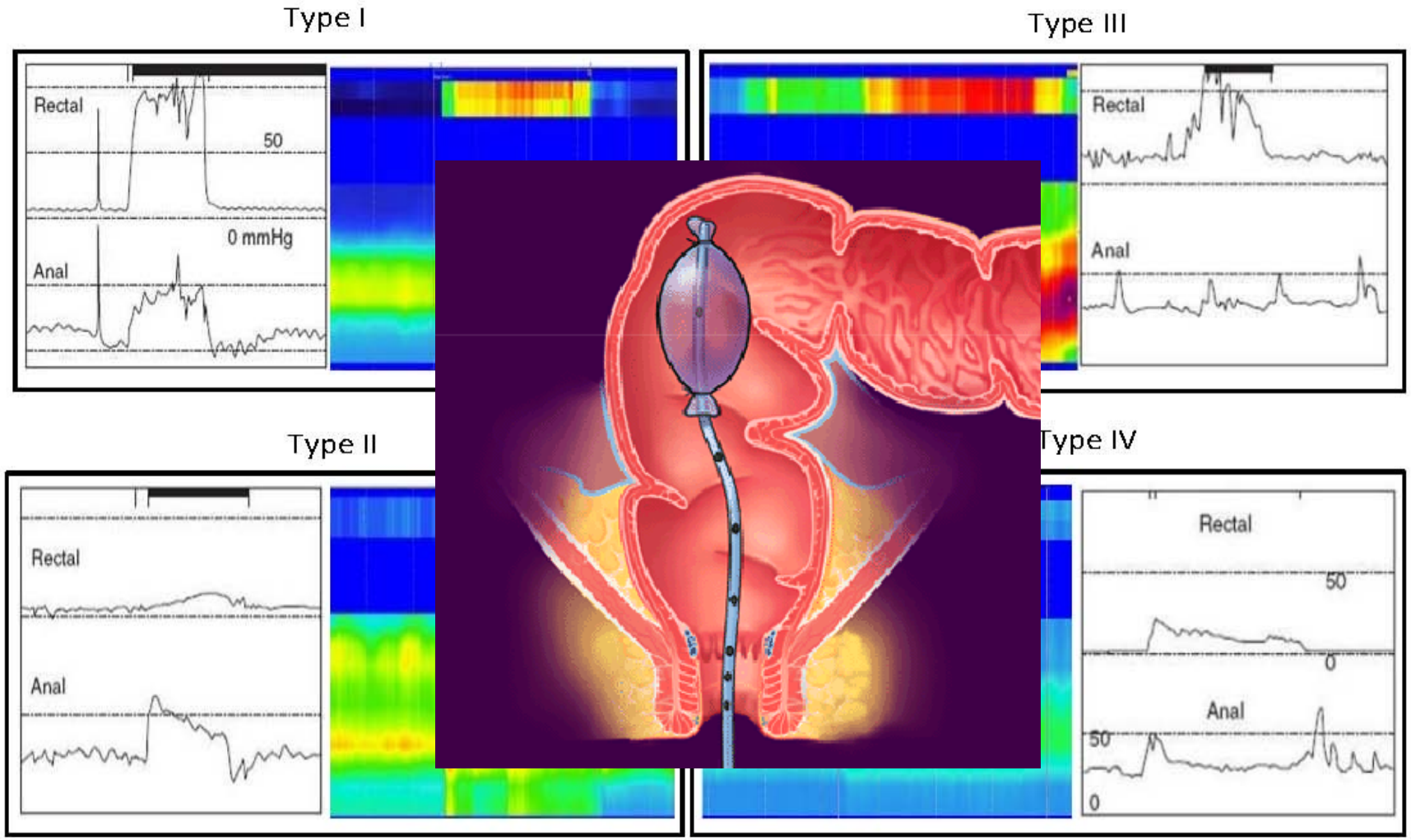
- Increasing constipation- 9 years
  - B.M once every 2 weeks, hard, pellet-like stool only after Fleet's enema + Suppository and laxatives
  - Frequent digital maneuvers, excessive straining, and incomplete evacuation
  - Tried OTC laxatives, MOM, PEG-no relief
  - DRE: paradoxical anal contraction-?dyssynergia
  - What would you do Next?

Types of Dyssynergic Defecation



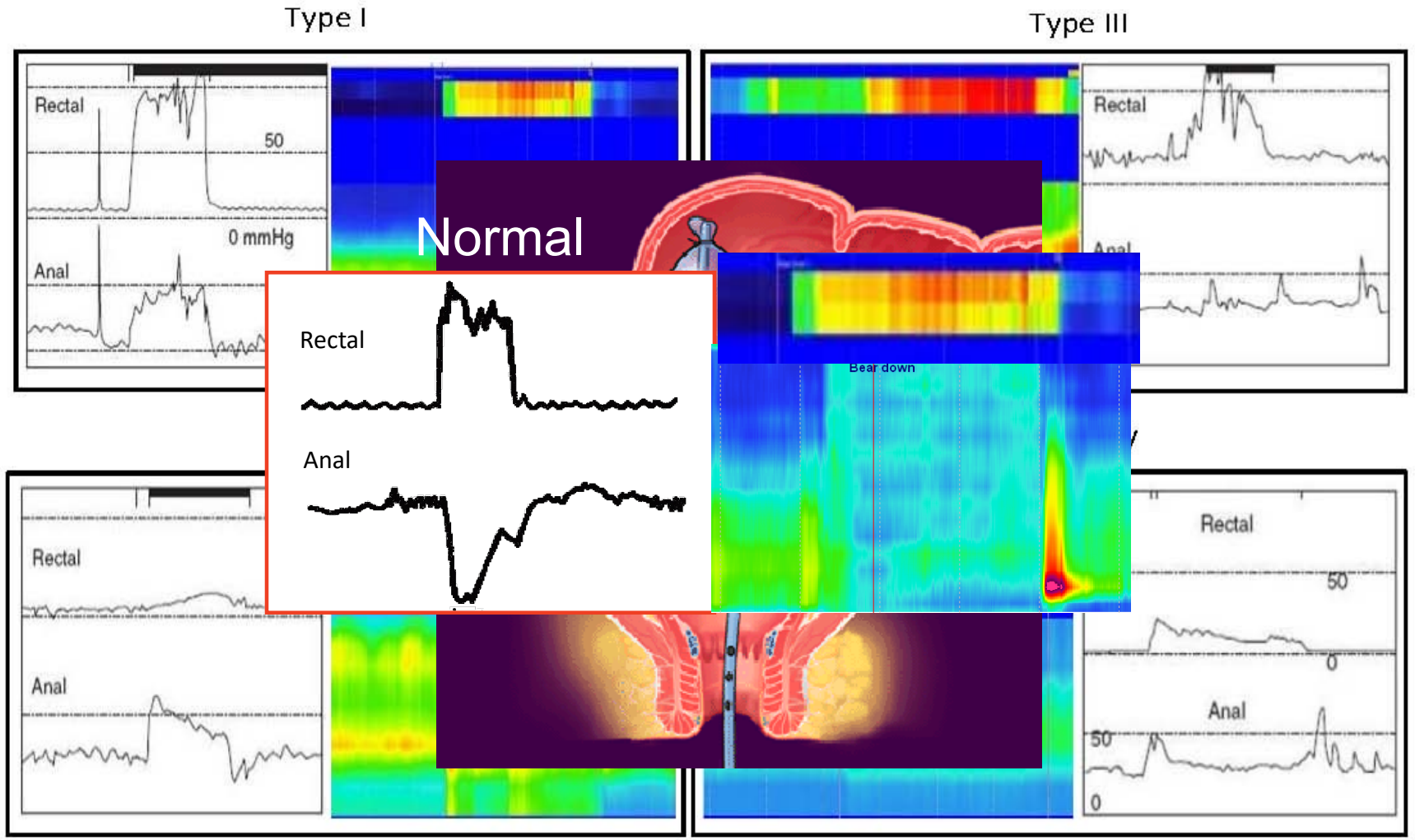
Rao SS, et al. *Neurogastroenterol Motil*. 2004;16:589-596.

Types of Dyssynergic Defecation



Rao SS, et al. *Neurogastroenterol Motil*. 2004;16:589-596.

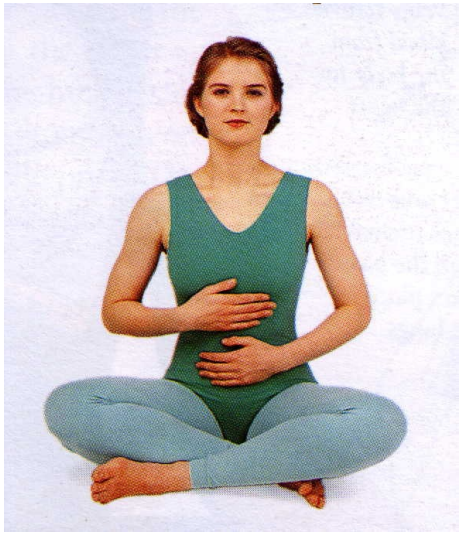
Types of Dyssynergic Defecation

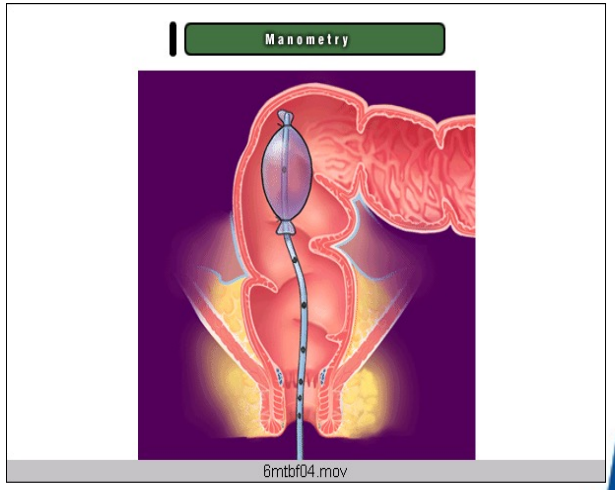


Rao SS, et al. *Neurogastroenterol Motil*. 2004;16:589-596.

Biofeedback-Dyssynergia

- Goals of Therapy :
  - A) Teach Diaphragmatic breathing exercise
  - B) Teach anal sphincter & pelvic floor relaxation
  - C) Improve Rectal Sensation
  - D) Eliminate Sensory Delay
  - E) Improve Recto-anal Coordination





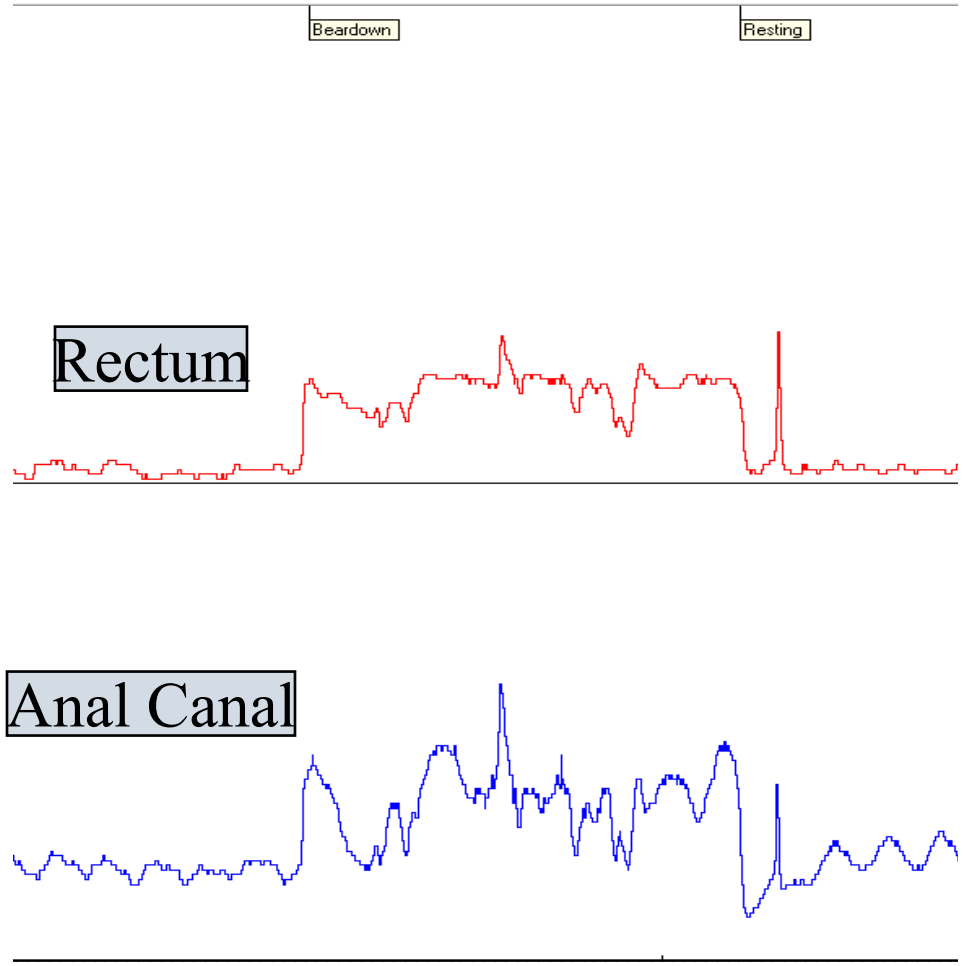
Rao SS, Go JT. *Curr Gastroenterol Rep*. 2009;11:278-287.

Biofeedback Therapy-RCTs

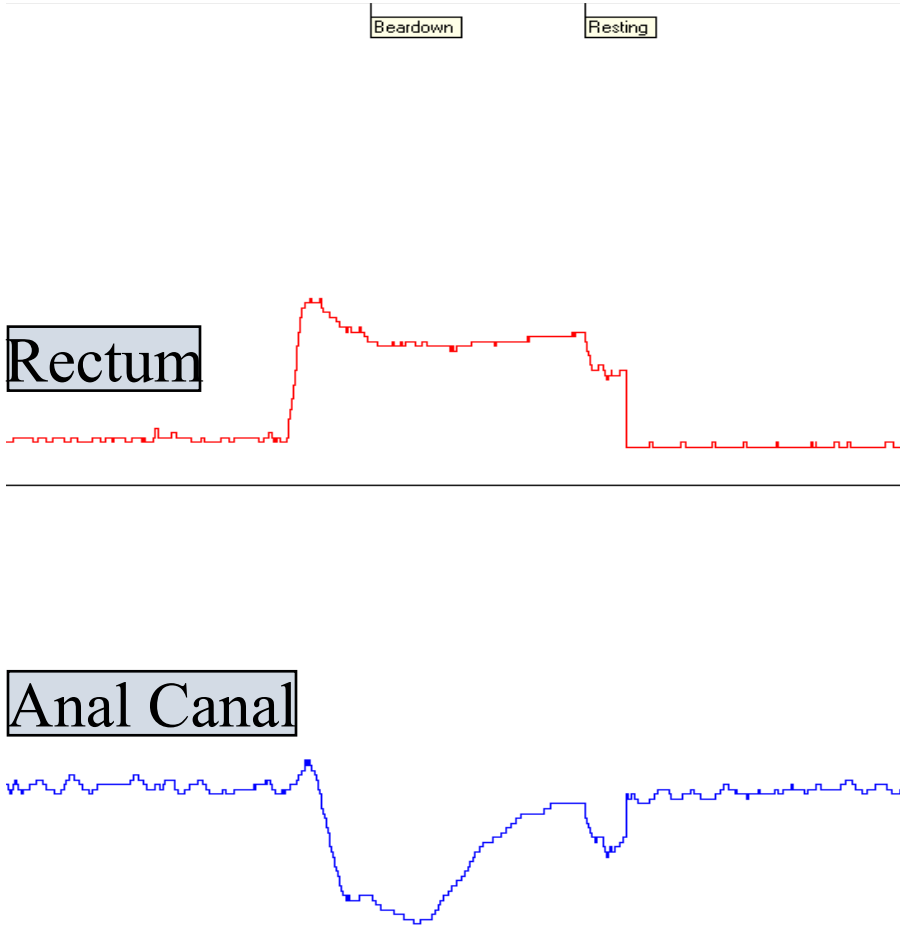
- Biofeedback Vs PEG 14.6 g for Dyssynergia
  - Chiarioni G, et al *Gastroenterology*. 2006;130:657-664.
- Biofeedback vs Diazepam for Dyssynergia
  - Heymen S, et al. *Dis Colon Rectum.* 2007;50:428-441.
- Biofeedback vs Sham Therapy vs Standard Therapy
  - Rao SS, et al. *Clin Gastroenterol Hepatol*. 2007;5:331-338.
- Biofeedback vs Standard Therapy-One Year outcome
  - Rao SS, et al. *Am J Gastroenterol*. 2010;105:890-896.
- Home vs Office Biofeedback Therapy - Efficacy & Cost Effectiveness
  - Rao SS, et al. DDW 2011; Go J, et al. DDW 2011.

Dyssynergic Defecation-Effects of Biofeedback

Before



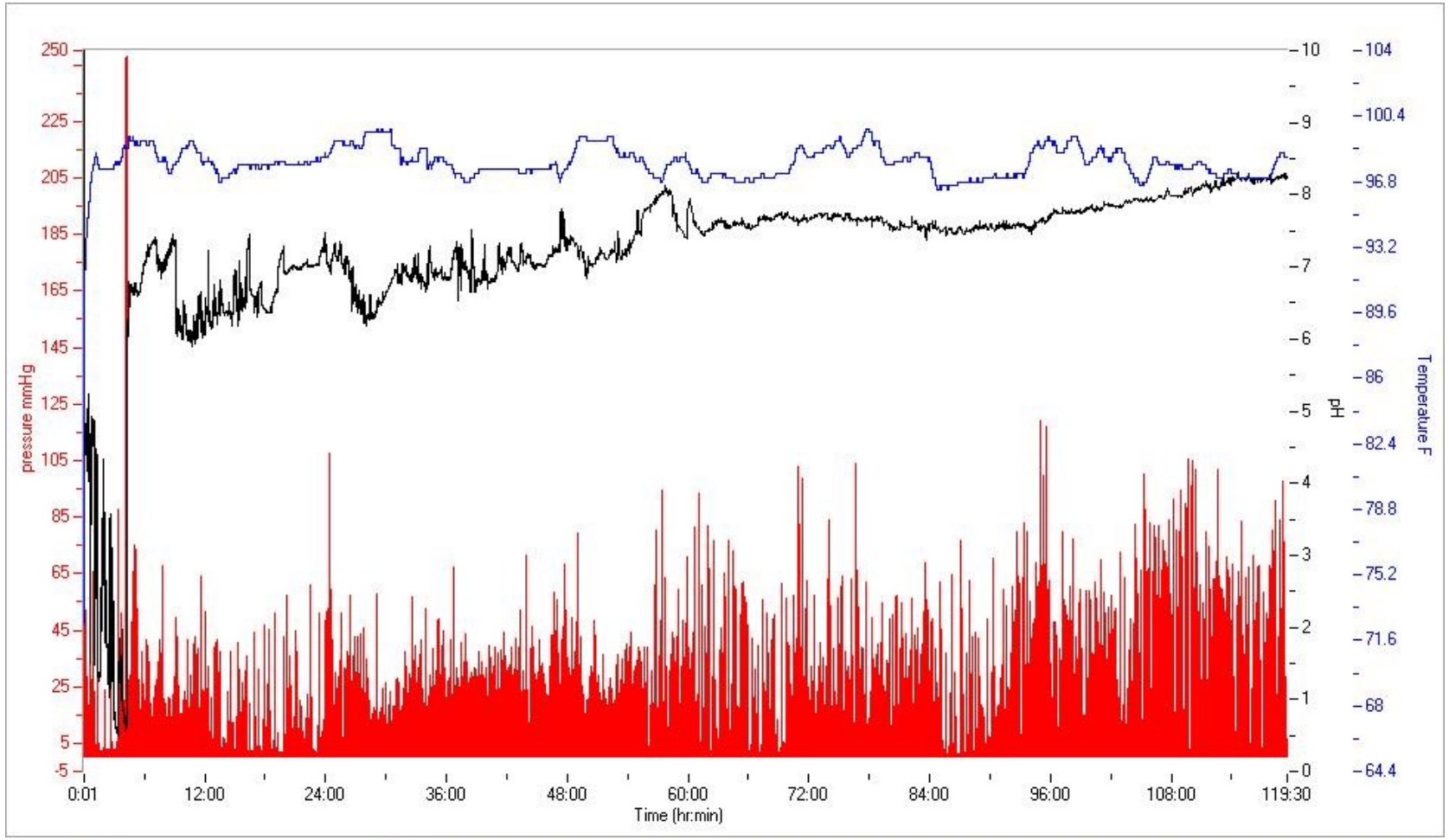
After

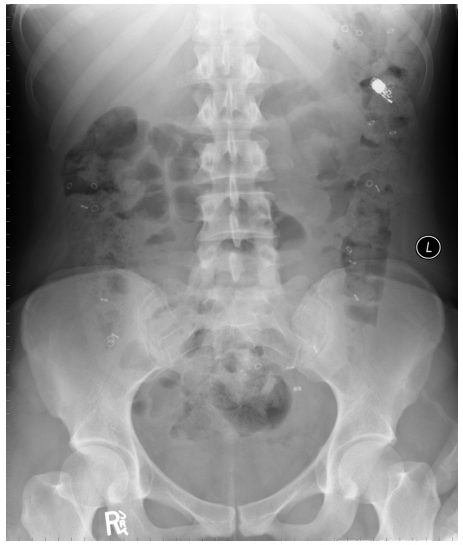


Images courtesy Rao SS.

40 yr Old Nurse, Severe Constipation, Pain, Gas & Bloating - Worse 2 yrs, On Depo-Provera

Refractory to laxatives; ? Colectomy





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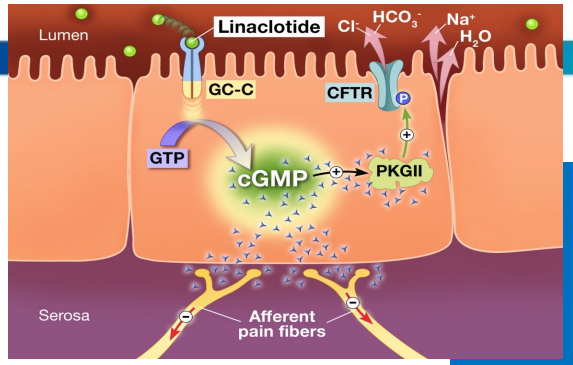
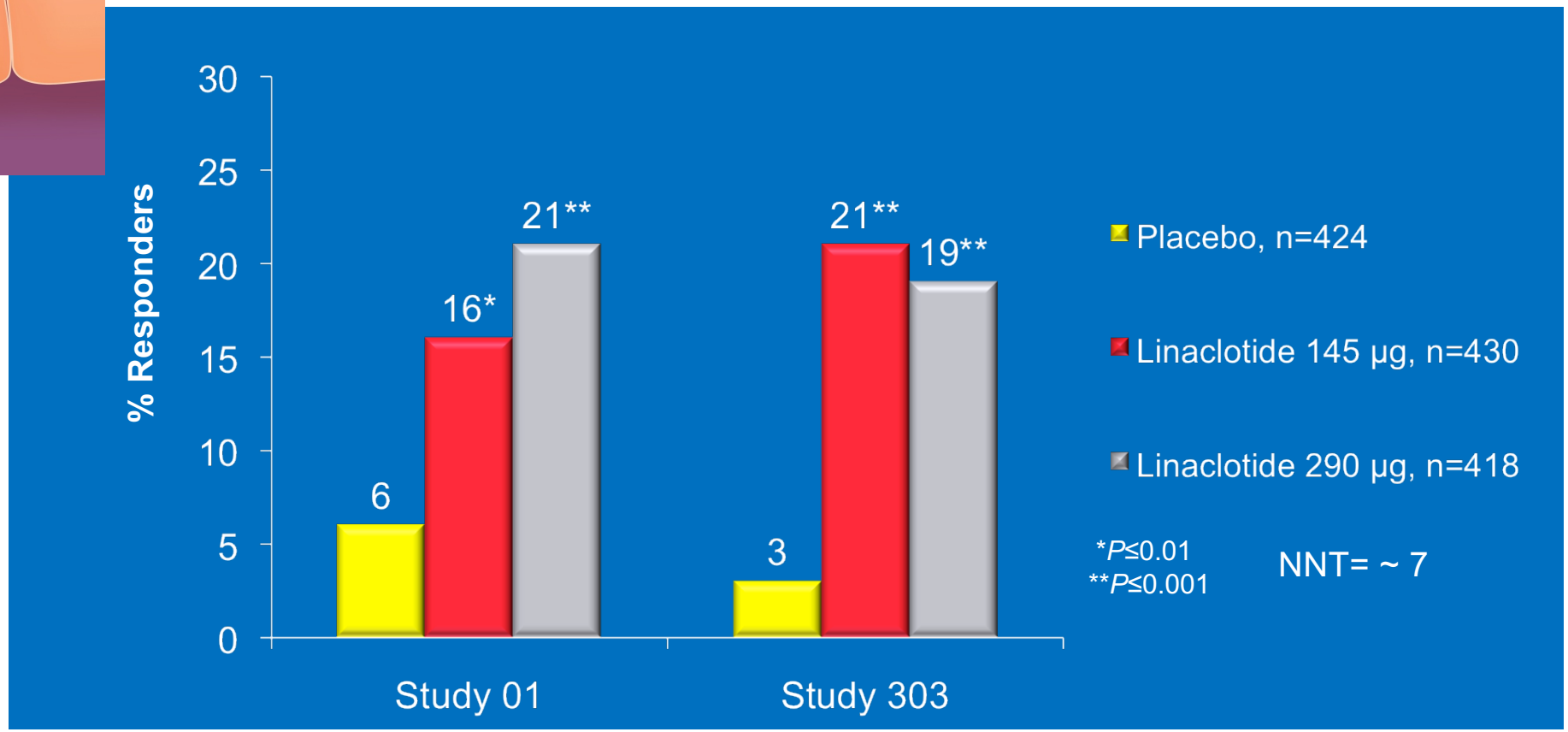
Efficacy of Linaclotide in Chronic Constipation





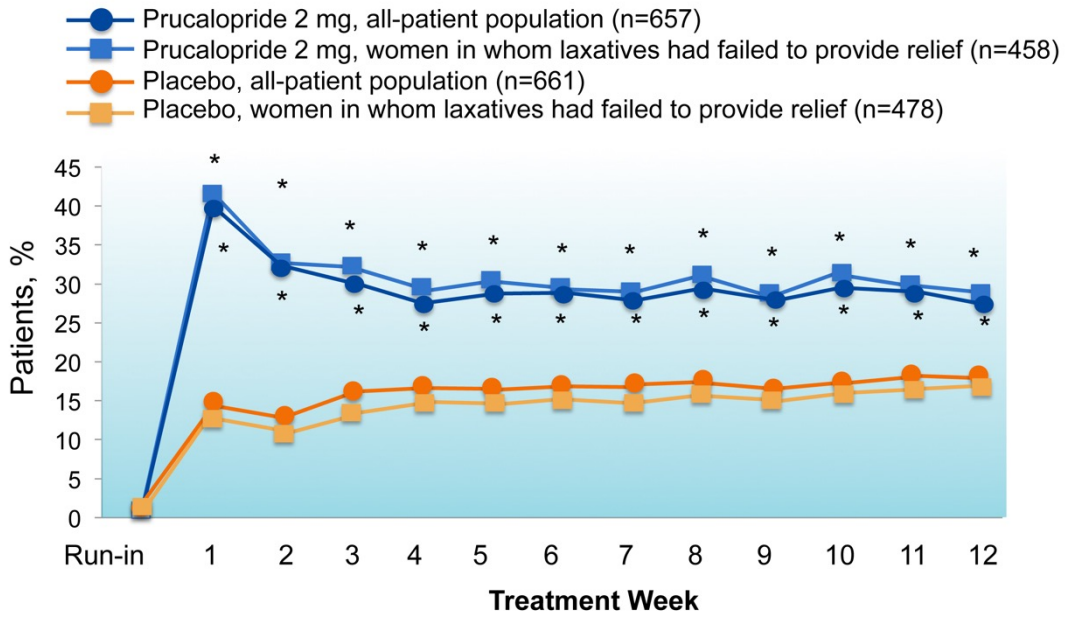
CSBM=complete spontaneous bowel movement.

Most common AE diarrhea (14%-16% vs 4.7%); Discontinuation (4% vs 0.5%).

Lembo AJ, et al. *N Engl J Med*. 2011;365:527-536.

Prucalopride in CIC: Integrated Analysis of Pivotal Phase 3 Trials

Patients with ≥3 SCBMs Over 12-Week Treatment Period†



Most Common Adverse Events‡

Adverse Events	Placebo (n=478) %	Prucalopride 2 mg (n=458) %
Nausea	9.8	10.7
Abdominal pain	8.1	10.0
Diarrhea	6.6	4.8
Headache	15.1	11.7

*P<0.001 for prucalopride vs placebo.

†Integrated analysis of 3 identical, double-blind, placebo-controlled, pivotal Phase 3 trials.

‡Occurring in >10% among patients in whom laxatives had failed to provide adequate relief. Results exclude adverse events on the first day of treatment.

SCBMs, complete spontaneous bowel movements.

Tack J, et al. *United European Gastroenterol J*. 2013;1:48-59.

Vibrating Capsule for Chronic Constipation

Vibration Capsule Program
Two Stimulation Cycles, each ~ 2 hours:
Each Vibration cycle: 3 seconds on and 16s rest

Vibrating capsule

Activation POD:

- Used for activating the capsule

E-Diary: Patient Reporting APP

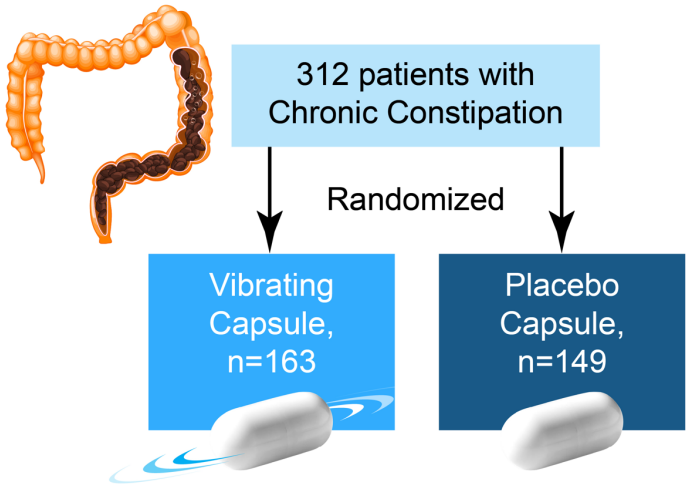
- Daily stool data
- Symptoms
- Capsule ingestion information
- Compliance
- Rescue
- Adverse Events

Rao SSC, et al. *Gastroenterology.* 2023;164:1202-1210.

Efficacy of Vibrating Capsule

Vibrating Capsule Treatment for Chronic Constipation

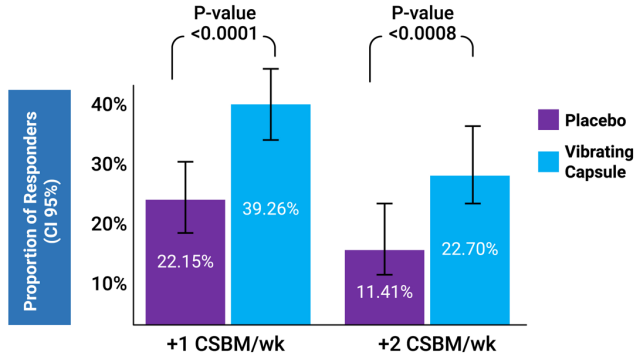
Phase 3, Double Blind, Multicenter, Placebo controlled trial



- Patients ingested one capsule at bedtime daily for 5 days a week
- Duration of study= 8 weeks

Primary Outcome Measures: Increase in one or more or two or more complete spontaneous bowel movements (CSBM) per week over baseline in 6 out of 8 weeks

Effect of Vibrating Capsule on CSBM, Primary Outcomes



Incremental CSBM (Complete Spontaneous Bowel Movement)

Vibrating Capsule was superior to Placebo capsule in improving constipation symptoms and quality of life, and was safe and well tolerated

Gastroenterology

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Rao SSC, et al. *Gastroenterology.* 2023;164:1202-1210.

Constipation: Take Home Points

- Investigation is key:
  - Colonic Transit, WMC, ARM, defecography, Colonic manometry are complementary & helpful
- Recognize comorbid illnesses, Burden & QOL
- Therapeutic options will depend on a clear understanding of pathophysiology
  - STC/CIC: Vibrating Capsule, Lubiprostone, Linaclotide, Prucalopride
  - OIC: Naloxegol, Methyl naltrexone
  - Dyssynergic Defecation: Biofeedback therapy

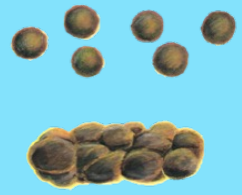
Irritable Bowel Syndrome

IBS is Chronic Disorder of Gut-Brain Interaction (DGBI)

- 30's-40's; ♀≥ ♂; 4-11% adult population
- Intermittent abdominal pain/discomfort/bloating and altered bowel function
- Symptoms are frequently aggravated by food/stress
- Coexisting conditions are common including:
  - chronic fatigue, fibromyalgia, migraine headaches, interstitial cystitis, etc

Lacy BE, et al. Am J Gastroenterol. 2021;116:17-44.
Ballou S. et al. Clin Gastroenterol Hepatol. 2019 Aug 13
Grover M, et al. Plos One 2021; 16(1)

Bristol Stool Form Scale[1,2]



Type 1
Separate hard lumps, like nuts

Type 2
Sausage-shaped but lumpy

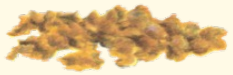
IBS-C

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

Lacy BE, et al. *Am J Gastroenterol*. 2021;116:17-44; Ballou S, et al. *Clin Gastroenterol Hepatol*. 2019;17:2471-2478.e3; Grover M, et al. *PLoS One*. 2021;16:e0245323.

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Rome IV Criteria for Irritable Bowel Syndrome

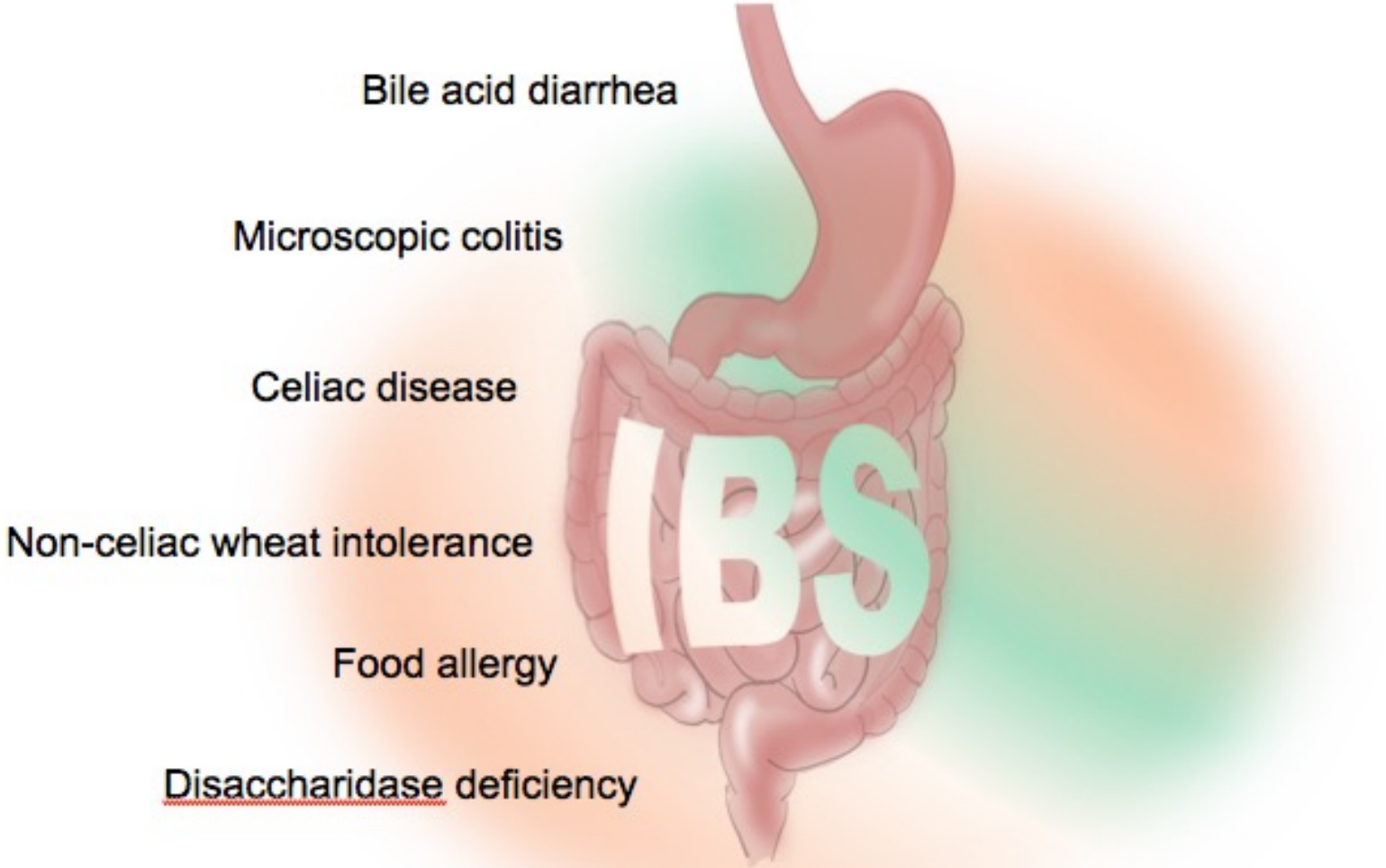
Recurrent abdominal pain at least 1 day/week
In the last 3 months associated with 2 or more:

- **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

Mearin F, et al. *Gastroenterology*. 2016;150:1393-1407.

Searching for IBS-D: Differential Diagnoses



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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;116:17-44.

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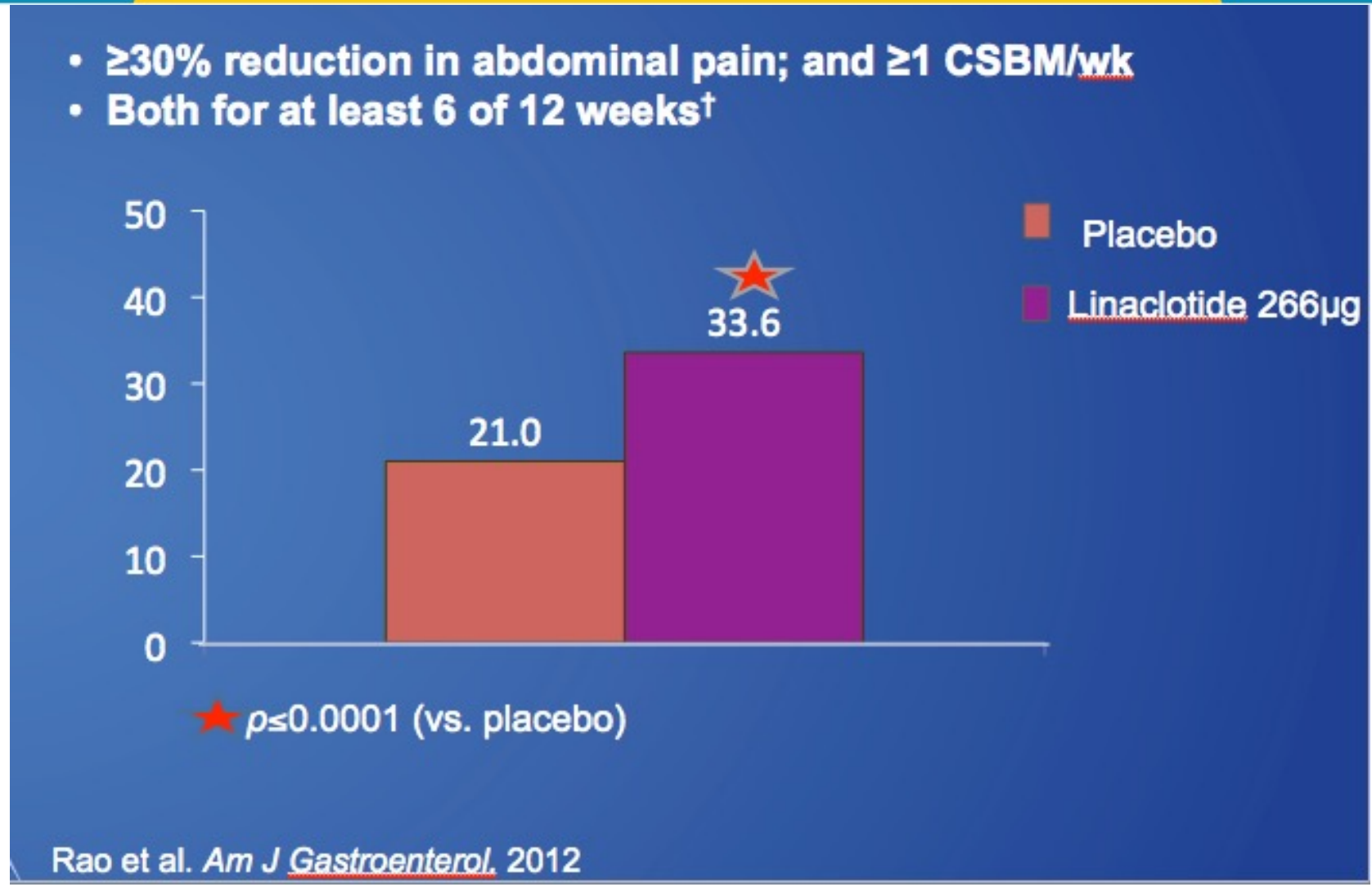
ACG Guidelines for IBS-D Treatment

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

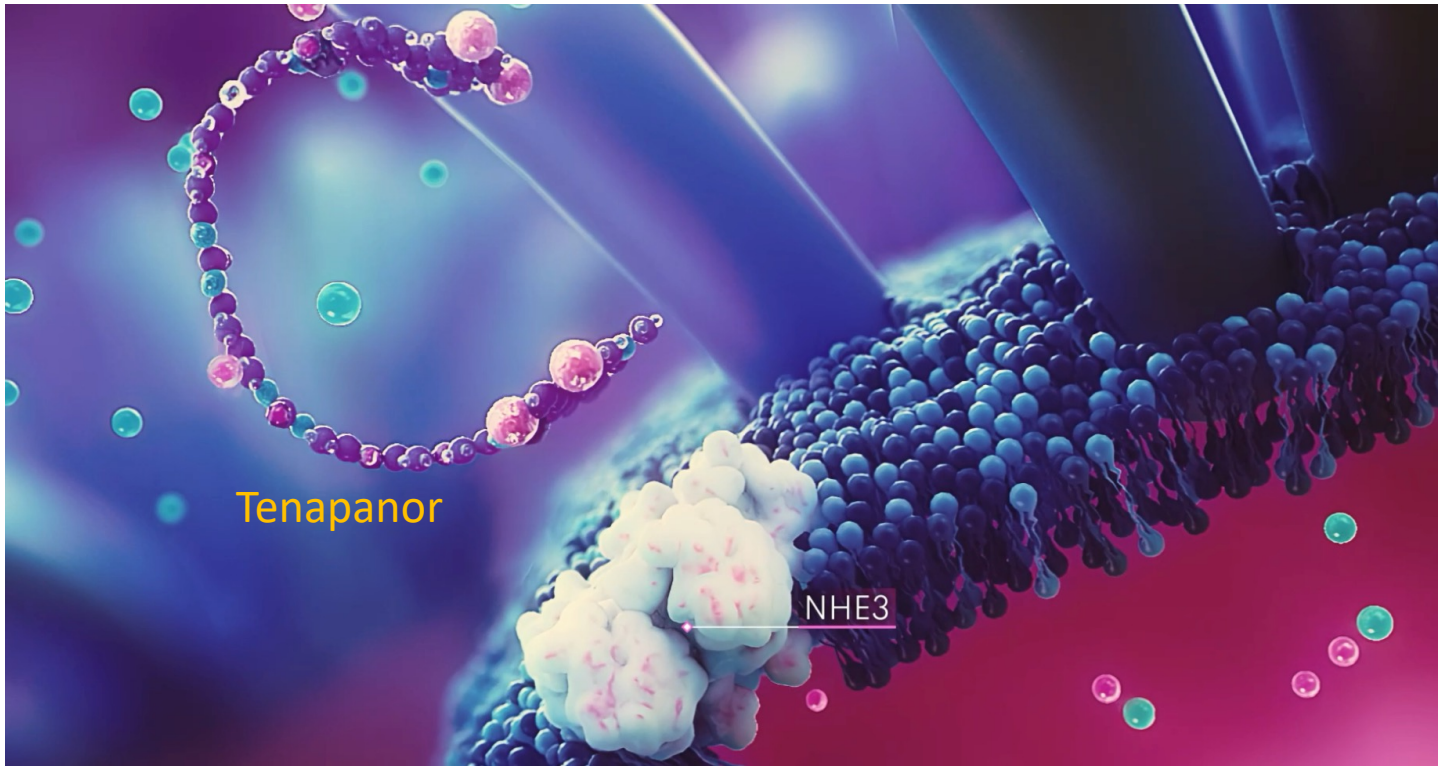
[a]For all recommendation statements, the comparator was no drug treatment.

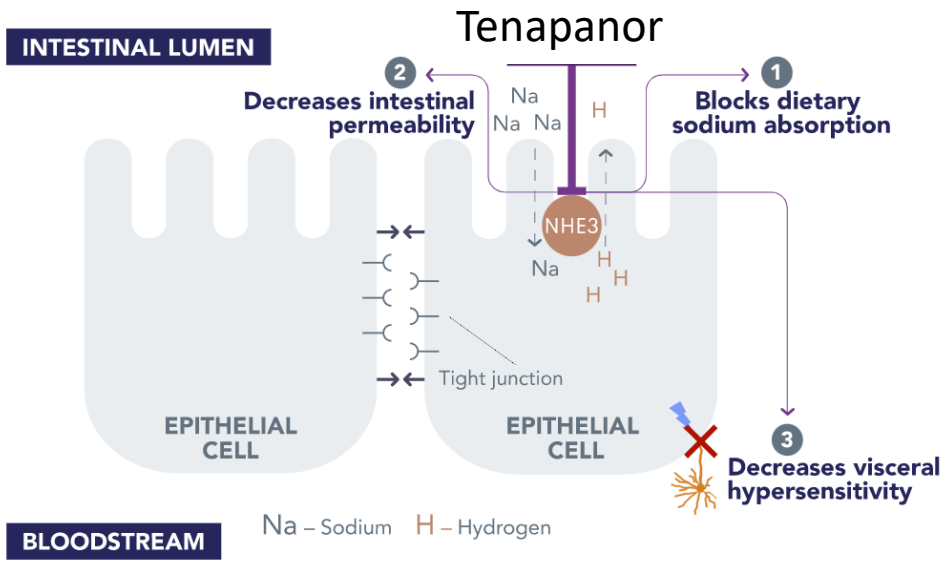
Lembo A, et al. *Gastroenterology.* 2022;163:137-151.

Efficacy of Linaclotide for IBS-C: Study 31, FDA Endpoint



Tenapanor: Sodium Hydrogen Exchanger 3 Blocker





1. Chey WD, et al. Am J Gastroenterol. 2020;115:281-293. 2. Chey WD, et al. Am J Gastroenterol. 2021;116:1294-1303.

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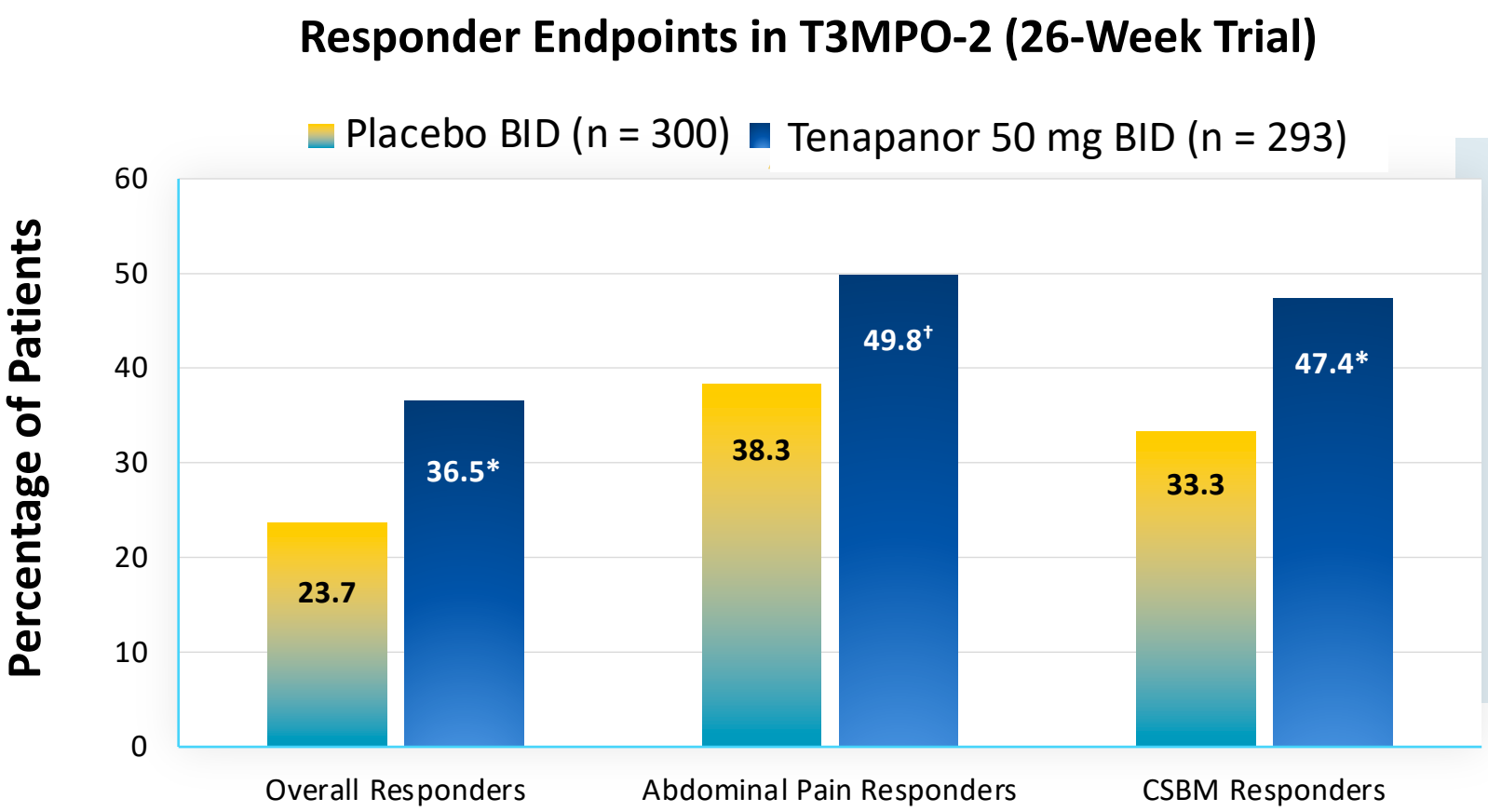
Efficacy of Tenapanor Compared With Placebo in RCT



36.5%

of patients treated with Tenapanor were overall responders‡

Primary efficacy endpoint: overall responder for 6 or more of the first 12 treatment weeks.
*P <0.001. †P <0.004. ‡Overall responder defined as: a decrease in average weekly worst abdominal pain of ≥30.0% from baseline AND an increase of at least 1 CSBM from baseline, both in the same week, for at least 6 of the first 12 weeks of treatment.
BID, twice daily; CSBM, complete spontaneous bowel movement.
Chey WD, et al. *Am J Gastroenterol*. 2021;116:1294-1303.

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AGA Guidelines for Treatment of IBS-C

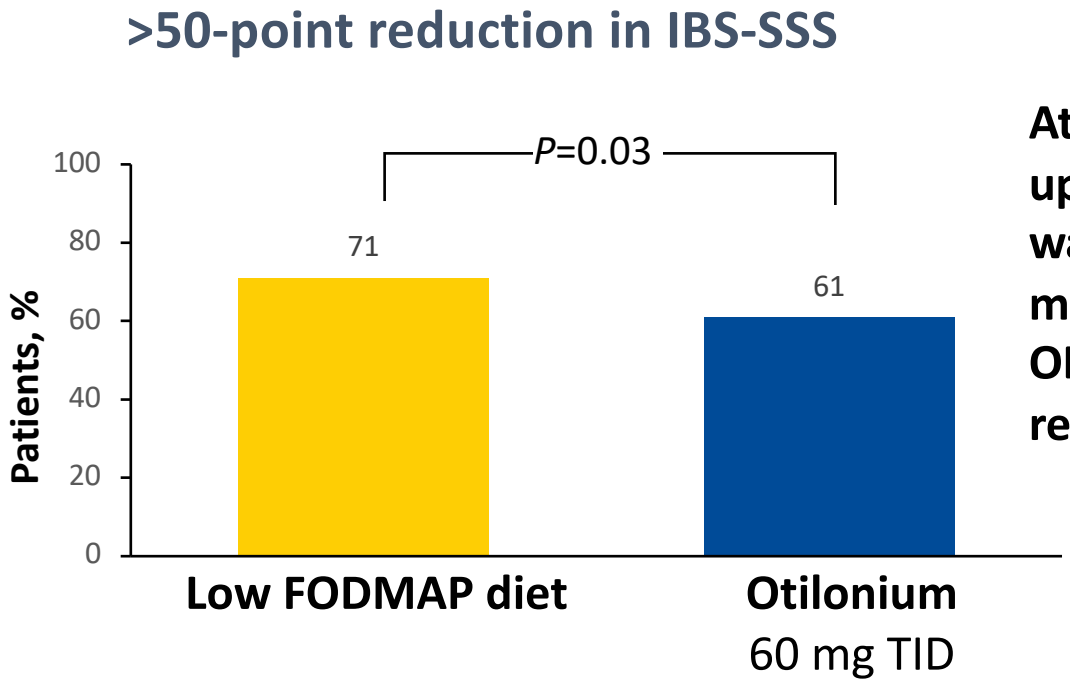
New or updated recommendations[a]	Strength of recommendation	Certainty of evidence
1. In patients with IBS-C, the AGA suggests using tenapanor	Conditional	Moderate
2. In patients with IBS-C, the AGA suggests using plecanatide	Conditional	Moderate
3. In patients with IBS-C, the AGA recommends using linaclotide	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;163:118-136.

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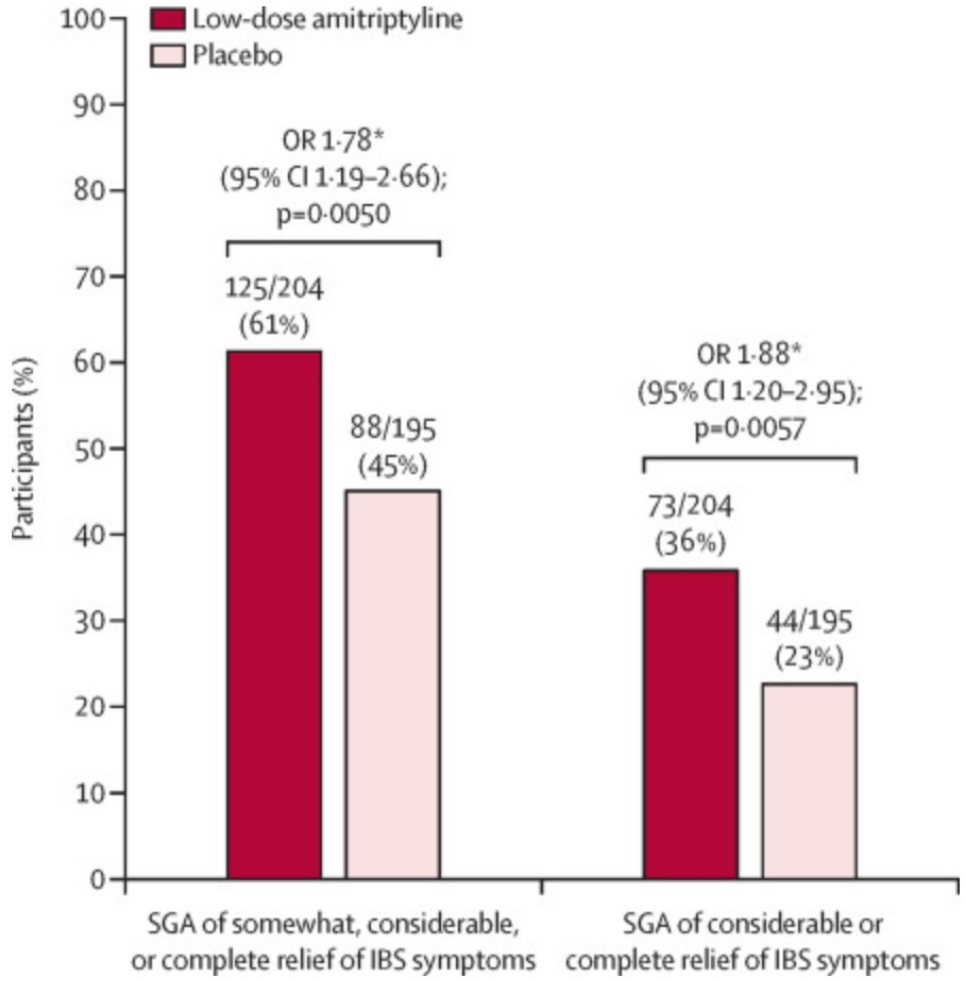
Amitriptyline for IBS in Primary Care (ATLANTIS Trial): 463 Patients; Amitriptyline (232 pts), 10-30 mg/day



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

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IBS: Take Home Points

- Make a Positive Diagnosis: Physician-patient communication is key
- Abdominal Pain, Visceral hypersensitivity and DGBI are Key features
- Evaluate for Alarming features and treat symptomatically (Diet, Loperamide, Peppermint oil, Fiber, laxatives-First line)
- 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: CHO deficiency, SIBO (Antibiotics), SIFO (Antifungals)

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Best of Evidence-Based GI: Lower GI Motility Disorders

Moderator: Darren Brenner, MD

Panel: Kavita Kongara, MD and Baha Moshiree, MD

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Importance

This summary reviews Ford AC, Wright-Hughes A, Alderson S, et al. **Amitriptyline at Low-Dose and Titrated for Irritable Bowel Syndrome as Second-Line Treatment in Primary Care (ATLANTIS): A Randomised, Double-Blind, Placebo-Controlled, Phase 3 Trial**. *Lancet*. 2023;402:1773-1785.

IBS is very common and debilitating, yet treatment is currently not optimal due to limited supporting evidence

→

ACG and AGA guidelines have conditional recommendation for the use of TCAs for global symptoms of IBS

→

The ATLANTIS study is a major effort to quantify the benefit of amitriptyline in a large RCT over 6 months

Conditional recommendation as per WHO GRADE system: when the evidence around the benefits and risks of an intervention is less certain.

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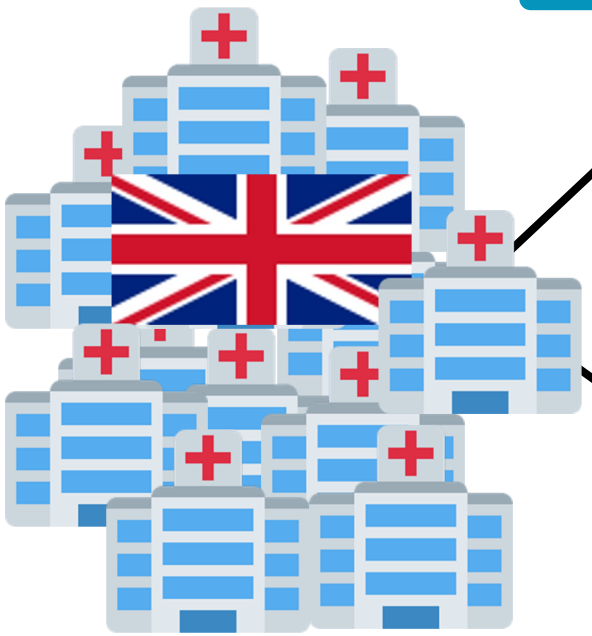
Study Design

This summary reviews Ford AC, Wright-Hughes A, Alderson S, et al. **Amitriptyline at Low-Dose and Titrated for Irritable Bowel Syndrome as Second-Line Treatment in Primary Care (ATLANTIS): A Randomised, Double-Blind, Placebo-Controlled, Phase 3 Trial**. *Lancet*. 2023;402:1773-1785.

QUESTION: Is amitriptyline 10-30mg at night superior to placebo for improvement in IBS symptoms at 6 months?

55 Primary Care General Practices



Placebo

RANDOMIZED 1:1

amitriptyline 10mg at night

Titrated up to 30mg over 3 weeks and participants able to titrate up or down their doses based on IBS symptoms or side effects

PATIENT POPULATION:

- Inclusion criteria:
- ≥18 yo
- IBS based on Rome IV criteria
- IBS-SSS > 75 (0-500)
- Failure to respond to 1st line tx (dietary modification, soluble fiber, antispasmodics, laxatives/antidiarrheal)
- Normal Hb, CRP, negative for celiac
- No suicidal ideations

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Definitions and Endpoints

This summary reviews Ford AC, Wright-Hughes A, Alderson S, et al. **Amitriptyline at Low-Dose and Titrated for Irritable Bowel Syndrome as Second-Line Treatment in Primary Care (ATLANTIS): A Randomised, Double-Blind, Placebo-Controlled, Phase 3 Trial**. *Lancet*. 2023;402:1773-1785.

Rome IV diagnostic criteria for Irritable Bowel Syndrome

Recurrent abdominal pain at least 1 day/week in the last 3mo, associated with 2 or more of the following:

1. **Related to defecation**
2. **Associated with a change in the frequency of stool**
3. **Associated with a change in the form of the stool**

*Criteria should be fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

INTENTION TO TREAT ANALYSIS

PRIMARY OUTCOME:
IBS-SSS score at 6 months

SECONDARY OUTCOME:
subjective global assessment (SGA) of relief of IBS at 6mo

Adapted from: Lacy, Brian E.; Pimentel, Mark; Brenner, Darren M.; Chey, William D.; Keefer, Laurie A.; Long, Millie D.; Moshiree, Baha.

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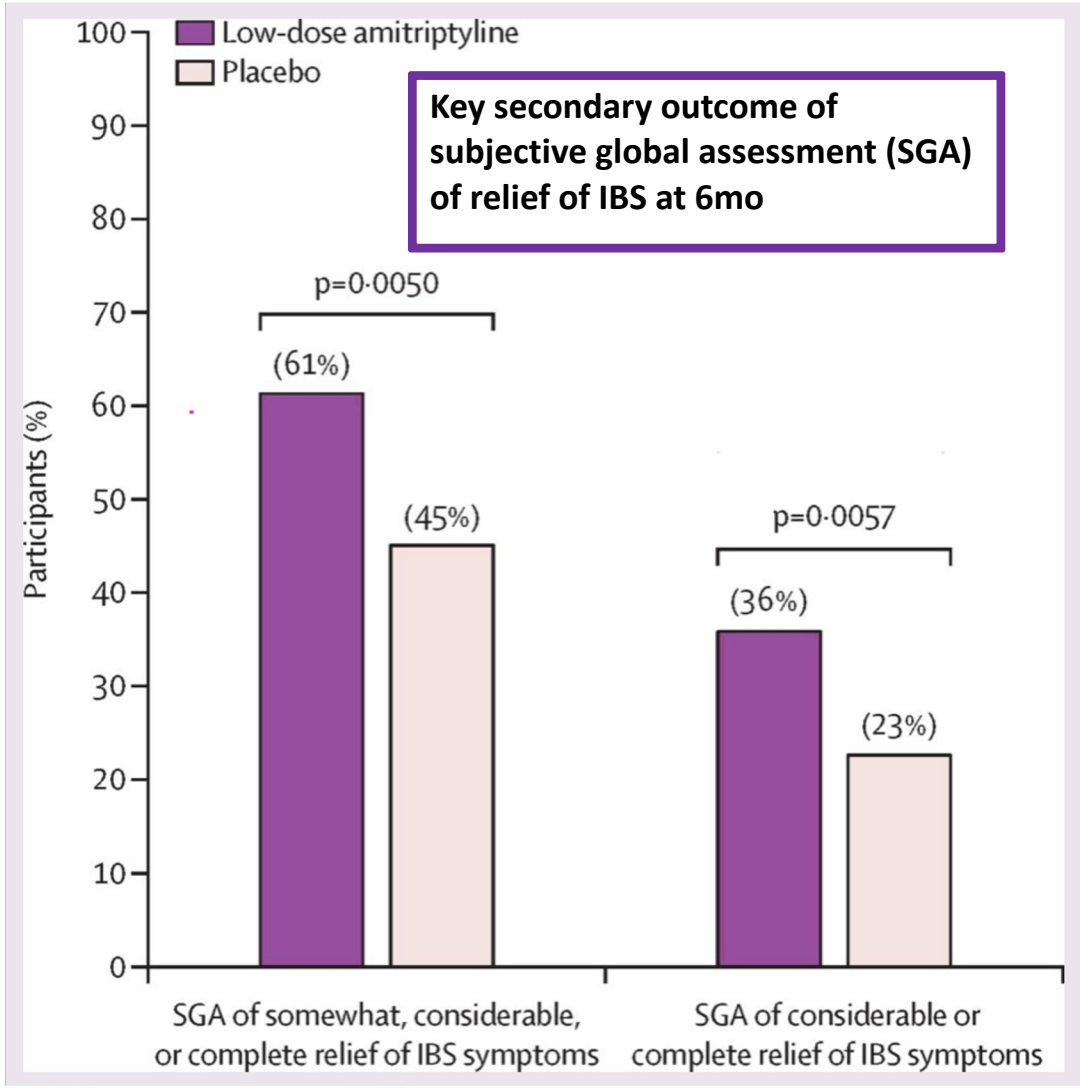
Results

This summary reviews Ford AC, Wright-Hughes A, Alderson S, et al. **Amitriptyline at Low-Dose and Titrated for Irritable Bowel Syndrome as Second-Line Treatment in Primary Care (ATLANTIS): A Randomised, Double-Blind, Placebo-Controlled, Phase 3 Trial**. *Lancet*. 2023;402:1773-1785.



At 6 months mean IBS-SSS:

- Amitriptyline group: ⇩ from 273 to 170
- Placebo group: ⇩ from 272 to 200
- Mean difference in IBS-SSS score of -27.0 95%CI [-46.9 to -4.6], *P* = 0.008

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Limitations

This summary reviews Ford AC, Wright-Hughes A, Alderson S, et al. **Amitriptyline at Low-Dose and Titrated for Irritable Bowel Syndrome as Second-Line Treatment in Primary Care (ATLANTIS): A Randomised, Double-Blind, Placebo-Controlled, Phase 3 Trial**. *Lancet*. 2023;402:1773-1785.

- Benefit observed with amitriptyline was modest
- Inclusion of IBS-C patients (17%) in this trial may have decreased the observed benefit of amitriptyline in the overall IBS population
- Did not meet the minimal clinically important difference in IBS-SSS reduction of 35 points compared to placebo
- Rigorous responder endpoints required by the US and European agencies for drug trials in IBS-D and IBS-C were not used.
- Performed in a Primary Care setting

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Questions

1. Which IBS patients are optimal candidates for treatment with TCAs? How do you educate them about benefits-risks of an “anti-depressant”?

2. What are your preferred neuromodulators for IBS-C patients?

3. How much benefit is likely to be achieved with TCAs? Do you combine with other treatments?

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Kiwifruit-A Specific Food to Improve Stool Frequency in Patients With Mild Constipation

Philip Schoenfeld, MD, MSEd, MSc (Epi)

Chief (Emeritus), Gastroenterology Section, John D. Dingell VA Medical Center, Detroit, MI.

This summary reviews Gearry R, Fukudo S, Barbara G, et al. Consumption of 2 Green Kiwifruits Daily Improves Constipation and Abdominal Comfort-Results of an International Multicenter Randomized Controlled Trial. Am J Gastroenterol 2023; 118: 1058-68.

Access the article through PubMed

Listen to the audio summary

Correspondence to Philip Schoenfeld, MD, MSEd, MSc. Editor-in-Chief. Email: EBGI@gi.org

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PGY-6, Loma Linda University

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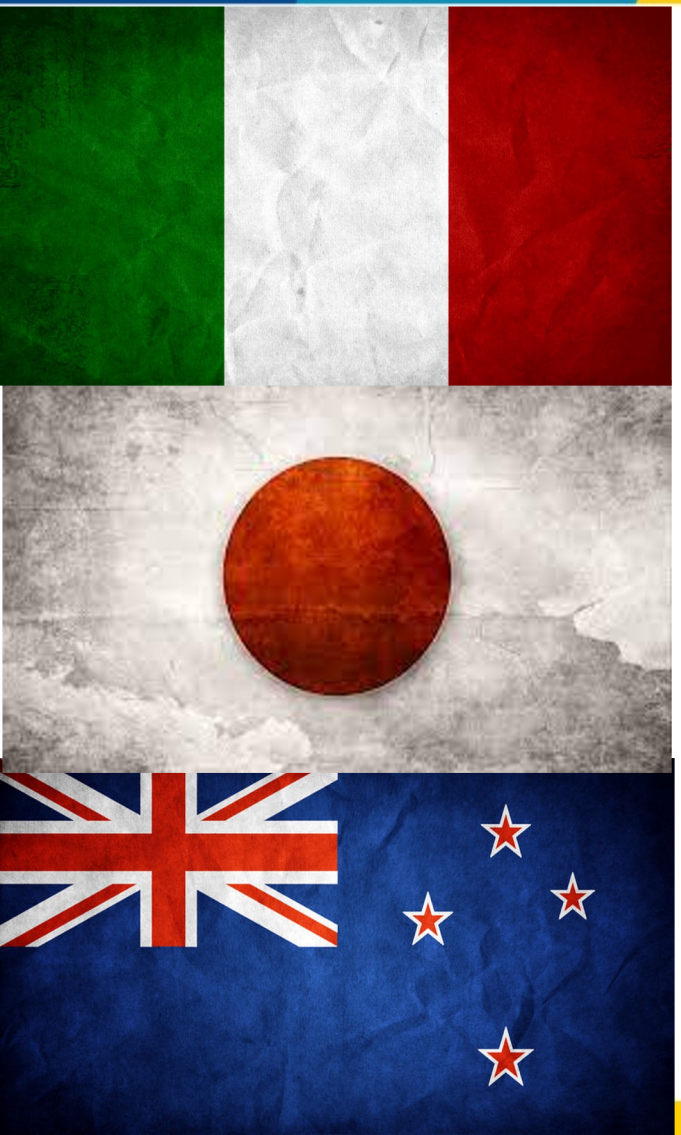
Study Design



Italy
Japan
New Zealand

Multicenter
Randomized
Crossover Trial

FC (n=60)
IBS-C (n=61)
Controls (n=63)

2 kiwis qd x 4 wks

7.5g psyllium qd x 4 wks

4 wk washout followed by crossover

Inclusion:
Patients meeting Rome III criteria at initial screening for functional constipation (FC), IBS-C, and healthy controls

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Outcomes

PRIMARY OUTCOME

Complete Spontaneous Bowel Movements (CSBM) / Week

Secondary Outcomes

- GI Comfort via GI Symptom Rating Scale
- Constipation Status via Rome III Questionnaire
- Stool Consistency via Bristol Stool Form Scale
- Changes in Mood via Profile of Mood State Questionnaire
- Degree of Straining via Daily Bowel Health Diaries
- Severity of GI Symptoms via IBS-Symptom Severity Index
- IBS-Associated Quality of Life via Questionnaire

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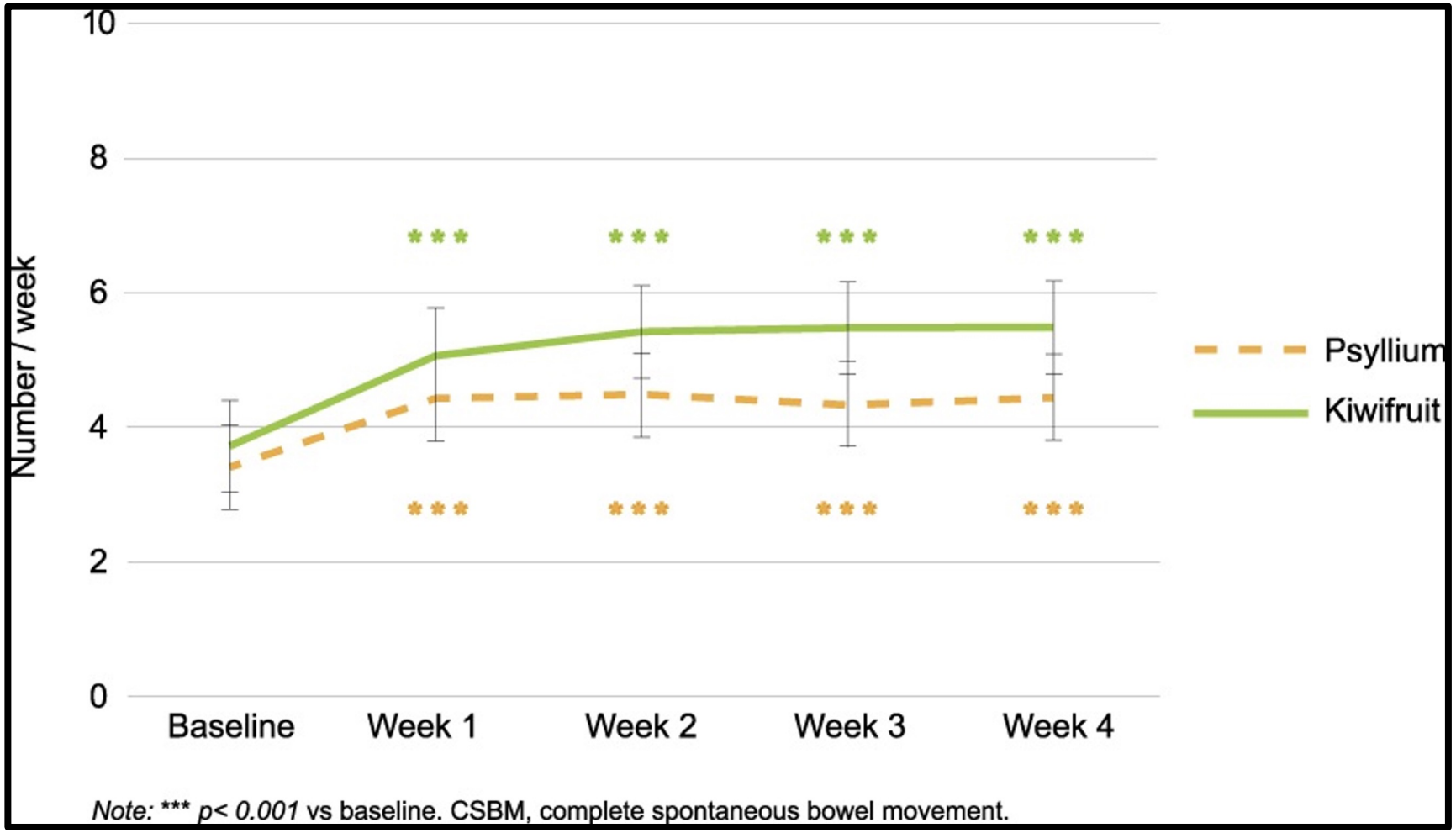
Results



Combo FC/IBS-C Group:
Mostly women and European
Mean age 39 and BMI 23

FC Group:
IBS-C Group:
Increase in mean CSBMs/week with **both** kiwifruit and psyllium

Combo FC/IBS-C Group:
Kiwifruit significantly increases CSBMs/week vs psyllium

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Questions

1. What dietary interventions do you recommend to your patients with CIC or IBS-C?

2. Are there other non-pharmacologic interventions that you've found helpful?

3. How do you quantify treatment success? With multiple dietary, behavioral, and pharmacologic interventions, when should you "step-up" therapy?

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EoE Treat-to-Target: Symptoms Improved but Histology Unchanged

Eric Low, MD MPH
University of California, San Diego

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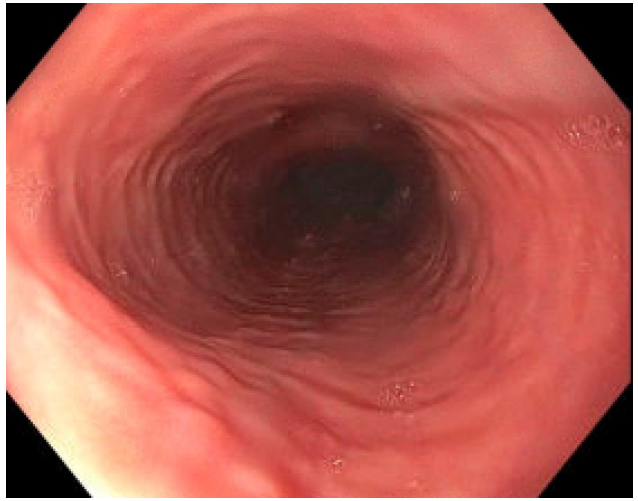
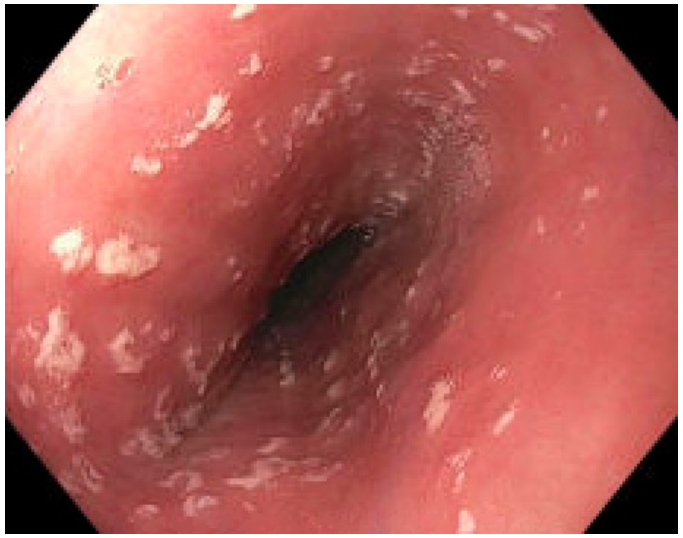
Case Vignette

- 33 year old male presents to clinic for dysphagia for solids >> liquids, intermittent heartburn and chest pain
- He has a history of childhood asthma (which is now “outgrown”), allergic rhinitis, and an anaphylactic reaction to eggs
- No prior food impactions but there have been “some close calls,” to the point of forcefully vomiting up a portion of his meal
- No prior endoscopies, antacid therapy, or steroid exposure in the past
- No weight loss, odynophagia, abdominal pain, or changes in bowel pattern
- Lab work is unremarkable

Case Vignette Continued

- An upper endoscopy is performed and shows the following:
  - Edema = 1
  - Rings = 1
  - Exudate = 2
  - Furrows = 1
  - Stricture = 1 (16)





- A 54Fr wire dilation with a Savary dilator was performed which results in a moderate mucosal disruption
- Biopsies were notable for 40 eos in the distal / 60 in the proximal

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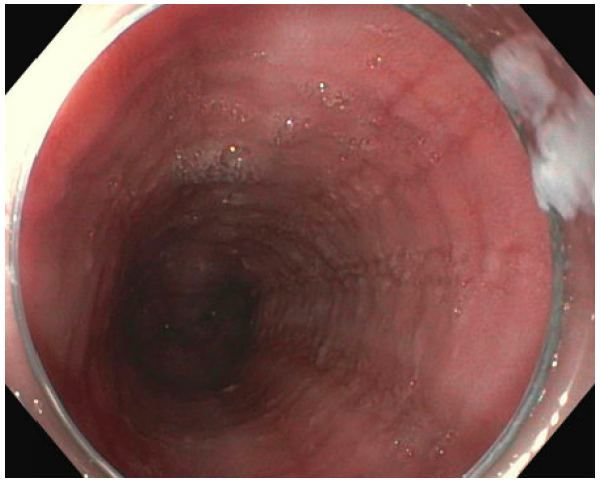
Case Vignette Continued

- You diagnose him with EoE and present all treatment options
- He elects to start PPI therapy with omeprazole 20mg BID
- After 12 weeks of treatment his dysphagia is 80-90% improved and he no longer experiences heartburn or chest pain
- Repeat endoscopy to assess treatment response is planned

Case Vignette Continued

- An upper endoscopy is performed and shows the following:
  - Edema = 1
  - Rings = 1
  - Exudate = 0
  - Furrows = 1
  - Stricture = 0



- Biopsies were notable for 20 eos in the distal / 50 in the proximal

Management Question #1

- Based on the endoscopic and histology findings, how to you council the patient?
- What do you recommend regarding treatment at this point?

Management Question #2

- When is it appropriate to introduce Dupilumab into the therapeutic algorithm?
- Do you ever consider using Dupilumab as a first-line therapy?

Case Vignette Continued

- He is switched to oral budesonide 2mg BID
- After 12 weeks of treatment his symptoms are 100% resolved
- A repeat EGD is performed which shows mild furrows but otherwise normal appearing esophagus (EREFS=1)
- Biopsies show 3 eos in the distal / 1 in the proximal

He asks:

”How long do I need to remain on topical steroids?”

Management Question #3

- How do you approach maintenance therapy for EoE?
- Have you every stopped therapy completely?

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Laryngeal Reflux Unresponsive to PPI

Judy Trieu, MD

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Case

A 48-year-old man was referred to GI clinic for a chronic cough that has been going on for 5 months.

- Daily coughing, maybe worse in evenings and night
- Unsure if triggered by food or other activities
- Had “heart burn” a few years ago that was successfully treated by antacids but has not symptoms recently
- Denies chest pain, abdominal pain, nausea, vomiting, or weight loss

History

Medical Hx

- Hypertension
- Diabetes
- Obesity (BMI 35)

Medications

- Amlodipine 10mg daily
- Metformin 500mg BID

Surgical Hx

- No prior surgeries

Social Hx

- Never used tobacco
- 1-2 Etoh drinks per month

Allergies

- No known allergies

Prior Work-Up

Labs: CBC, CMP unremarkable

Referral to ENT: fiber optic exam demonstrated erythema of the vocal cords, concerning for *laryngo-pharyngeal reflux disease*

Trial of Omeprazole 20mg BID: maybe slight improvement

Lifestyle changes: no improvement - avoided spicy and "acidic" foods, avoid eating before bedtime, elevated head-of-bed when sleeping

EGD: normal – no esophagitis, no hiatal hernia

Questions

What would be the next diagnostic step?
- pH test? *On or off PPI?*
- pH with impedance?
- Bravo?

At what point would you consider changing current PPI to another PPI or to potassium channel competitive acid blocker?

At what point would you consider the diagnosis/treatment of "functional heartburn"?

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Guideline Update: Fecal Microbiota Transplantation for Recurrent *C. difficile* Colitis…With Clinical Pearls

Paul Feuerstadt MD, FACG, AGAF
Assistant Clinical Professor of Medicine
Yale University School of Medicine
Attending Gastroenterologist
PACT-Gastroenterology Center
Hamden, CT

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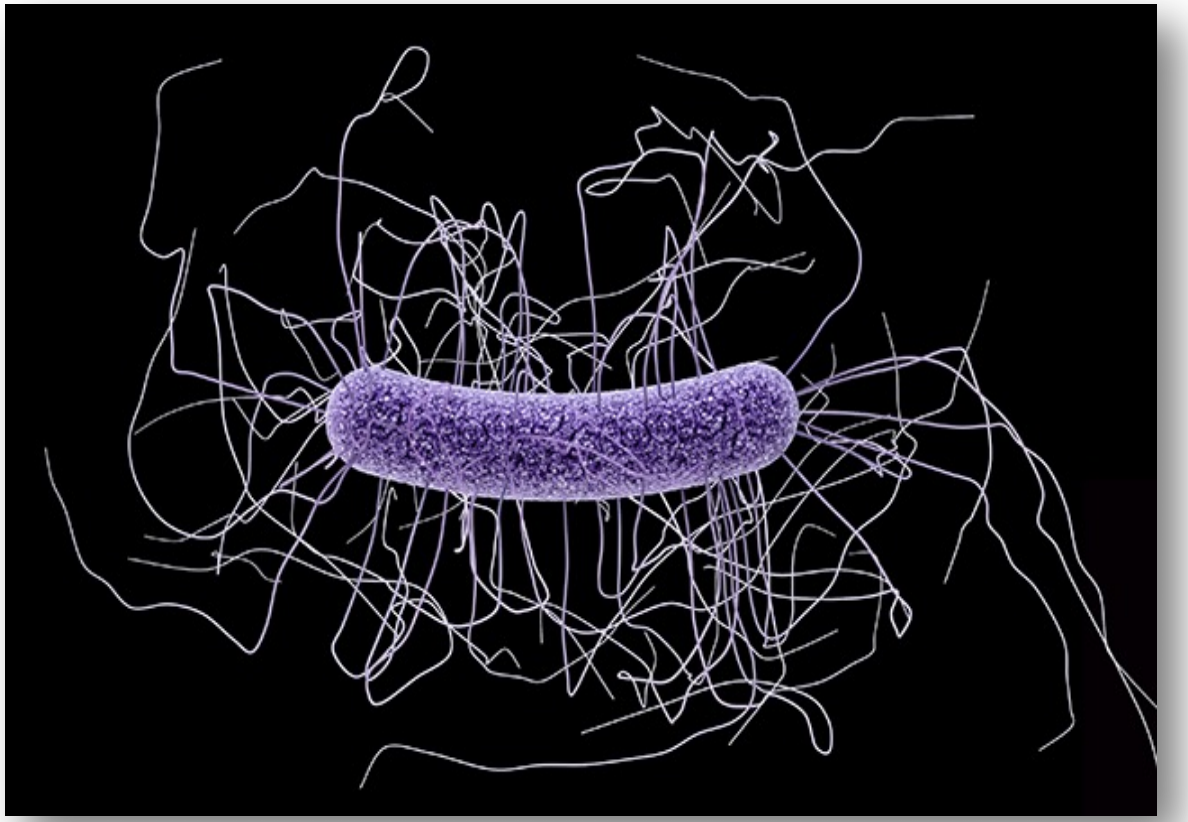
What is *Clostridioides difficile*?



- Gram positive
- Spore forming
- Anaerobic
- Rod

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Microbiology

Vegetative Form

Survives on moist surfaces for up to 6 hours[1]

Susceptible to:[2]

- Gastric acid
- Antibacterial soaps
- Alcohol-based hand sanitizers

Spore Form[2,3]

Survives on surfaces for months

Resistant to:

- Gastric acid
- Antibacterial soaps
- Alcohol-based hand sanitizers
- Rapidly changes to vegetative form

1. Jump RL, et al. *Antimicrob Agents Chemother.* 2007;51:2883-2887; 2. Fordtran JS. *Proc (Bayl Univ Med Cent).* 2006;19:3-12; 3. Cohen SH, et al. *Infect Control Hosp Epidemiol*. 2010;31:431-455.

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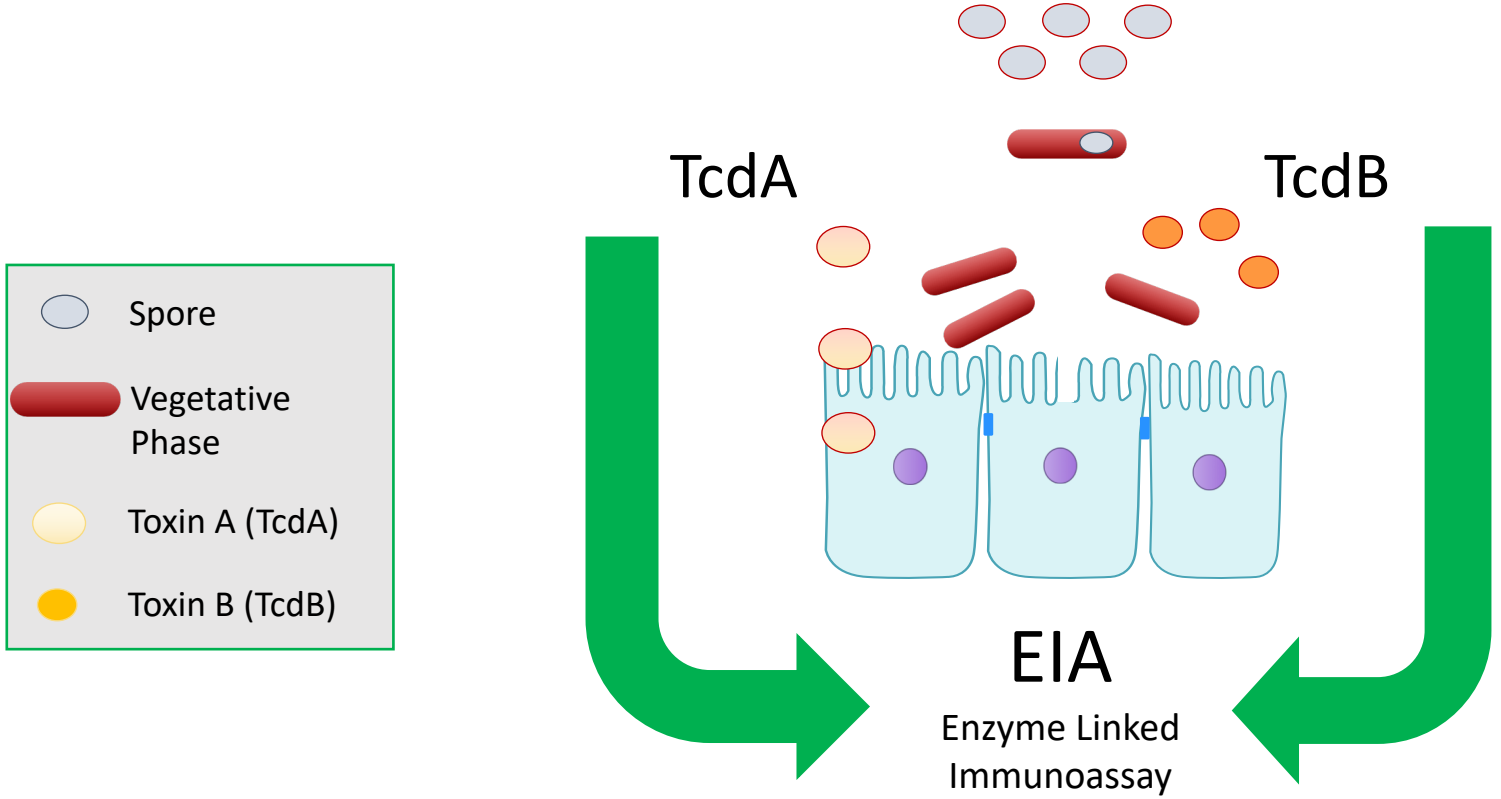
Common Mistake

Relying solely on the PCR assay for diagnosis

Diagnostic Tool: Toxin Detection



Sensitivity: Low
Specificity: Moderate

Adapted from: Shen J. *Innate Immun*. 2012;4:149-158; McDonald LC, et al. Clin Infec Dis. 2018;66:e1-e48.

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Diagnosis: Organism Detection

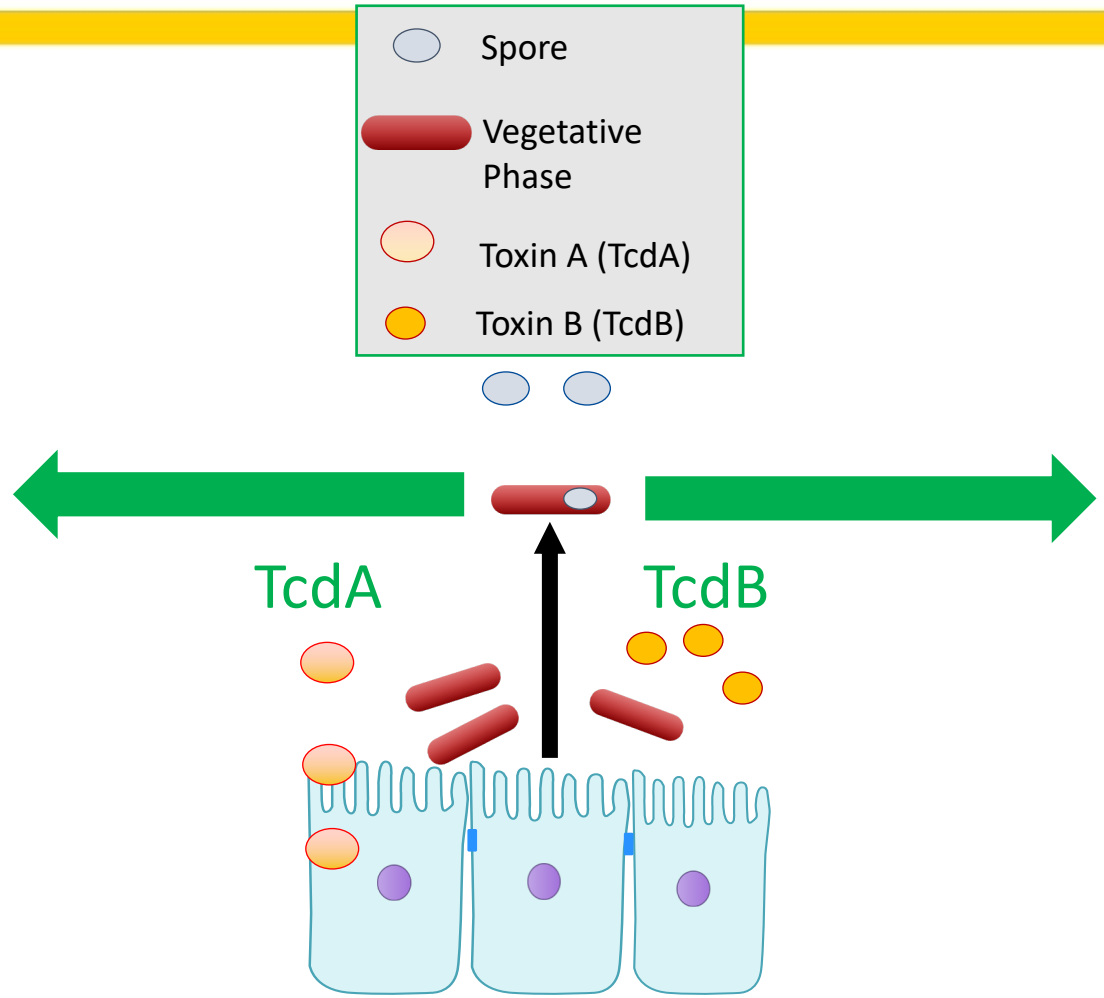
GDH

(Glutamate Dehydrodense)

Detects: Enzyme release by *Clostridioides*

Sensitivity: High

Specificity: Low



PCR

(Polymerase Chain Reaction)

Detects: Toxin Genes

Sensitivity: High

Specificity: Mod

Adapted from: Shen J. *Innate Immun*. 2012;4:149-158; McDonald LC, et al. Clin Infec Dis. 2018;66:e1-e48.

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Clinical Pearl: Diagnosis

- Understand what you are ordering
- 2 assays are better than 1
  - At least one should include the EIA
  - The other can be the GDH or PCR
  - If the GDH is used and results are discordant, than reflex to the PCR to confirm the diagnosis

Common Mistake

Thinking someone is recurring when they have post-infection IBS

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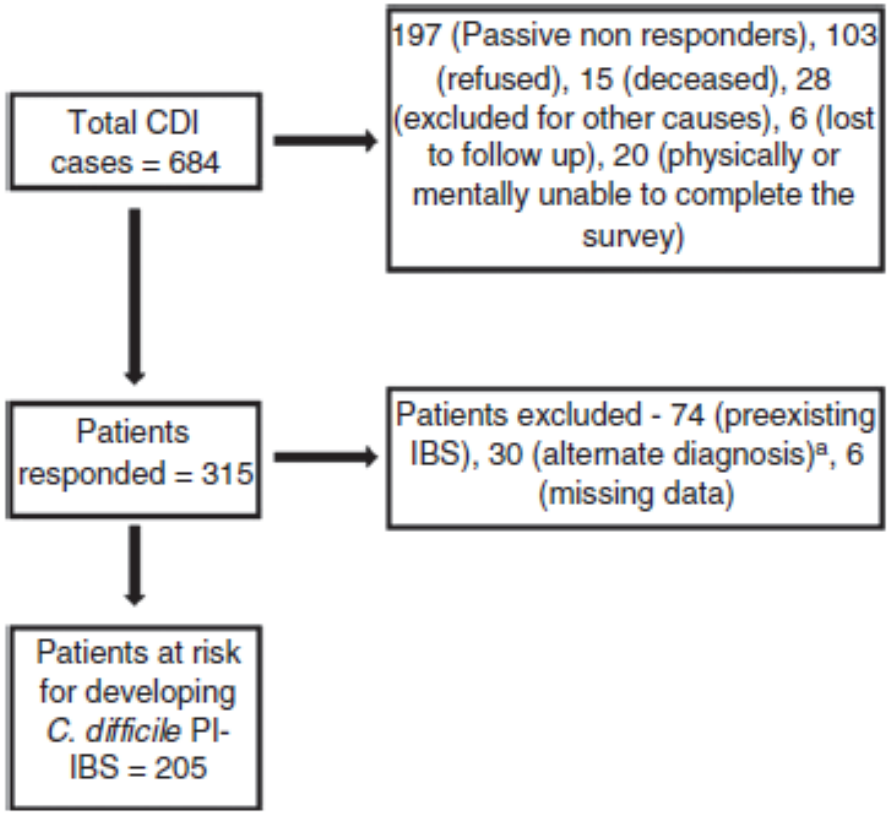
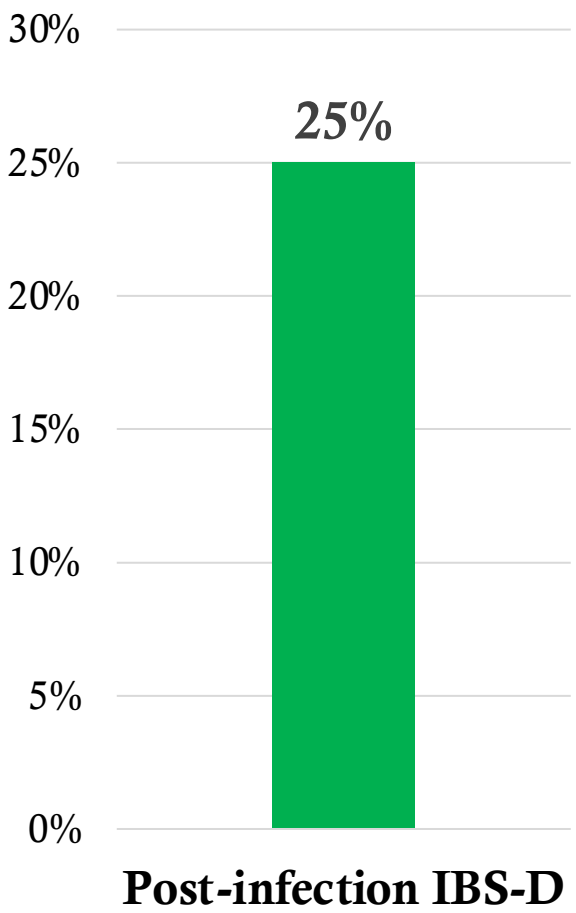
Post-Infection IBS After *C. difficile* Infection





Risk factors for development of post-infection IBS-D:

- Diarrhea greater than 7-days (p=0.01)
- Current Anxiety (p<0.001)
- Higher BMI (p=0.004)

Wadhwa et al. *Aliment Pharmacol Ther* 2016; 44: 576–582

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Clinical Pearl: Differentiating Post-Infection IBS Versus Recurrent CDI

	Post-Infection IBS	Recurrent CDI
IBS Questions		
Abdominal pain	Worsened or alleviated with bowel movement	No significant change with BM or only briefly improved with BM
Bowel movement frequency	About half of what it was at initial presentation	Similar to initial presentation
Consistency of stool	Bristol 5-6	Bristol 6
***C. Difficile* Questions**		
Fevers and sweats	Not seen	Common
Nausea	Not seen	Common
Odor of stool	Similar to prior to CDI	Patient describes this as similar to when they had active infection

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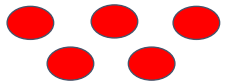
Treatment: What Are We Targeting?

Attack the Vegetative Phase

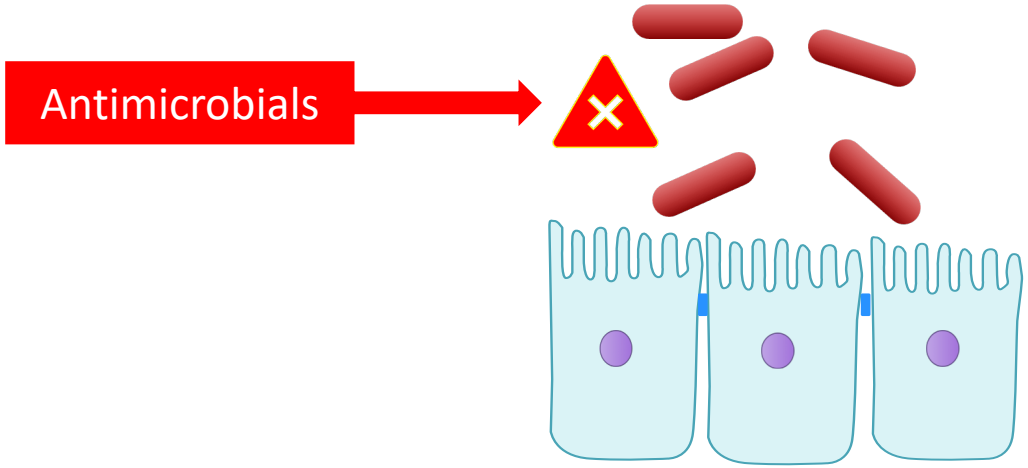
Ingestion of *C. difficile* spores



Germination

Bile salts induce germination

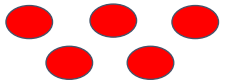
Antimicrobials



Glucosylating toxin production

Boost Immune Response

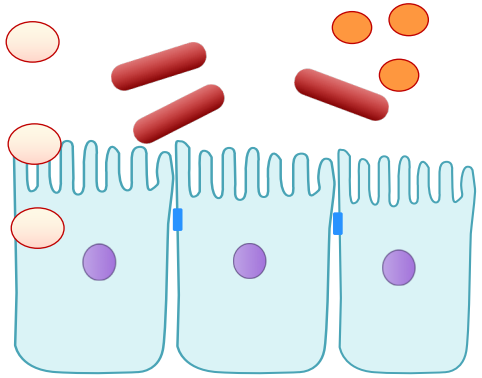
Transmission of spores



Sporulation

TcdA

TcdB



Adapted from: Shen J. *Innate Immun*. 2012;4:149-158.

Common Mistake

Assuming vancomycin and fidaxomicin are the same/similar

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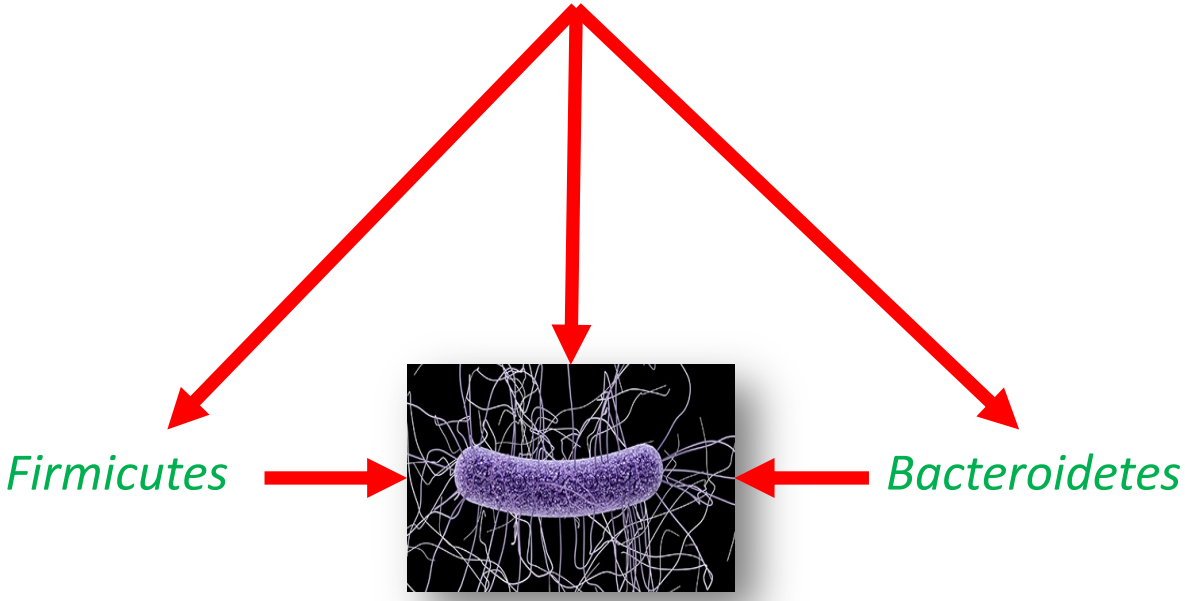
Guideline Recommendations for Primary CDI Episode

Recommendation	IDSA/SHEA[1,2]	ESCMID[3]	ACG[4]
Preferred	**Fidaxomicin** 200 mg PO BID x 10 days	**Fidaxomicin** 200 mg PO BID x 10 days	**Fidaxomicin** 200 mg PO BID x 10 days **Vancomycin** 125 mg PO 4x/day x 10 days
Alternative	**Vancomycin** 125 mg PO 4x/day x 10 days *If no other available agents (nonsevere):* Metronidazole 500 mg PO 3x/day x 10-14 days	**Vancomycin** 125 mg PO 4x/day x 10 days *If no other available agents:* Metronidazole 500 mg PO 3x/day x 10 days	*If no other available agents (nonsevere):* Metronidazole 500 mg PO 3x/day x 10 days
Comments	In settings where logistics are not an issue, consider **addition of bezlotoxumab** in high risk of recurrence	Risk stratify for recurrence with selective use of **fidaxomicin** in limited access/resources Consider **addition of bezlotoxumab** in high risk of recurrence	Consider **addition of bezlotoxumab** in high risk of recurrence Consider **FMT** on case-by-case basis in severe CDI unresponsive to standard therapy

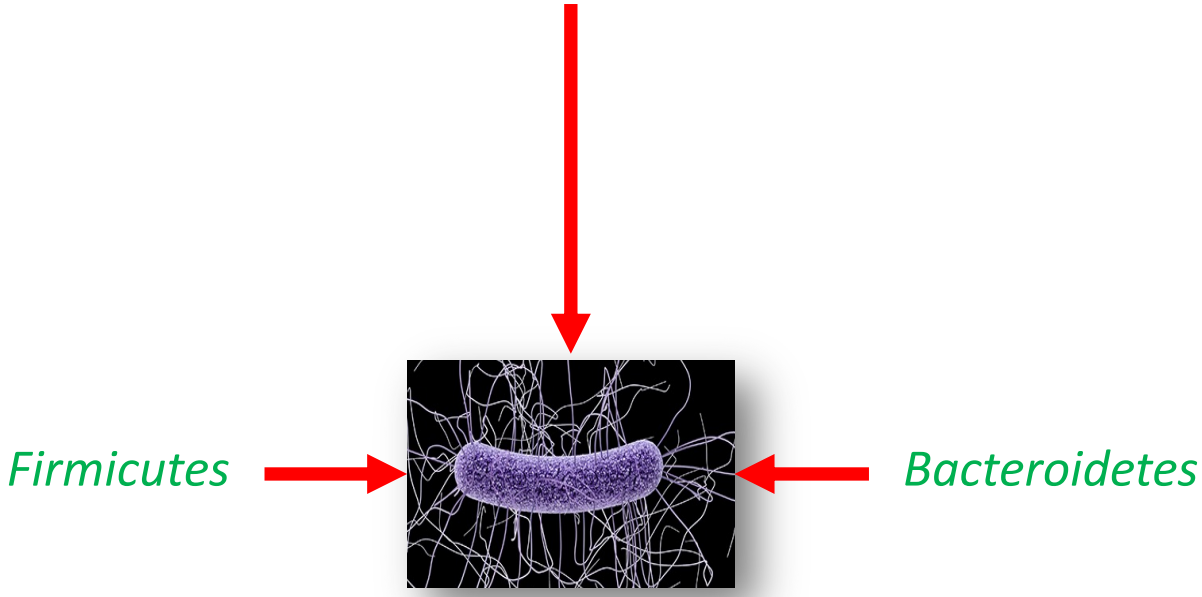
1. McDonald LC, al. Clin Infect Dis. 2018;66:e1-e48; 2. Johnson S, et al. *Clin Infect Dis*. 2021;73:e1029-e1044; 3. van Prehn J, et al. *Clin Microbiol Infect*. 2021;27 Suppl 2:S1-S21; 4. Kelly CR, et al. *Am J Gastroenterol*. 2021;116:1124-1147.

Clinical Pearl: Why is Fidaxomicin Associated with Lower Recurrence?

Vancomycin



Fidaxomicin



Louie TJ, et al. *N Engl J Med*. 2011;364:422-431.

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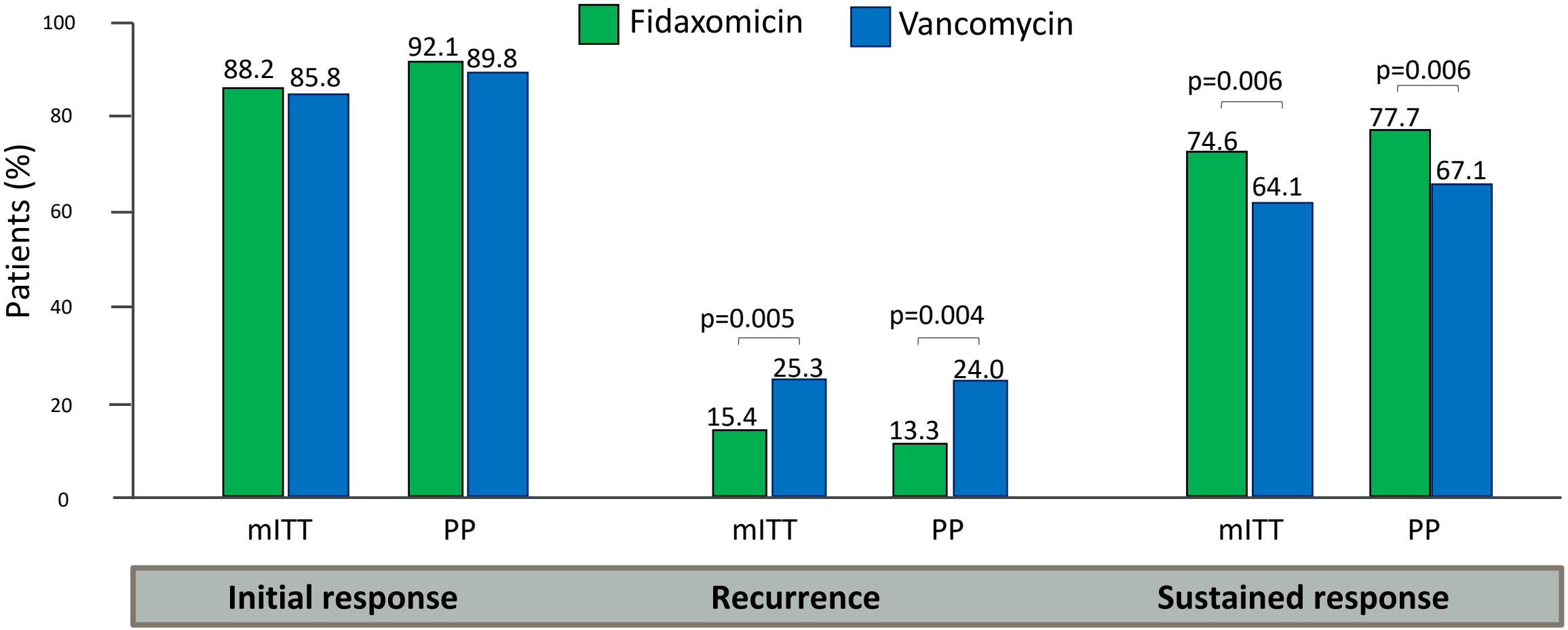
Fidaxomicin and Vancomycin for Initial *C. difficile* Infection



Louie TJ, et al. *N Engl J Med*. 2011;364:422-431.

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2021 IDSA/SHEA Treatment Recommendations for CDI in Adults: First Recurrence

Clinical Presentation	Recommendation	Comments
First Recurrence	**Preferred** **Fidaxomicin** standard or extended dosing	
	Alternative **Vancomycin in tapered and pulsed regimen**	**Vancomycin tapered/pulsed example regimen: 125 mg 4x/day x 10-14 days, 2x/day x 7 days, 1x/day x 7 days, then every 2-3 days x 2-8 wk**
	Vancomycin standard dosing	Consider if metronidazole was used for treatment of first episode
	Adjunctive **Bezlotoxumab 10 mg/kg IV once during administration of SoC antibiotics**	May be considered during first episode if other **risks for CDI recurrence** are present

Johnson S, et al. *Clin Infect Dis*. 2021;73:e1029-e1044.

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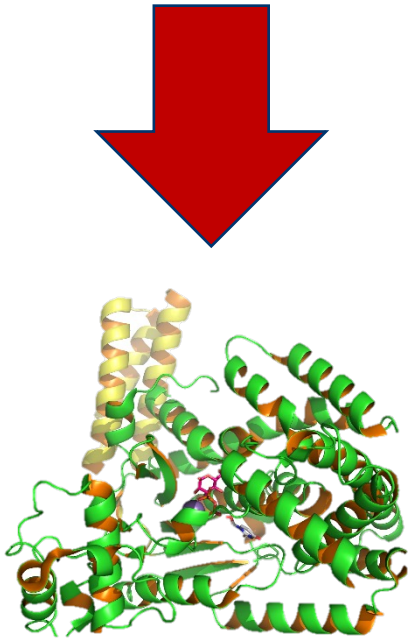
Multimodal Approach to Therapy

Bezlotoxumab



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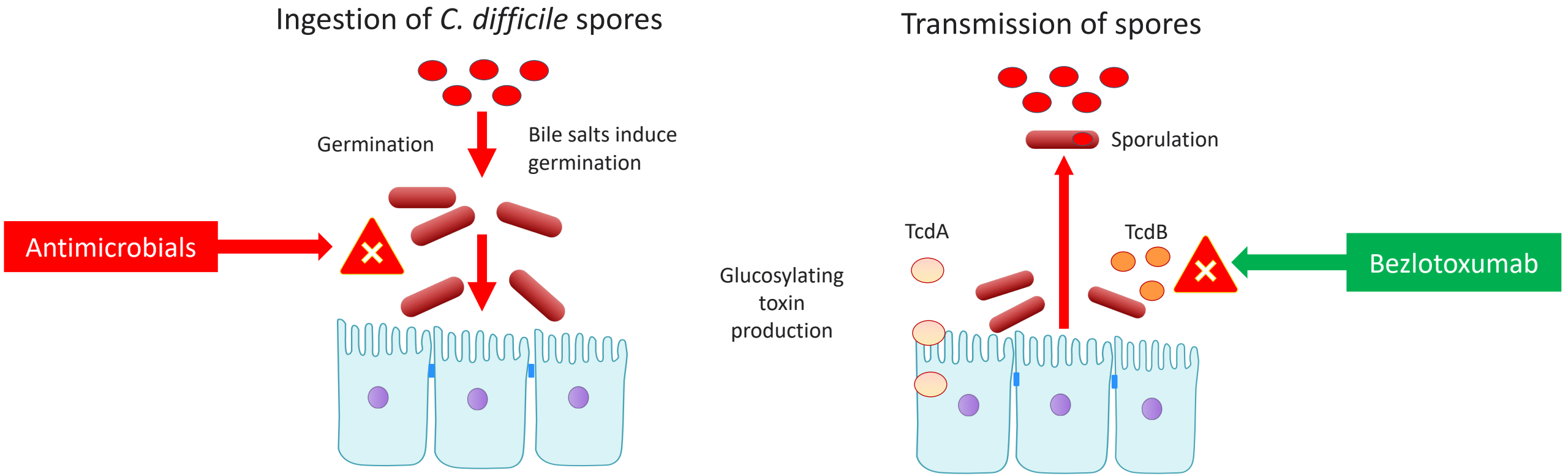
Treatment: What Are We Doing?

Attack the Vegetative Phase

Boost Immune Response



Adapted from: Shen J. *Innate Immun*. 2012;4:149-158.

Common Mistake

Not considering bezlotoxumab as a treatment option

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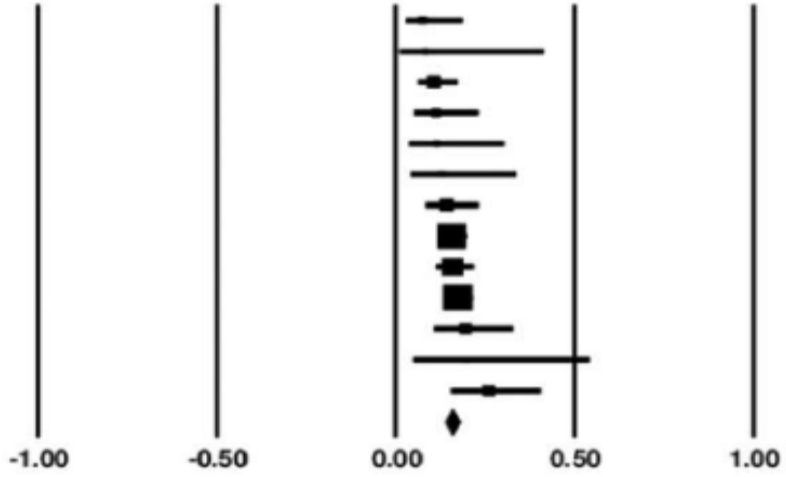
Efficacy of Bezlotoxumab-Metanalysis

Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total	Relative weight	Relative weight
Lopez R.S. 2022	0.075	0.029	0.184	-4.818	0.000	4 / 53	1.94	
Kerr 2019	0.083	0.012	0.413	-2.296	0.022	1 / 12	0.48	
Pena 2022	0.107	0.064	0.172	-7.507	0.000	14 / 131	6.54	
Johnson 2022	0.113	0.052	0.230	-4.748	0.000	6 / 53	2.78	
Perreault 2020	0.115	0.038	0.303	-3.318	0.001	3 / 26	1.39	
Askar 2022	0.130	0.043	0.335	-3.064	0.002	3 / 23	1.37	
Escudero-Sánchez 2020	0.143	0.085	0.231	-5.981	0.000	13 / 91	5.83	
Wilcox/ MODIFY II 2017	0.157	0.124	0.196	-12.153	0.000	62 / 395	27.36	
Hengel 2020	0.159	0.114	0.217	-8.506	0.000	31 / 195	13.65	
Wilcox/ MODIFY I 2017	0.174	0.139	0.215	-11.612	0.000	67 / 386	28.98	
De La Villa 2023	0.196	0.109	0.327	-4.001	0.000	10 / 51	4.21	
Bradely 2022	0.200	0.050	0.541	-1.754	0.080	2 / 10	0.84	
Oksi 2019	0.261	0.155	0.405	-3.102	0.002	12 / 46	4.64	
	0.158	0.140	0.178	-23.135	0.000	228 / 1472		



P-value: **0.00**; Q-value: **12**; I^2**0%**; Tau Squared: **0.00**

- 13 studies, 2 randomized controlled trials, 11 observational trials
- 2,337 patients in total
- **rCDI receiving SOC followed by Bezlo: 15.8%, SOC alone: 28.9%**

Mohamed MFH, et al. *J Clin Gastroenterol*. 2024;58:389-401.

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Clinical Pearl: Use Risk Factors for Recurrent *C. difficile* Infection to Dictate Indications for Bezlotoxumab

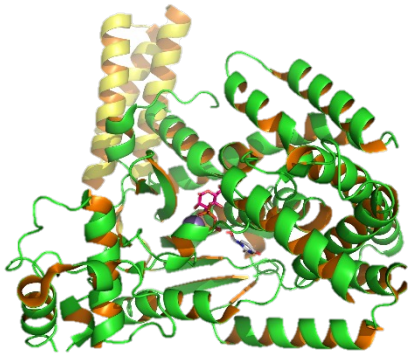
Demographics	Exposures	Environment

• Age older than 65
• Female gender
• Immunocompromised
  • Diabetes
  • HIV
  • Chronic Kidney Disease
  • IBD on biologic
• Prior episode of CDI
	• Exposure to antimicrobial agents
	• Chemotherapy
	• Gastrointestinal surgery
	• Acid suppression medications
		• Extended stay at a hospital and/or residence in a long-term care facility
		• Contact with contaminated environment and/or health worker hand colonization
		• Direct contact with a patient with CDI

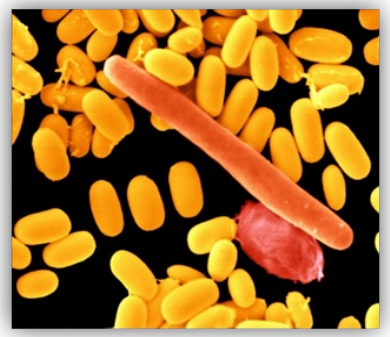
Cohen SH, et al. *Infect Control Hosp Epidemiol*. 2010;31:431-455; Fekety R, et al. *Clin Infect Dis*. 1997;24:324-333; Shakov R, et al. *Am J Infect Control*. 2011;39:194-198.

Multimodal Approach to Therapy

Bezlotoxumab



Fecal Microbiota Transplantation



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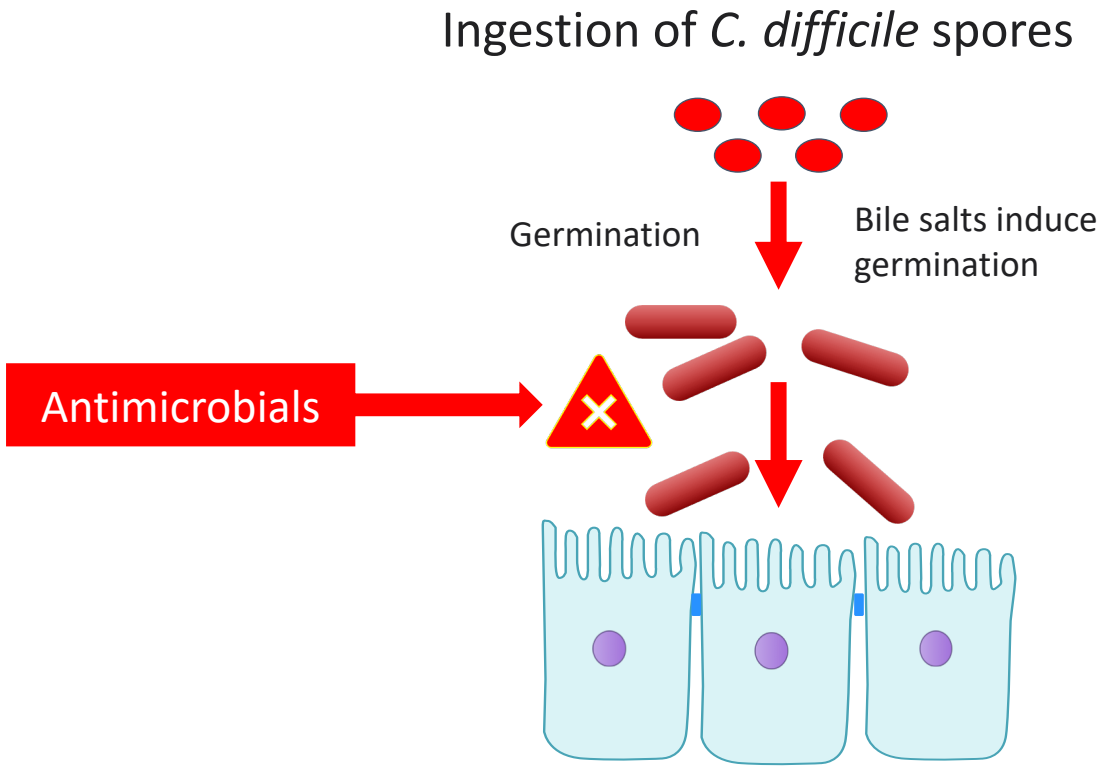
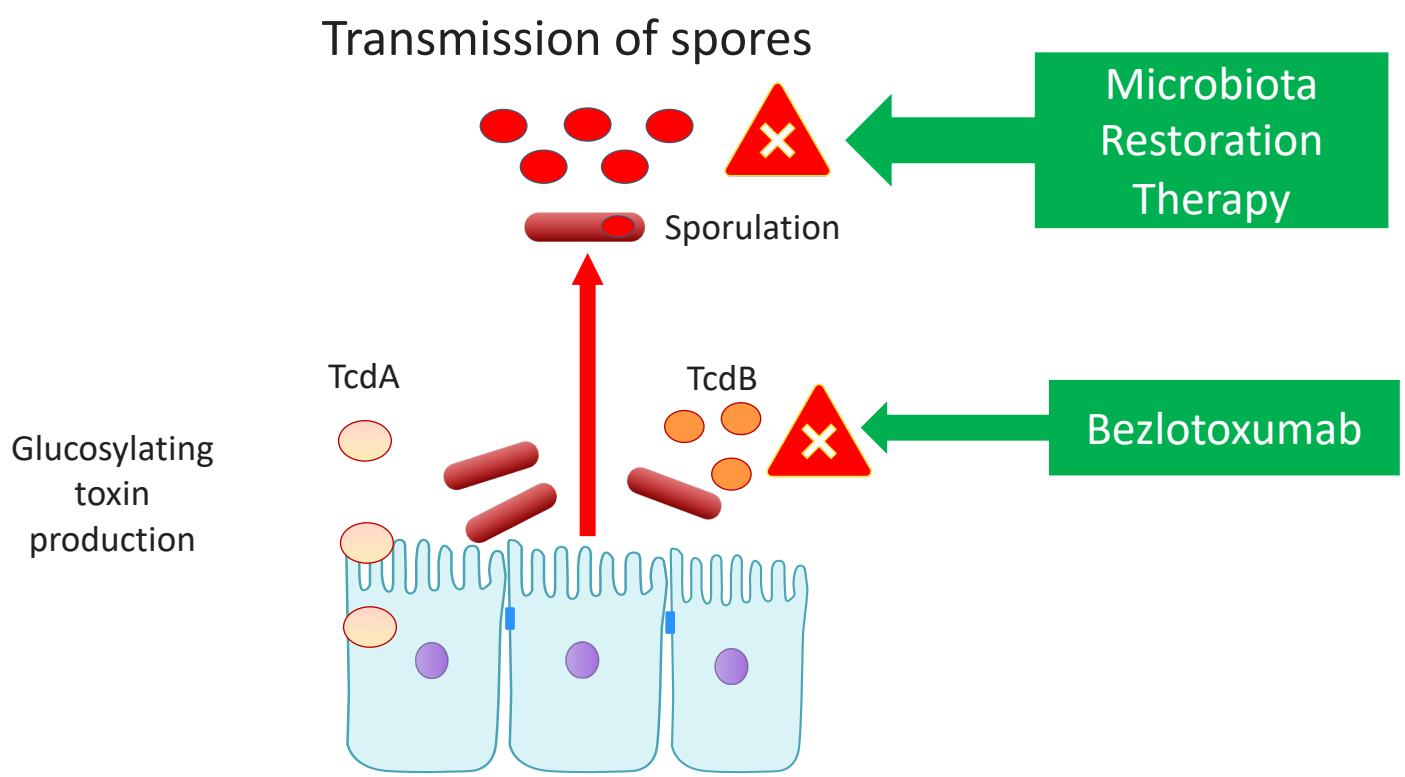
Treatment: What Are We Doing?

Attack the Bacteria



Boost Immune Response



Adapted from: Shen J. *Innate Immun*. 2012;4:149-158.

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AGA Microbiota Transplant Guideline

Recurrent *C. difficile* Infection

Is the patient at high risk for recurrence?

Immunocompetent adults

Recommend use of fecal microbiota-based therapies upon completion of SOC ABX

⊕⊕◯◯

Immunocompromised adults

Mild-Moderate Immunocompromise

Recommend use of conventional FMT upon completion of SOC ABX

⊕◯◯◯

Severe Immunocompromise

Recommend against use of fecal microbiota-based therapies upon completion of SOC ABX

⊕◯◯◯

Peery AF, et al. *Gastroenterology*. 2024;166:409-434.

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AGA Microbiota Transplant Guideline

Severe or Fulminant *C. difficile* infection

↓

Use SOC antimicrobial

↓

Is patient not improving?

↓

Recommend use of conventional FMT

⊕◯◯◯

Peery AF, et al. *Gastroenterology*. 2024;166:409-434.

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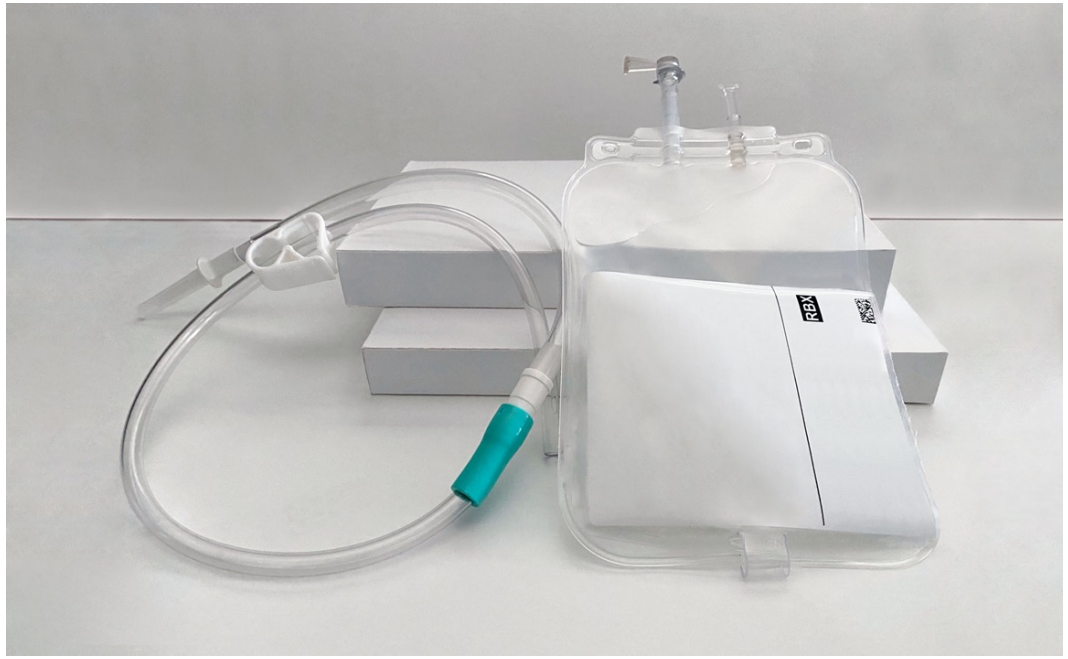
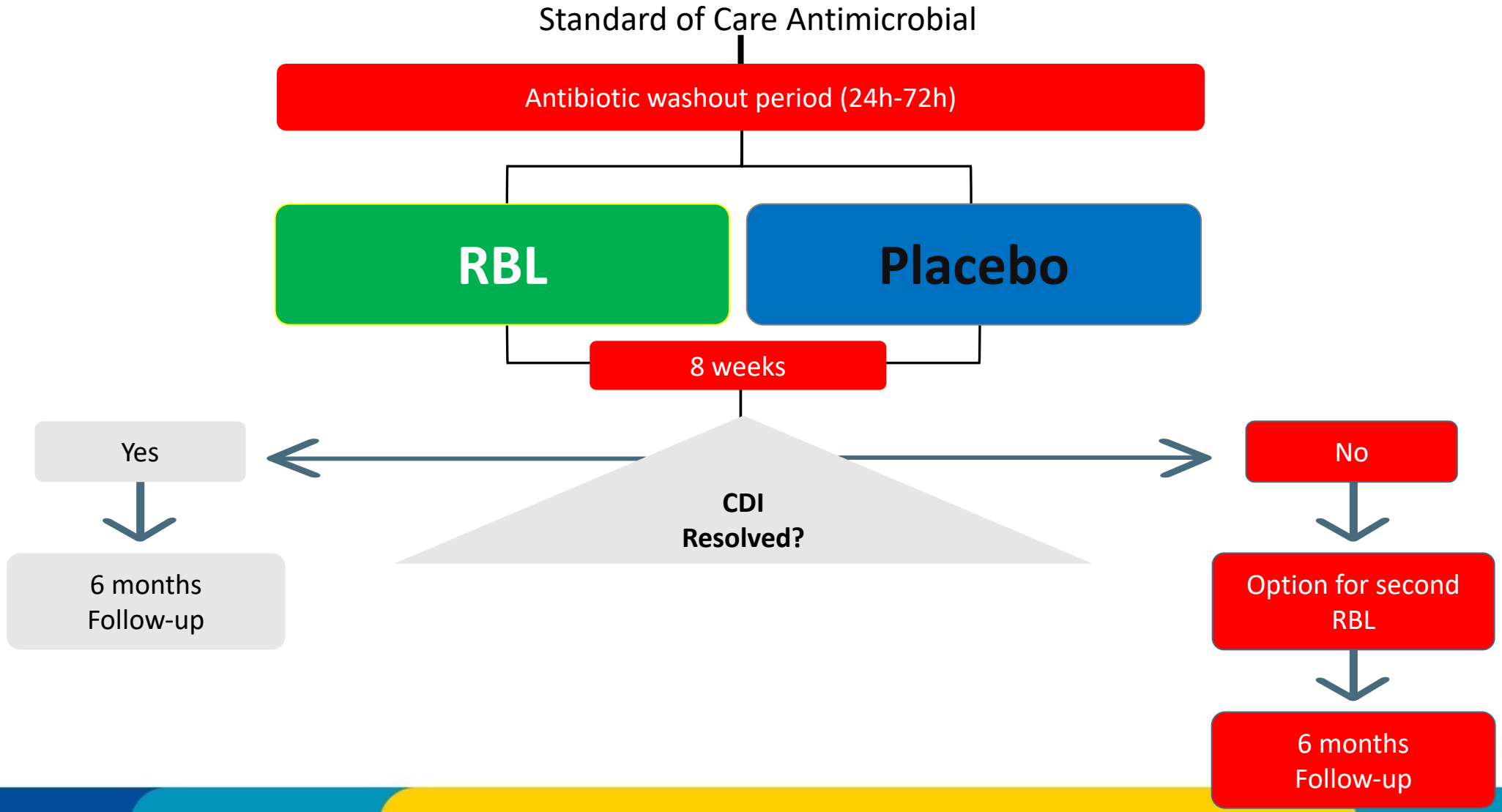
Fecal Microbiota Live-JSLM (Rebyota™, RBL)

- Single-dose, microbiota-based live biotherapeutic agent
- Rectally administered
- 150 mL of therapeutic material
- 10^7 microbes per mL or 15 x 10^8 microbes per treatment
- Broad consortium
- A proprietary manufacturing process preserves diverse spore-forming and non–spore-forming bacteria, including *Bacteroides*



Orenstein R, et al. *Clin Infect Dis*. 2016;62:596-602; Blount KF, et al. *Open Forum Infect Dis*. 2019;6:ofz095; Ray A, Jones C. *Future Microbiol*. 2016;11:611-616.

PUNCH-CD3: Phase 3 Trial Design



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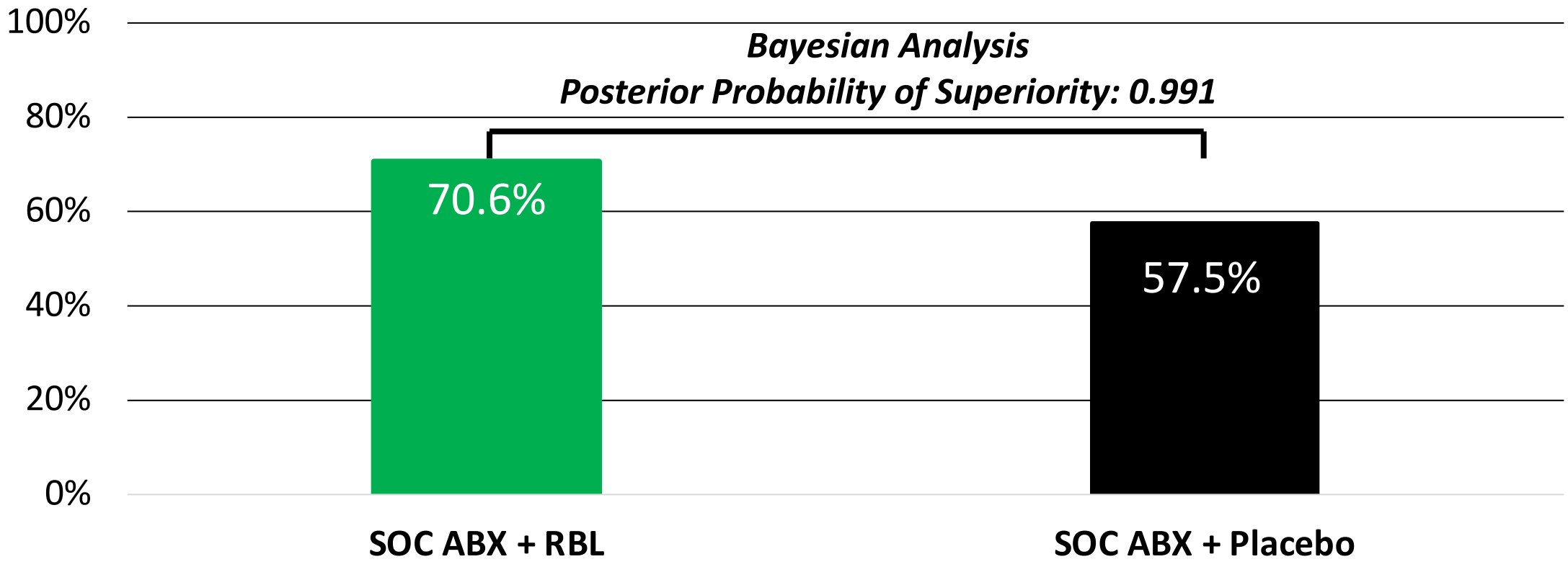
PUNCH-CD3: Phase 3
RBL Superior to Placebo



Khanna S, et al. *Drugs.* 2022;82:1527-1538.

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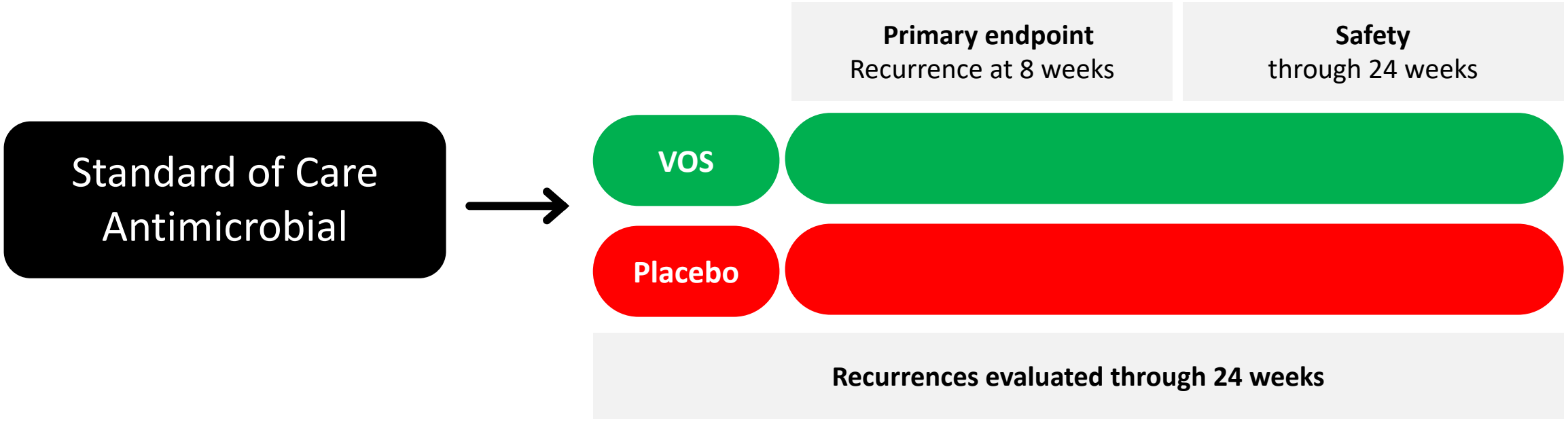
Fecal Microbiota Spores, Live-BRPK (Vowst™, VOS)

- Microbiota-based live biotherapeutic agent administered with 4 capsules daily over 3 days
- Orally administered
- 3 x 10^7 CFU per full treatment
- Narrow consortium
- A proprietary manufacturing process removes most fungi, parasites, viruses and non-spore forming bacteria resulting in predominantly Firmicutes spores

Korman L, et al. *Gastroenterology*. 2021;160:S-368; Feuerstadt P, et al. *N Engl J Med*. 2022;386:220-229.

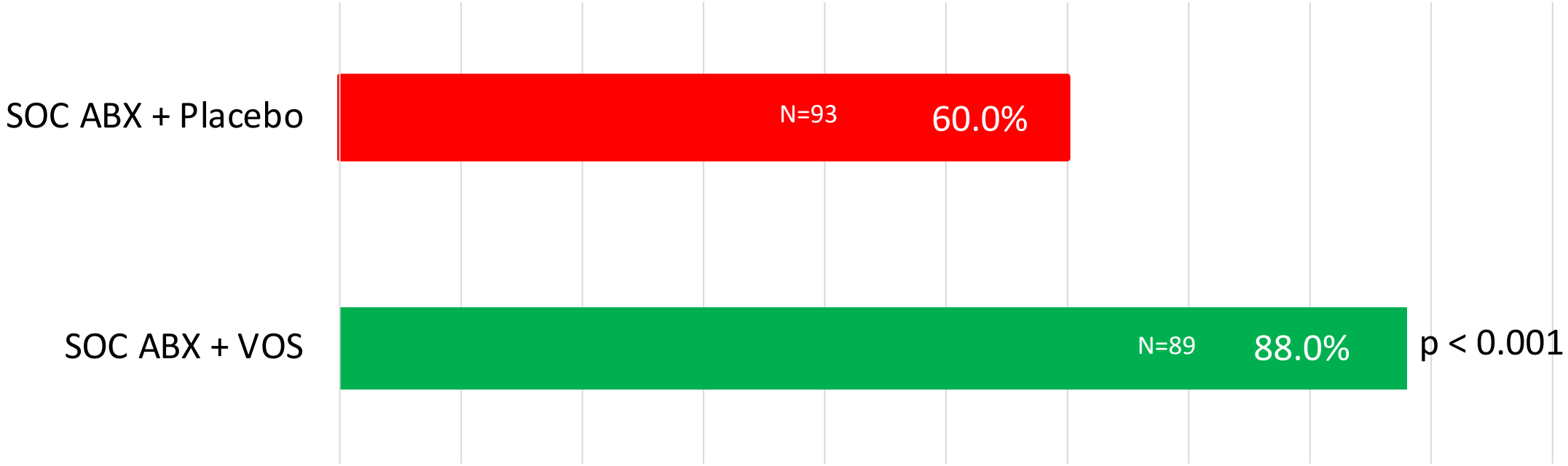
ECOSPOR-III: Phase 3 Trial Design



Feuerstadt P, et al. *N Engl J Med*. 2022;386:220-229.

ECOSPOR-III: Phase 3
VOS Superior to Placebo

Sustained Clinical Response, 8 weeks



Feuerstadt P, et al. *N Engl J Med*. 2022;386:220-229.

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Common Mistake

Giving microbiota restoration without a SOC antimicrobial *a priori* or at the same time as SOC antimicrobial

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Washout Period

- ✓Time from completion of standard of care antimicrobial to administration of LBP
- ✓Minimize the impact of the standard of care antimicrobial on the administrated microbial species
- ✓Goal: Clear as much of the antimicrobial from the patients system but also don't offer *C. difficile* the opportunity to re-germinate and recur
- ✓Optimal timing unclear

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Clinical Pearl: Washout Period

- No clear data for what is most optimal
- Anywhere from 1-4 days is best
- Goal: At least one formed bowel movements from the patient, but 2 or 3 might be better.

Clinical Pearl: Bowel Lavage

- No clear data for what is most optimal
- Since FDA package insert recommends for VOS, would consider this to be important to replicate the efficacy
- Fertile ground for clinical trials

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Conversation Regarding LBPs: VOS v. RBL

- Introduction of what MRT is and why it helps decrease recurrence
- Discuss both LBPs (RBL and VOS)
- Different administrative methods
- No formal informed consent is needed
- **Side effects:** Diarrhea, distension, flatulence, bloating and abdominal pains

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Common Mistake

Giving a probiotic at the same time or following microbiota restoration

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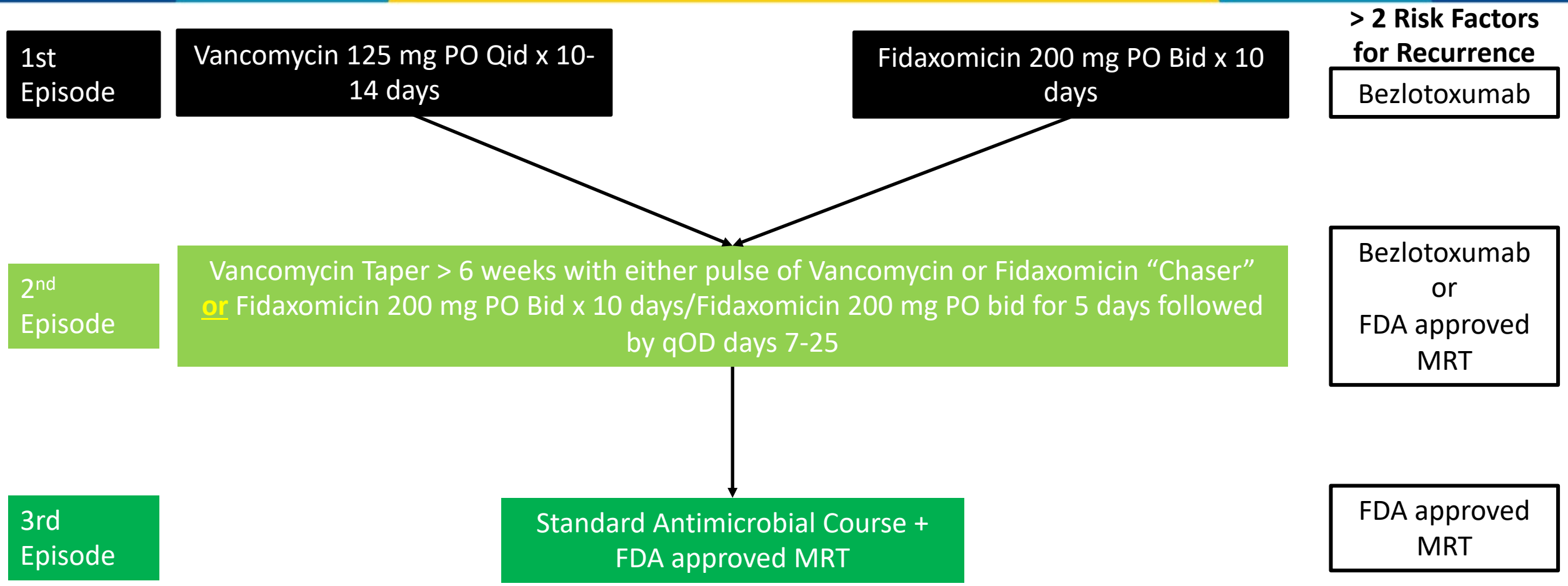
Clinical Pearl: Probiotics

- Definition:
  - Substance which stimulates the growth of microorganisms, especially those with beneficial properties (such as those of the intestinal flora).
- Mixed data
- Probiotics
  - Should **not** be used following microbiota restoration
  - Probiotics might cause no harm if given to prevent recurrence

Kelly CR, et al. *Am J Gastroenterol*. 2021;116:1124-1147.

Treatment Algorithm



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Short Bowel Syndrome

Joshua Novak MD
Associate Director, Small Bowel Disease at the Mount Sinai Center for GI Physiology & Motility
Mount Sinai West & Morningside
Associate Professor of Medicine Icahn School of Medicine at Mount Sinai

Conflict of Interest

- None

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Goals

- To understand the definition of Short Bowel Syndrome
- Improve the providers knowledge in the management of a patient with Short Bowel Syndrome

Short Bowel Syndrome

"Clinical condition associated to having less than 200 cm of residual small bowel in continuity, measured from the duodenojejunal flexure (ligament of Treitz), with or without colon, in an adult and for children (<18yrs), less than 25% of the normal length of small intestine for their respective age."

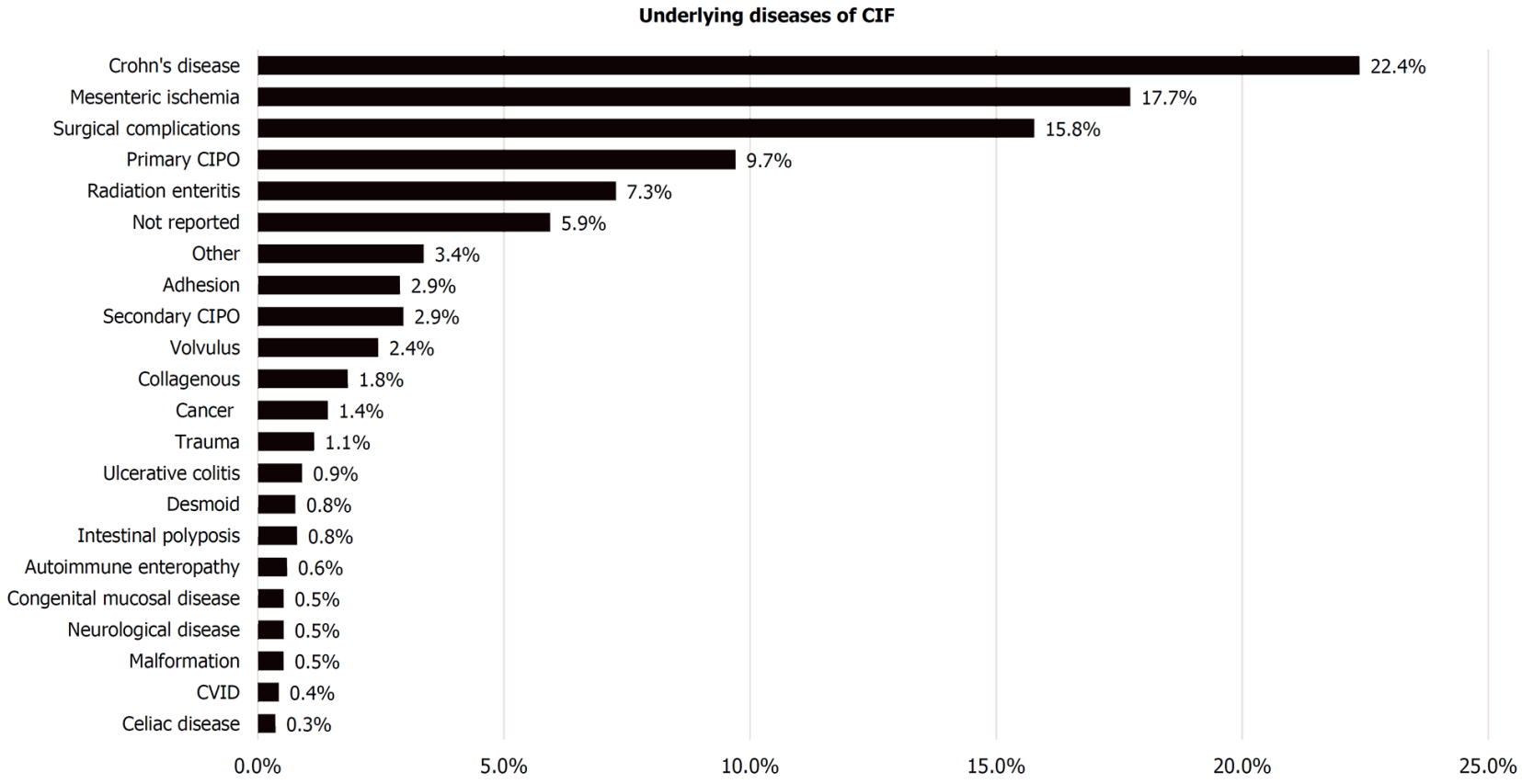
Estimates of SBS

TABLE 1 Geographical prevalence estimates of home parenteral nutrition

Country	Prevalence estimate per million
Argentina[7]	20
Denmark[8]	19
Finland[9]	9
Germany[10]	34
Ireland[11]	10–15
Spain[12]	6
The Netherlands[13]	12
United Kingdom[14]	21
United States[6]	75

Winkler M. at al Nutr Clin Pract 2023

Causes of SBS



Pironi et al Clin Nutr 2018

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Types of Intestinal Failure

- Type 1 “Acute”
  - Self-limiting intestinal failure “following abdominal surgery”
    - Short term TPN or IV fluids
    - Recover without complications
- Type 2 “Prolonged Acute”
  - Severely ill patients with major resections of the bowel
  - Septic, metabolic and nutritional complications
  - Requiring multidisciplinary intervention with metabolic and nutritional support to permit recovery
- Type 3 “Chronic”
  - Requiring long-term nutritional support (TPN)
  - Ultrashort gut syndrome due to massive enterectomy or extensive abdominal pathology not amenable for restorative surgery

Lal S. et al. Aliment Pharmacol Ther 2006

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Types of Short Bowel Syndrome

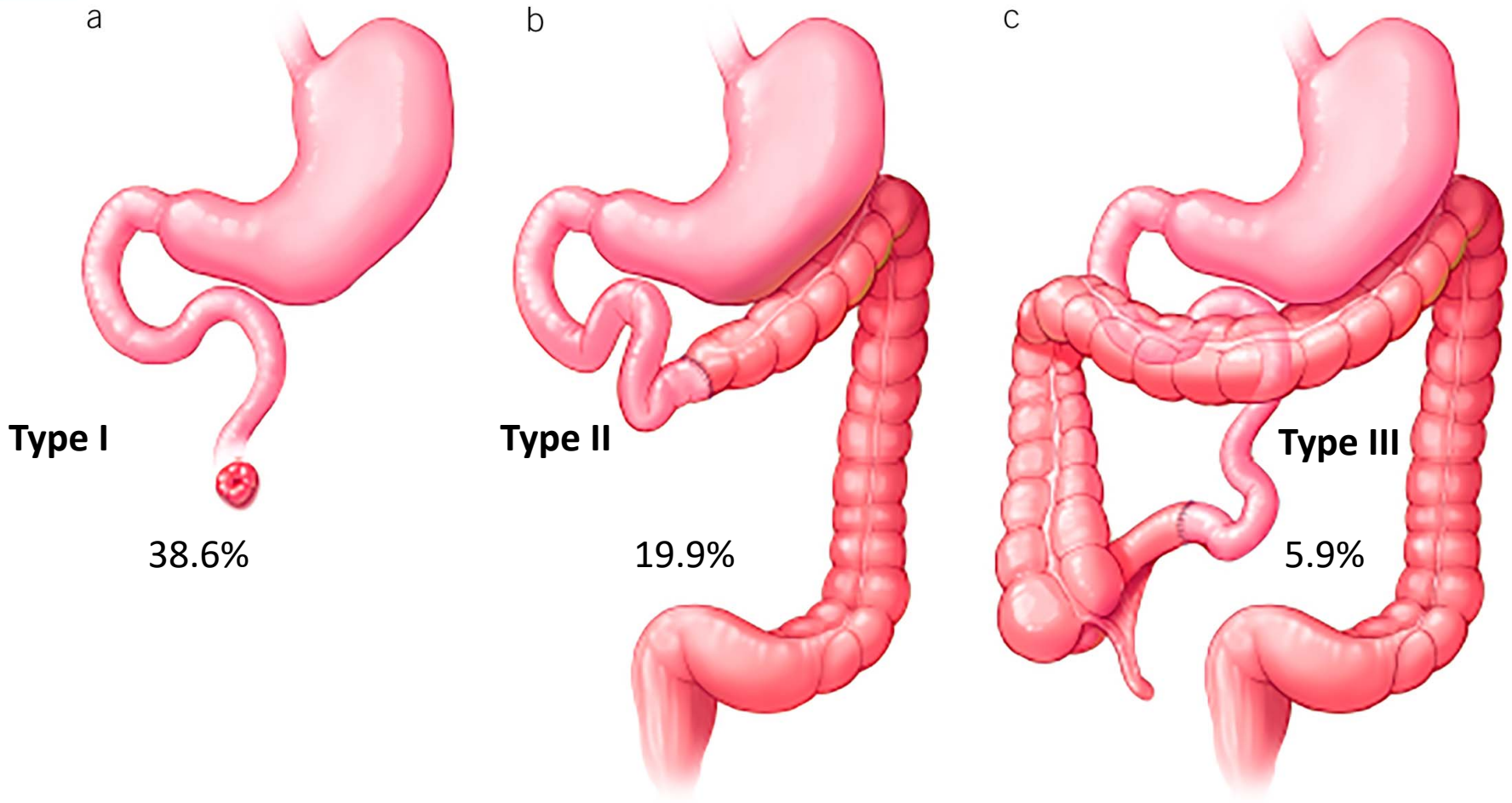

Figure 1. Bowel anatomy types in short bowel syndrome. Figure created by the Mayo Clinic.

Bering et al. Am Jour Gastro 2022; Pironi et al Clin Nutr 2018.

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Postoperative Phase

- Chance of rehabilitation to wean off TPN
  - SBS type 1- 20%
  - SBS type 2 - 40%
  - SBS type 3- 80%
- Adaptive changes that improve absorption
  - villous hyperplasia
  - increased blood flow
  - increased enzyme secretion
  - changes in motility and bowel dilation

Pironi L Nutr Clin Pract 2023; O'Keefe SJ, et al. Clin Gastroenterol Hepatol. Jan 2006; Buchman AL. MedGenMed : Medscape general medicine. 2004

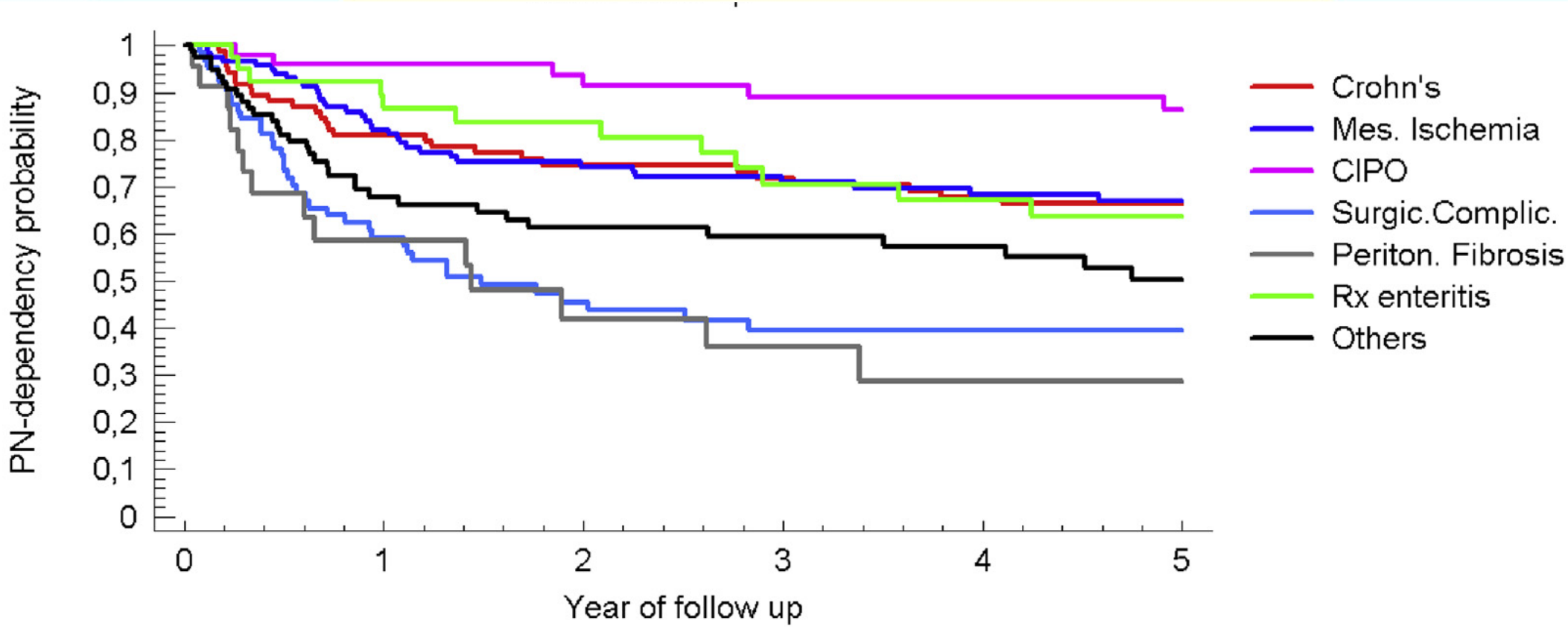

Fig. 2. PN-dependency probability.

Joly et al. Clinical Nutrition (2018)

Role of the Colon

- Large reserve absorptive capacity for electrolytes and water
  - Estimated: Capacity up to 800 mmol of Na^+ and 6L of isotonic salt solution per day in SBS
  - Even part of the colon can reduce fecal electrolyte and water losses
- ***Right colon*** - mainly involved in the fluid and electrolyte reabsorption
- ***Left colon*** - storage and contractile functions.
- Suggested ½ of the colon = 50 cm of small bowel

Wong JM et al. J Clin Gastroenterol. 2006; Nightingale JM Gut 1992.

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After a Meal

- Endocrine L cells (Distal small intestinal and proximal colon)
  - Peptide YY
  - Glucagon Like Peptide -1
  - Glucagon Like Peptide -2
- Enhance small bowel and colon cell growth
- Slow gastric emptying and small bowel transit ***"Ileo-colonic brake"***
- Increases contact time and absorption

Tappenden KA JPEN 2014; Pironi et al Gastroenterology 1993.

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End Proximal Jejunostomy (Type 1)

- Impaired release of GLP-1, GLP-2, and PYY
  - Rapid gastric emptying of liquids and rapid intestinal transit
- Inadequate mixing food with biliary and pancreatic secretions + enzymes
  - Nutrient maldigestion + Malabsorption
- ***Net secretors*** of salt and fluid
  - *Hypovolemia, hyponatremia, and hypokalemia*
- Unrestricted diet (free access to food and water)
  - Significant diarrhea >4L day (2-3 kg of wet weight)
- ***At least 100 cm of intact jejunum is required to maintain positive water and electrolyte balance***

Nightingale JM, et sl. Lancet 1990

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Medical Management

Diet

- Macronutrient absorption - first 100 cm of the small intestine
- Fat
  - Rich in essential fatty acids (FA) to prevent essential FA deficiency
  - Patients that are not receiving PN with lipid emulsions
  - No restriction if no colon present
  - Colon present – limit to 20-25% of total calories
- Protein
  - Well absorbed
  - At least 20% of the patient's caloric intake
  - 0.8 g/kg -2.0 g/kg of IBW
- Carbohydrates
  - Complex carbohydrates
  - Readily absorbed throughout the small intestine
  - 40-50% of total calories
- Soluble fiber and resistant starch
  - Short chain fatty acids (SCFA)
  - Butyrate
  - Preferred energy source - colonic epithelium
  - 100g of unabsorbed carbohydrate can produce 75mmol of SCFA which ***decreases fecal energy loss by 310-1000 kcal/day***

Joly F, et al. . Gastroenterology. 2009; Messing Bet al. Gastroenterology. 1991; Pironi et al Clin Nutr 2015; Vipperla K, et al..Nutr in clin pract. 2012; Bond JH, et al. Gastroenterology. 1980; Tappenden KA, et al. Gastroenterology. 1997; Nordgaard I, et all. Lancet. 1994

Ileal Resection

- **Ileal resection (<100 cm)** with or without right hemi-colectomy
  - Diarrhea or steatorrhea with consumption of a regular diet
  - Secretory diarrhea *without* steatorrhea
    - Treatment with a bile acid binding resin
      - Cholestyramine (2 to 4 g with meals)
      - Colestipol (1 to 2 g with meals)
  - Vitamin B12 malabsorption
    - parenteral B12- usually in a dose of 1 mg IM
- **Ileal resection (>100 cm)**
  - Calcium oxylate nephrolithiasis
  - Deficit of bile salts → excess of malabsorbed fats in the colon
    - Fats bind to calcium, ***which would otherwise bind oxalates***
  - Free oxalates pass into the bloodstream → precipitate in the kidney
  - Treatment
    - Restriction of oxalate-containing foods
    - If persists oral administration of calcium citrate (1000-1200 mg/d

Medical Management

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Fluids

- Small frequent sips
- Avoid hypoosmotic (water, tea) and hyperosmotic solutions (regular Gatorade, juice)
- Vicious cycle of thirst, drinking and increased stomal losses can result in the **“washout syndrome”**
- WHO oral rehydration solutions (ORS) formulation = 2.5g of NaCl, 20g glucose, 1.5g KCl and 2.5g Na_2CO_3 in one liter of water
- Variety of ORS formulas
  - Homemade
  - Commercial
    - Drip Drop
  - Optimal sodium concentration of at least 90mmol/L up to 120mmol/L

Lennard-Jones JE. Clinical therapeutics. 1990

Medical Management

Medications

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Medications

- Decrease intestinal transit and diarrhea volume
- First six months following significant enterectomy
  - gastrin secretion is ↑ → ↑ gastric acid production
  - Increasing the risk of peptic ulceration and secretory fluid loss
  - Start proton pump inhibitor
    - Taper after **6 months**

Buchman AL. *Gastroenterology*. 2006

Medications

- Loperamide:
  - 2-6 mg four times a day
  - activates m-opiate receptors in the myenteric plexus
    - Intestinal smooth muscle
- Diphenoxylate-atropine:
  - 2.5-10 mg four times a day
- Tincture of opium:
  - 0.6ml (6mg) four times a day

Cosnes J et al. Am J Clin Nutr 1985

Vitamins + Trace Elements

- Water soluble vitamin deficiency rare
  - Absorbed in proximal small intestine
- Fat Soluble Vitamins (A, D, E, K) more common
- Zinc
- Copper and Selenium Deficiency
- Supplementation with vitamins, calcium, and possibly magnesium should be initiated before overt signs of vitamin deficiency or hypocalcemia and hypomagnesemia develop
  - Magnesium is a *cathartic*

Trace elements (on TPN)

- Mn and Cu toxicity is encountered
  - Hepatic cholestasis
  - Bile transported heavy metals
- Mn toxicity –
  - Series of Australian patients with SBS and associated in some with *Parkinson-like symptoms* associated with Mn basal ganglia deposition.
- Chromium induced nephrotoxicity
  - Concern in the TPN patient
  - The American Society for Parenteral and Enteral Nutrition (ASPEN)
    - concern about toxicity of current parenteral micronutrient formulation and asked the (FDA) for a mandated change in the manufacture and formulation of these micronutrient products.

Hardy G. Gastroenterology. 2009; Moukarzel A. Gastroenterology. 2009.

Table 3. Vitamin and Mineral Supplementation for Patients With Short Bowel Syndrome Weaning From Parenteral Nutrition.

Nutrient	Strength	Dose
Vitamin B_{12}	1000 µg	Injection once monthly
Vitamin A	25,000 IU	1 tablet PO daily
Vitamin D	1000 IU	1 tablet PO daily
Vitamin E	400 IU	1 tablet PO daily
Calcium	500- to 600-mg tablet	1–2 tablets PO tid
Magnesium lactate	8-mg tablet	1–2 tablets PO tid
Magnesium gluconate	1000-mg tablet (or liquid)	1–3 tablets PO tid
Potassium chloride	20-mg tablet	1–2 tablets PO daily
Phosphate (NeutraPhos)	250-mg package	1 package PO tid
Sodium bicarbonate	650-mg tablet	1 tablet PO tid
Chromium	100-µg tablet	1–2 tablets PO tid
Copper	3-mg tablet	1–2 tablets PO daily
Selenium	200-µg tablets	1 tablet PO daily
Zinc sulfate	220-mg tablet	1–3 tablets PO daily

IU, International Unit; PO, by mouth; tid, 3 times daily. Adapted with permission from Matarese LE. Síndrome de intestino corto: principios actuales de tratamiento. In: Prado RA, Márquez HA, Moya DA, eds. *Nutricion Enteral y Parenteral*. 2nd ed. New York, NY: McGraw-Hill; 2012:484-496.

Medical Management

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Other considerations in SBS

- Gallbladder
  - Suggest that *nearly 100 % of patients* will develop symptomatic gallstone disease over time
  - Prophylactic cholecystectomy
  - Acalculous Cholecystitis - Decreased gallbladder contraction in patients that do not eat
- Osteoporosis
  - Occurs in up to 84% of SBS patients on PN
- Catheter Related Bloodstream Infections (CRBSI's)
  - 0.89 per 1000 catheter days
- Ethanol locks
  - 70% solution
  - 19 fold decrease in infection
  - Adverse events were rare and included thrombotic events

Buchman AL, Moukarzel A.. Clin Nutr. 2000; Pironi L, et al. Clin Nutr. 2002; Braga CB et al. Arch Endocrinol Metab. 2015; Davidson JB. et al. Parenter Enteral Nutr. 2015; Gundogan K et al. J Parenter Enteral Nutr. 2020; Xue Z, et al. Parenter Enteral Nutr. 2020; Roslyn JJ, et al. Am J Surg. 1984; Thompson JS. Arch Surg. 1996.

Teduglutide

- GLP-2 analogue
- **S**tudy of **E**ffectiveness in **P**arenteral **N**utrition **D**ependent **S**ubjects (STEPS) Phase III trial of 86 patients with SBS
- Teduglutide group (0.05 mg/kg/d) experienced a greater response (20% reduction in PN) than the placebo group (63% versus 30%)
  - 3 teduglutide-treated patients completely weaned from PN
  - Villous height, serum citrulline levels, and lean body mass ↑ with teduglutide
- Extension study (52 weeks) - 52 teduglutide-treated patients
  - 96% of patients reporting adverse events
  - headache (35%)
  - nausea (31%)
  - abdominal pain (25%)
  - nasopharyngitis (25%)
  - vomiting (17%)
  - catheter-related sepsis (17%), and urinary tract infection (17%)

Kocahr B et al. J Clin Gastroenterol 2017; Jeppesen PB,, et all. Gut. 2011; O'Keefe SJ, et al.. Clin Gastroenterol Hepatol. 2013; Jeppesen PB et al. Gastroenterology 2018; Chen et al. Ther Clin Risk Manag 2018; Seidner DL. JPEN 2020

Teduglutide

- No adenomatous polyps, colon cancers, or deaths observed
  - Colonoscopy within 6 months before drug initiation and surveillance thereafter is important
- Ad hoc analysis :
  - 2018 PS volume reduction greatest in patients with higher initial PN requirements
  - Greater response in CD
- Predictors of Response to Teduglutide
  - Older age
  - Volvulus as the cause of SBS
  - Baseline PS volume >6 L /wk
  - Longer ties since start of PS dependence
  - Lower percentage of colon remaining
  - All patients who achieved enteral autonomy required >6 months of treatment
  - Patients with >50% colon in continuity had a ↑ for obtaining a greater number of days off PS

Kocahr B et al. J Clin Gastroenterol 2017; Jeppesen PB,, et all. Gut. 2011 ; O'Keefe SJ, et al.. Clin Gastroenterol Hepatol. 2013; Jeppesen PB et al. Gastroenterology 2018; Chen et al. Ther Clin Risk Manag 2018; Seidner DL. JPEN 2020.

Teduglutide

- STEPS-2 (24 month extension)
  - Initially previously treated with teduglutide, placebo or no treatment (due to full study)
  - Clinical response – 20 - 100% reduction from baseline in weekly PS volume
  - No Treatment
    - 67% response
    - 39% volume reduction in PN
  - Placebo/Teduglutide
    - 55% response
    - 28% volume reduction in PN
  - Teduglutide/Teduglutide (30 months)
    - 93% response
    - 66% volume reduction
    - Response continued to improve through 30 months
- >1 addition day per week off PS for 58% patients
- 13 patients achieved fuller enteral autonomy

Schwartz et al. Clin Transl Gastroenterol. 2016

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Long Term Treatment with Teduglutide

- Slow responders (24-104 weeks) of treatment
  - All had colon in continuity ➡️ 30-130 cm of small bowel remaining
- STEPS-3
  - 13 pts, all treated
  - Previously not treated group- 41 weeks
    - 48% reduction in PN volume
    - 2 day decrease in PN delivery
  - Previously treated group - 34 weeks
    - 50% reduction in PN volume
    - 3 day decrease in PN delivery
  - 2 pt's achieved autonomy wks 126 and 130
  - Treatment up to 3.5 years associated with further reduction in PN

Seidner et al. Nutr Clin Pract 2018; Hvistedahl MK et al. JPEN 2020

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Teduglutide- Non-STEP Trials

- 54 French Patients with SBS-IF
- Mean 62cm small bowel length, 65% had colon in continuity
- 85% responders (>20% reduction on TPN requirement)
- 24% weaned off TPN
  - Presence of colon

- 32 pts with Crohn's Disease and SBS receiving teduglutide
- Retrospective case series comparing clinical outcomes before and after teduglutide
  - 26 of 32 patients achieved the primary outcome of ≥20% PS reduction
  - 23 patients received PN prior to teduglutide, decreasing to 14 pts after tx
  - Weekly PN volume reduced from 7.00 to 3.55 L and weekly frequency decreased from 7.00 to 3.00 days ($p < 0.01$)
  - Decrease in antidiarrheal medications, subjective symptoms, stool output, without any significant affects on immunosuppressive therapy

Joly et al Clinical Nutrition 2020; Siu R et al. Crohn's & Colitis 360 2024.

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Long Term Treatment with GLP-2

- Can you stop?
  - Limited observational studies
  - 11 SBS pts, 8 week washout period after 24 months of tx
  - Return of fecal weight back to baseline during washout period
  - Also decrease in urine volume during this time
  - Not Recommended
- ***Patients need colonoscopy prior, 1 year after treatment initiation and then no less then every 5 years***

Seidner et al. Nutr Clin Pract 2018; Schwartz LK. Clin Transl Gastroenterol 2016.

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Apraglutide

- Novel long acting Glucagon-like peptide -2 (GLP-2)
- Once weekly dosing (5mg or 10 mg)
- Phase 1 and 2 Open-label Metabolic Balance Trial
- SBS patients secondary to surgical resection with or without colon at least 6 months since previous surgical resection
  - Excluded active IBD patients
  - Patients with >1500 g/day of fecal wet weight
- Only serious treatment related AE was abdominal pain

Eliasson J et al. JPEN 2022.

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Apraglutide

- Placebo controlled Phase II double-blind, randomized cross-over study of 8 adults
- 5 mg vs placebo for 4 weeks, followed by 10 mg for 4 weeks, with washout period of 6-10 weeks
- Significantly increased wet weight and energy absorption
  - 741 g/day (P=0.015)
  - 1095 *kj/day (calculated by energy Bomb calorimetry)*
  - Increased Na and potassium absorption
  - Increased mean urine output vs placebo
    - 5 mg = 714 ml/day
    - 10 mg= 795mg/day
    - No difference between the dose

Eliasson J et al. J Pen 2021.

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Apraglutide Phase III Trial

- 24 week double blind placebo Trial
- Reduction in TPN at least one day per week 43 % vs 27.5 % *(p=0.04)*
- Relative reduction in weekly PS volume at week 24 in stoma population (25.6% vs %7.8 (p < 0.001)
- Colon-in-continuity patients
  - One day/week off PS vs baseline and reaching enteral autonomy at week 48 were not achieved
- Numerically favorable but not statistically significant relative to placebo
  - Improving days off PS 51.8% vs 44.4%
  - Enteral autonomy in 7/56 (12.5%) patients vs 2/27 (7.4%) on placebo

Ironwood Pharm press release 2024.

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Intestinal Failure Associated Liver Disease (IFALD)

- Liver injury due to intestinal failure and TPN in the absence of another cause of liver disease or biliary obstruction
- Elevated LFT's
- Steatosis and steatohepatitis
- Intrahepatic Cholestasis
- Fibrosis → cirrhosis → end stage liver disease
- Evidence of Cirrhosis by radiological of histological (gold standard)
- In a prospective study of 90 patients with intestinal failure receiving TPN
  - probability of developing a severe complication of liver disease:
    - 26% at 2 years
    - 50% at 6 years
    - 53% at 8 years

Bond et al. Alimen Parmacol Ther 2019; Cavicchi M, et al.Ann Intern Med. 2000; O'Keefe SJ, et al. J Clin Gastroenterol Hepatol. 2006; Limketkai BN et al. Inflamm Bowel Dis 2016.

Manage IFALD

- Avoiding sepsis
- Treat Biliary obstruction
- Avoid excessive calories in TPN
- Optimization of lipid emulsion
  - <1g/kg/d
  - Use of other third generation emulsion
    - Optimize omega 3:omega polyunsaturated FA
      - Fish oil
      - SMOF (soybean oil, MCT, olive oil and fish oil)
        - Lower LFT at 4 weeks compared to standard soybean lipid
        - More long term data needed
- Cycling TPN to 12 hrs
- Use enteral route

Klek S. et al Clin Nutr. 2013.

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Accepted Criteria for Small Bowel Transplantation

- Impending or overt liver failure
  - Increasing bilirubin, liver enzymes, spleen size, pro-thrombin time reduced platelet counts, varices, stomal bleeding, hepatic fibrosis, and cirrhosis
- Thrombosis of central veins (two of the subclavian, jugular, or femoral veins)
- Frequent catheter-related sepsis
  - More than two episodes per year of life-threatening bacterial infections
    or
  - One episode of fungemia associated with shock and acute respiratory dysfunction syndrome
- Severe recurrent dehydration

Limketkai B et al Clin Gastro and Hepat 2016

Thank you !

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Best of Evidence-Based GI: Inflammatory Bowel Disorders

Moderator: Philip Schoenfeld, MD, MSEd, MSc (Epi)

Panel: Marla Dubinsky, MD and Bincy Abraham, MD

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SEAVUE: A Sea of Change in Biologic Positioning for Crohn's Disease

Bharati Kochar, MD, MS
Associate Editor

Bharati Kochar, MD, MS

Division of Gastroenterology, Massachusetts General Hospital Investigator, The Mongan Institute, Assistant Professor of Medicine, Harvard Medical School, Boston, MA

This summary reviews Sands BE, Irving PM, Hoops T, et al. Ustekinumab versus adalimumab for induction and maintenance therapy in biologic-naive patients with moderately to severely active Crohn's disease: a multicentre, randomised, double-blind, parallel-group, phase 3b trial. Lancet 2022;399(10342):2200-2211.

Conflicts of interest: *Dr. Kochar is an advisory board member for Pfizer Pharmaceuticals. Dr. Ozturk and Dr. Grover have no conflict of interests.*

Tweetorial provided by EBGI Ambassadors:

Begum Ozturk, MD
@NBegumOzturk
PGY-1, Beaumont Health

Dheera Grover, MD
@GroverDheera
PGY-3, UConn

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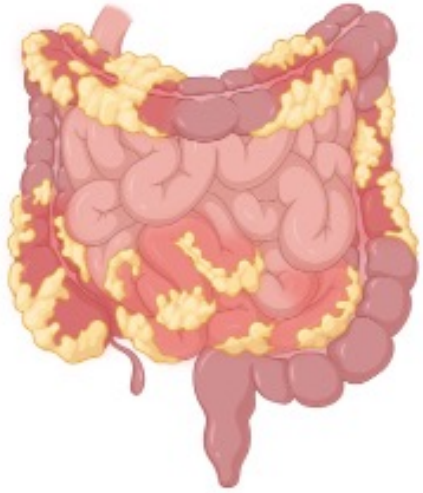
Ustekinumab vs. adalimumab in biologic-naïve moderately to severely active Crohn's disease (CD)

Ustekinumab

(Anti IL-12/23)

Adalimumab

(Anti TNF)



Severity of CD

↓

Crohn's disease activity index (CDAI)

- Frequency of liquid stools
- Use of anti-diarrheals
- Severity of abdominal discomfort
- General well-being
- Presence of extra-intestinal symptoms
- Hematocrit, weight loss, presence/absence of abdominal mass, anal fissure, fistulae, or fever

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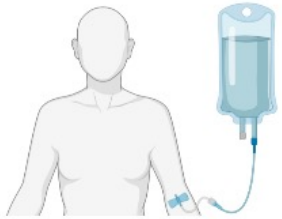
June 2018 – December 20

Randomized
Double blind
Parallel-group
Active comparator
Phase 3b trial

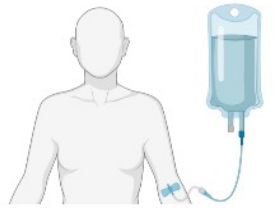
633 screened

386 enrolled



191 patients

195 patients



Ustekinumab 6mg/kg IV
→ 90 mg SQ every 8 weeks

Adalimumab 160 mg SQ
→ 80 mg SQ at week 2
→ 40 mg SQ every 2 weeks

SEAVUE: A Sea of Change in Biologic Positioning for Crohn's Disease

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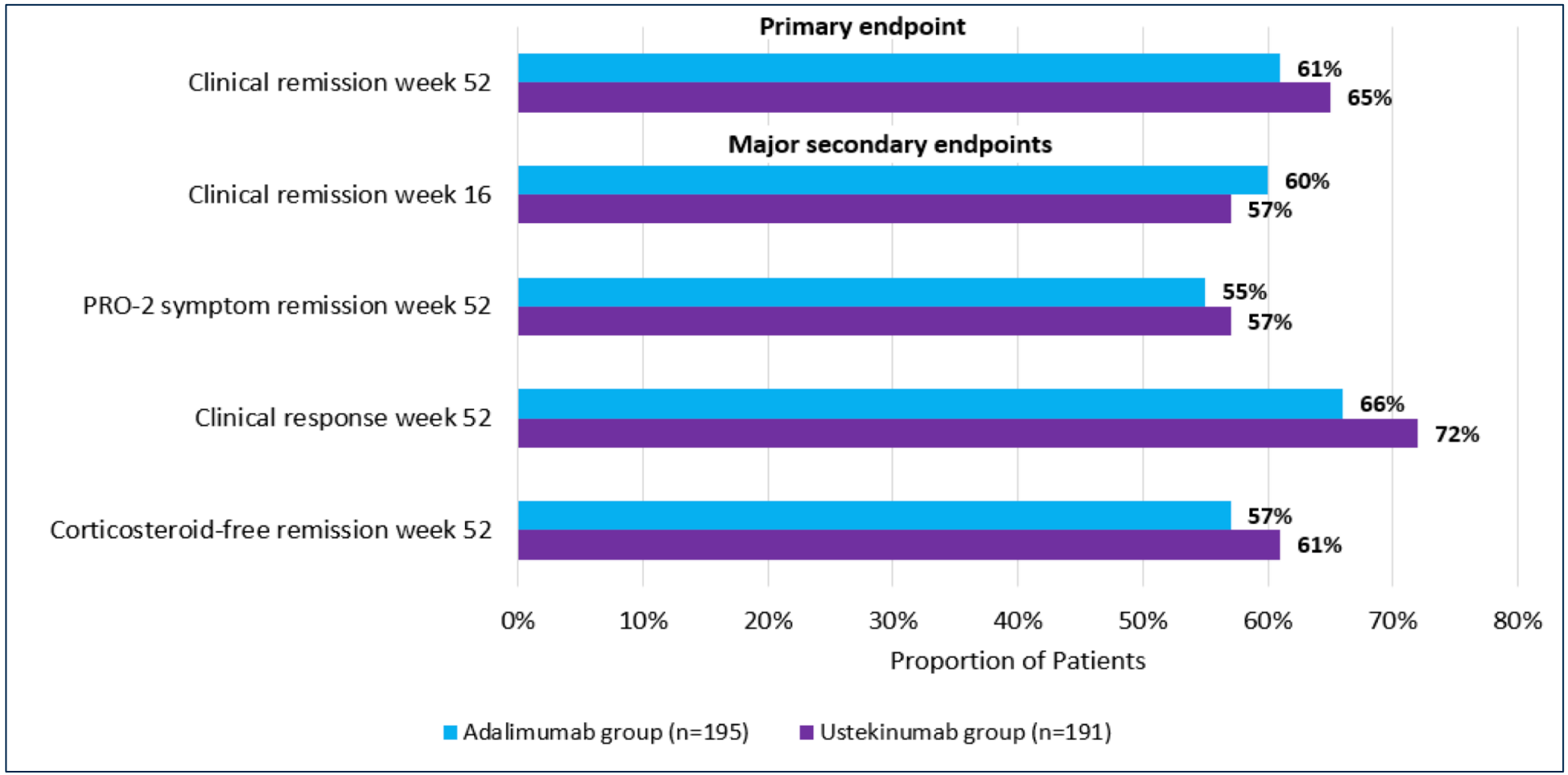

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ADVERSE EVENT DATA		
Adverse Event	**Adalimumab (41%)**	**Ustekinumab (34%)**
Serious infection	3%	2%
Abdominal pain	8%	13%
Headaches	7%	12%
Crohn's disease event	16%	12%

Questions

1. When do you prefer anti-TNF therapy vs anti-IL 12/23 in Crohn's disease?

2. What is role of anti-integrin antibody in Crohn's colonic inflammation?

This EBGI summary reviews Sands BE, Irving PM, Hoops T, et al. **Ustekinumab versus adalimumab for induction and maintenance therapy in biologic-naïve patients with moderately to severely active Crohn's disease: a multicentre, randomized, double-blind, parallel group, phase 3b trial**. *Lancet*. 2022;399:2200-2211.

MY PRACTICE

Bharati Kochar, MD, MS
Associate Editor

Ustekinumab may confer advantage related to treatment persistence and numerically low risk of infections

Vedolizumab also great first-line selective biologic agent for IBD patients with colon inflammation

Prefer Infliximab as first line therapy for penetrating Crohn's disease

Choose anti-TNF agents as first-line therapy if patients have significant rheumatological disorders

Most other patients, especially with mild Crohn's disease, anti-interleukin therapy with Ustekinumab preferred

SEAVUE: A Sea of Change in Biologic Positioning for Crohn's Disease

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The New Frontier of Combination Therapy for IBD: The VEGA RCT


Tarun Chhibba, MD[1] and Bharati Kochar, MD, MS[2]

[1]Advanced Fellow in Inflammatory Bowel Diseases, Division of Gastroenterology, Massachusetts General Hospital, Harvard Medical School , Boston, MA

[2]Assistant Professor of Medicine, Division of Gastroenterology, Massachusetts General Hospital, Investigator, The Mongan Institute, Harvard Medical School, Boston, MA

This summary reviews Feagan BG, Sands BE, Sandborn WJ, et al. Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA): a randomised, double-blind, controlled, phase 2, proof-of-concept trial. Lancet Gastroenterol Hepatol 2023; 8: 307-20 .

Tweetorial Provided by:

Chukwunonso Benedict Ezeani

@bengnonny

PGY-2, Baton Rouge General

Conflicts of interest: Dr. Chhibba reports no conflicts of interests. Dr. Kochar reports serving as an advisory board member for Pfizer Pharmaceuticals

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Importance

"[The New Frontier of combination therapy for IBD: The VEGA RCT]"
Summary of Feagan BG, Sands BE, et al. Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA): a randomised, double-blind, controlled, phase 2, proof-of-concept trial. *Lancet Gastroenterol Hepatol*. 2023;8:307-320.

Multiple new medications for Ulcerative Colitis

Clinical remission rate still LOW!

Combination Biologics Better?

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Definitions & Endpoints

"[The New Frontier of combination therapy for IBD: The VEGA RCT]"
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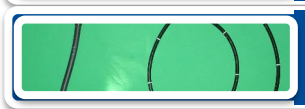
Primary Outcome

Clinical response

Secondary Outcomes


Clinical Remission


Endoscopic Improvement


Endoscopic Normalization


Histologic Remission

Histologic Remission and Endoscopic Normalization


Histologic Remission and Endoscopic Improvement


IBDQ Improvement

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Study Design

"[The New Frontier of combination therapy for IBD: The VEGA RCT]"
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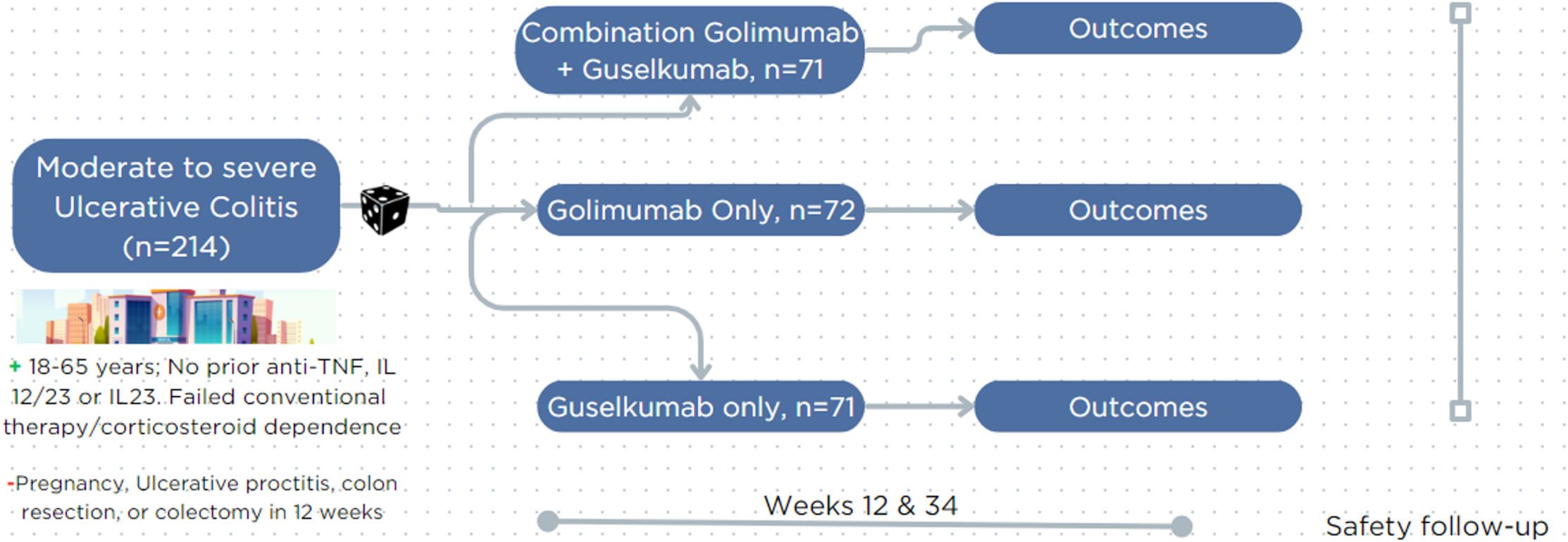

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Results

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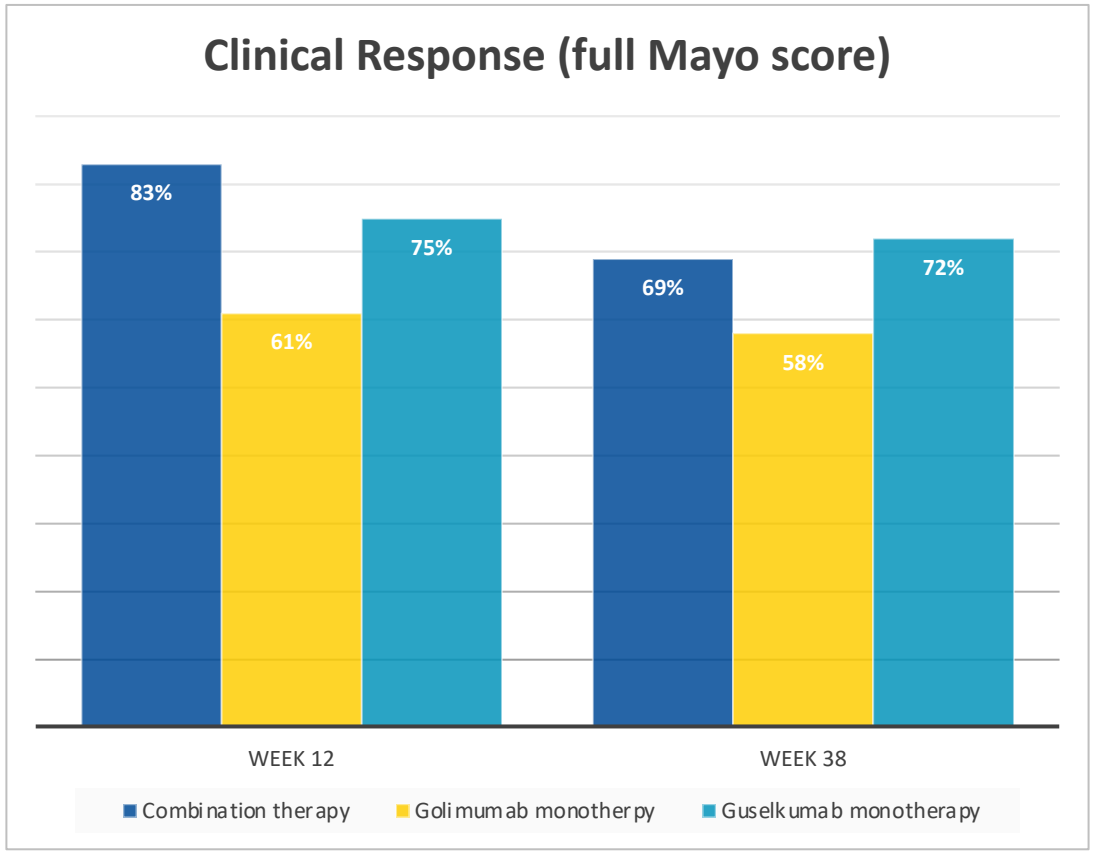

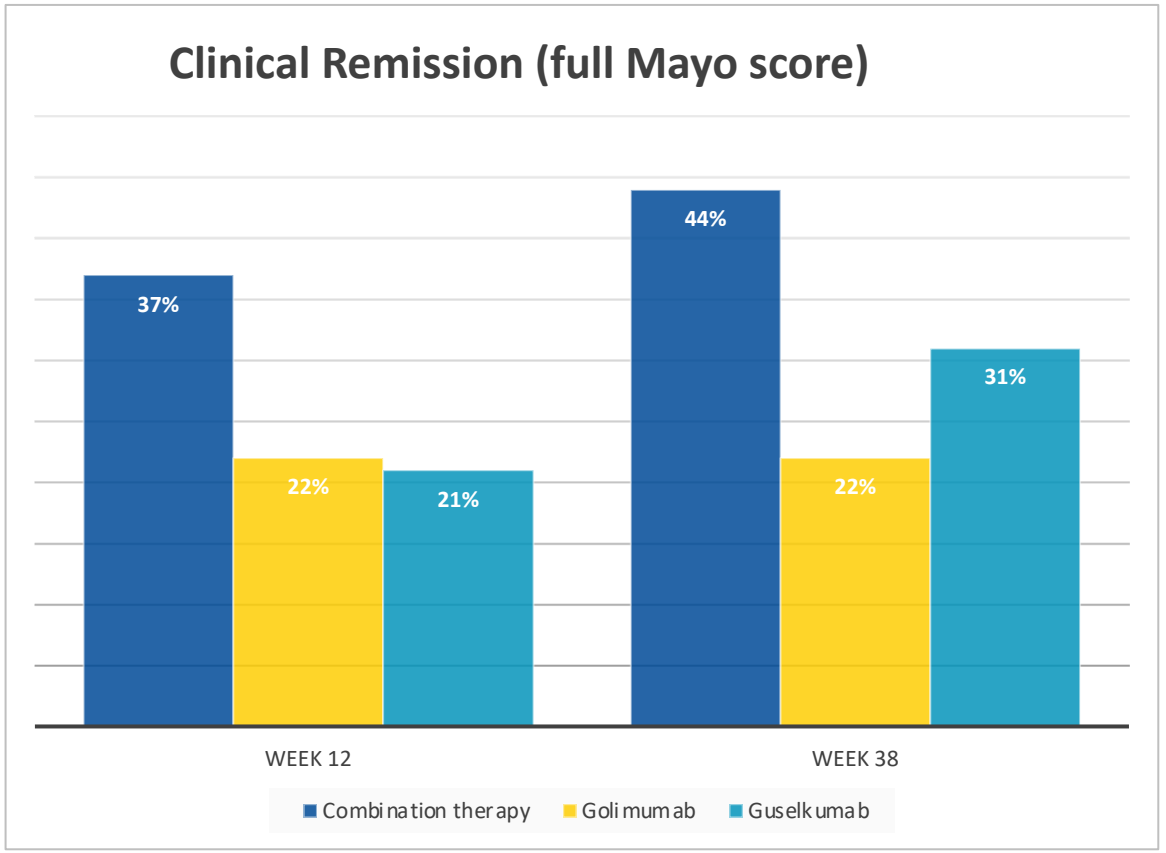

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Caution

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A Phase 2 proof-of-concept study!!! Needs Large scale efficacy and safety data to confirm findings

Treatment limited to those without prior anti-TNF or other biologic agents

Small sample size and underpowered to show difference <20%

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Questions

1. When do you consider combination biologic therapy beyond anti-TNF + immunomodulators?

2. What combinations of biologic agents have you used? Which combinations seem most promising?

My Practice

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Dr. Bharati Kochar, MD, MS

- JAK inhibitor has potent inductive properties, plus they are not immunogenic, i.e. can start and stop as needed
- Multimodal approach needed to address severe refractory disease in non-surgical patients
- Combination biologics is becoming mainstay in medical conditions including non-immune mediated diseases

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CASE STUDY

What's First Line in Ileal Crohn’s?

Case Presenter: Sameer Berry, MD, MBA

Moderator: Samir Shah, MD

Panel: Aja McCutchen, MD, Maia Kayal, MD, Sandra Quezada, MD

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A 24 yo Female with RLQ Abdominal Pain

- Presented to PCP 1 week ago with 6-month history of recurrent, gradually worsening RLQ abdominal pain, 3-month history of intermittent diarrhea, and decreased appetite.
- No hematochezia. Thinks she has had 5-10 lbs weight loss in past 6 months.
- Occasional mouth ulcers. No joint pain or skin rashes.

- No tobacco or NSAIDs.
- No other PMH. No abdominal surgeries.
- Meds: oral contraceptive.
- No family history of IBD or CRC.
- Engaged, no kids, but plans to have kids in the future.

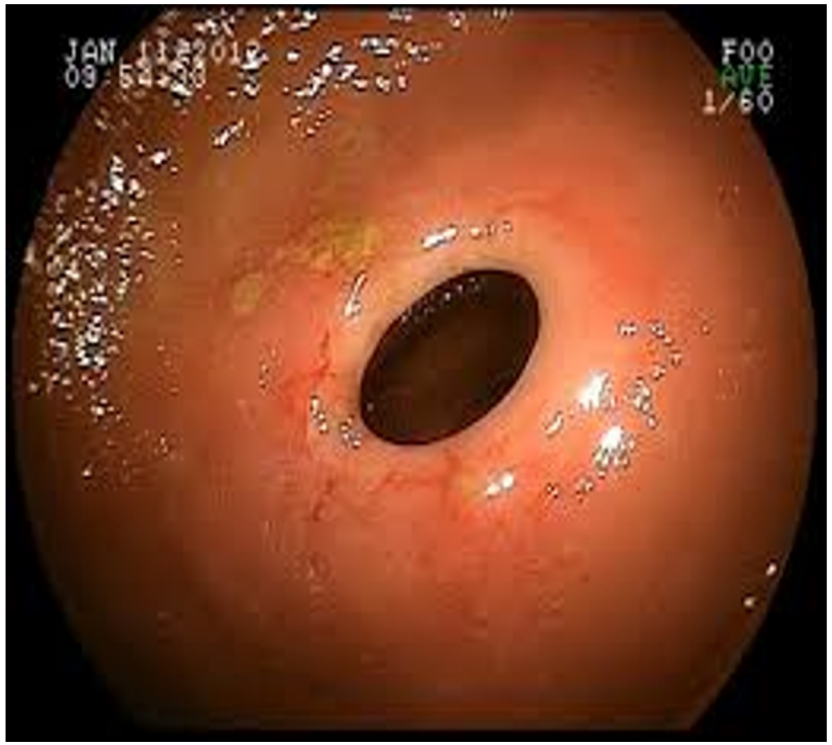
Diagnostic Evaluation

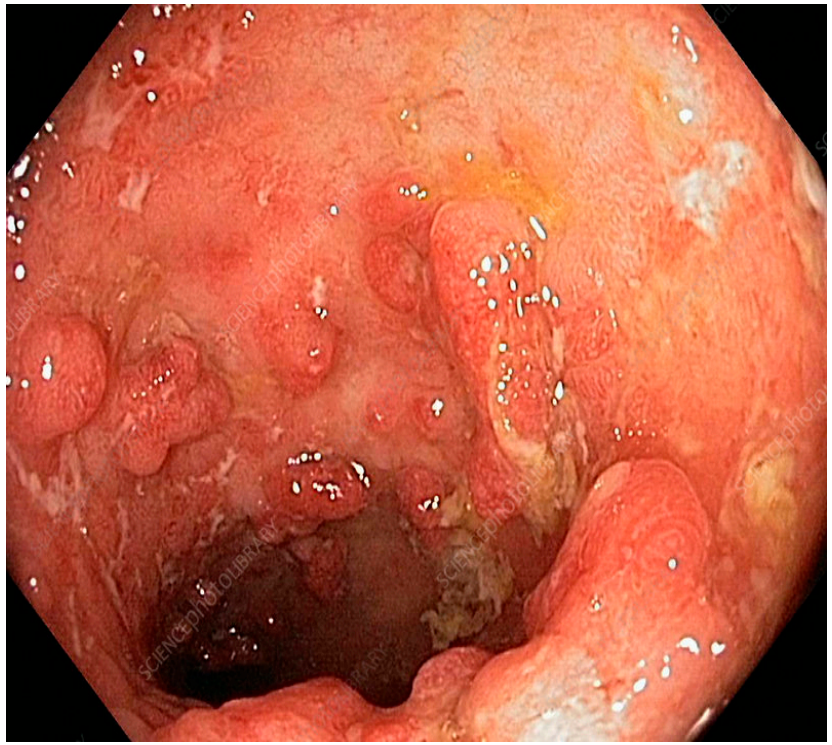
Physical Exam: Tender to palpation in RLQ and umbilical area. Otherwise, normal exam, including normal skin exam and normal digital rectal exam.

LABS:

- WBC 7.0, Hgb 11, Ferritin 50, Iron sat 20%
- Normal liver tests. Albumin 3.7. Normal B12, ffolate, zinc, Vit D
- CRP 15
- Negative stool pathogen panel, negative viral hepatitis panel, normal Quantiferon Gold

Colonoscopy-terminal Ileum Exam





Colon exam is endoscopically normal, including random biopsies.

Biopsies: Chronic active severe inflammation consistent with Crohn's disease.

Case Continues…

- Diagnosed with terminal ileal Crohn's disease
- Treated with prednisone 40 mg x 1wk – dose tapered over 1 month.
- Comes to see you in GI clinic:
  - Recurrent abdominal pain is improving, but still present. Diarrhea improved.

Question: What is the benefit of CTE or MRE at this time?

Questions

1. Given that patient had clinical response to oral steroids, what would be your first choice for an advanced medical therapy?
   - Anti-TNF, anti-IL 23, anti-integrin, JAK1 inhibitor

2. How would you counsel her about the side effect profile? Infusions vs subq injections? Frequency of laboratory follow-up? Any special concerns for a young female patient?

3. What if the patient had peri-anal disease, too? What if the patient had significant structuring on CTE/MRE?

Initial Therapy

1. IL 23 https://www.skyrizihcp.com/gastroenterology/crohns-disease/efficacy
    a. 61 % with clinical remission at week 12 in all patients. 50% in endoscopic response at week 12 in bio-naive.
    b. Higher risk of AE's in placebo compared to patients on therapy
    c. Consider in patients with comorbid psoriasis/psoriatic arthritis
2. TNF-A https://www.remicadehcp.com/crohns-disease/clinical-information.html
    a. 39% with clinical remission at week 12, 30% mucosal response at week 10 in bio-naive patients
    b. Boxed warning for increased serious infections, TB, sepsis, fungal infections, lymphoma
    c. Consider in patients with comorbid rheumatoid/psoriatic arthritis, ankylosing spondylosis, plaque psoriasis
    d. Can develop immunogenicity
    e. First line for Fistulizing Disease per ACG
3. Anti-Integrin https://www.entyviohcp.com/safety-profile
    a. 35% clinical remission at week 10 in bio-naive and 34% endoscopic response at week 26
    b. Infection risks similar to placebo
    c. No benefit for EIM's (gut specific)
4. JAK https://www.rinvoqhcp.com/crohns-disease
    a. 36% clinical remission at week 12, 34% endoscopic response at week 12
    b. Week 12 serious infection/adverse events similar to placebo (including MACE/malignancy) Increased single for Shingles in unvaccinated
    c. Consider in patients with comorbid rheumatoid/psoriatic arthritis, ankylosing spondylitis, atopic dermatitis
    d. Second line for fistulizing disease per ACG (post hoc analysis with fistula closure)
    e. FDA requires TNF-A failure first

PATIENT CONSIDERATIONS: Needle phobia, distance from infusion centers/frequent traveling

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CASE STUDY

Recurrent Pouchitis in a Patient With UC After IPAA

Case Presenter: Joseph Sleiman, MD

Moderator: Samir Shah, MD

Panel: Aja McCutchen, MD, Maia Kayal, MD, Sandra Quezada, MD

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Case Study:
Recurrent Pouchitis in a Patient With UC After IPAA

A 33-year-old male Puerto Rican patient, with uncontrolled UC leading to 3-stage IPAA, reports a **1-week increase in bowel frequency** from 6 to 8 movements daily, with 1 incontinent movement at night.

- Blood per rectum rarely.
- Has abdominal cramping, but no tenesmus.
- No change in appetite or weight No fever, cough, skin rashes, or joint pains.
- He infrequently has receptive intercourse.
- Non-smoker, socially drinks,
- Works at a gas station.

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Case Study:
Recurrent Pouchitis in a Patient With UC After IPAA

- **Medical History:**
  - Ulcerative **pan**Colitis diagnosis at 19.
  - Nonresponse to adalimumab then azathioprine/infliximab.
  - 3-stage IPAA at 25.
  - 4 years off-meds (loss of insurance due to surgery time off), asymptomatic.
  - Pouchoscopy at age 30: Crohn-like pouchitis (pouch/efferent limb ulcers).
  - Treated successfully with Vedolizumab, stopped after 3 years (normal pouchoscopy).
  - Current symptoms 1-year post-vedolizumab holiday.

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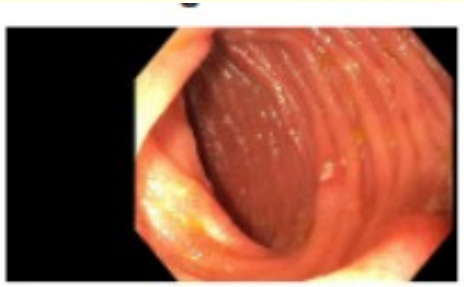
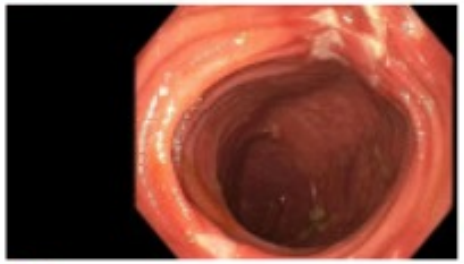
Case Study:
Recurrent Pouchitis in a Patient With UC After IPAA

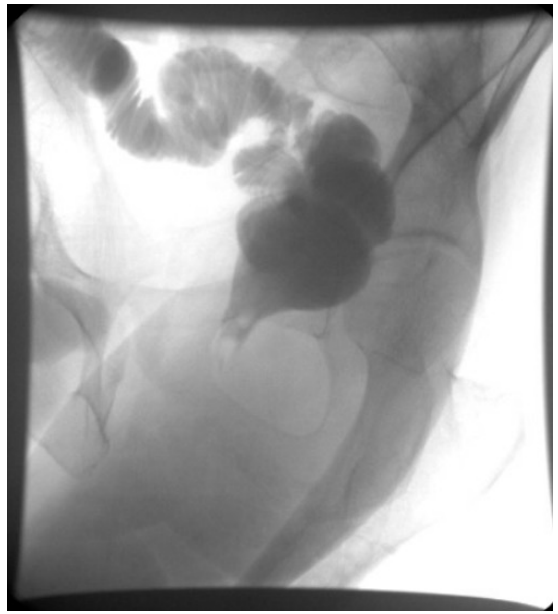
	Latest Ref Rng	Third stage IPAA surgery, age 25	Age 30, first pouchoscopy since return to insurance, asymptomatic	Currently, age 33, with symptoms
WBC	3.8 - 10.6 X10E+09/L	8.5	9.5	**11.2 (H)**
Hgb	12.9 - 16.7 g/dL	14.6	14.1	15.2
MCV	80.0 - 94.0 fl	84.3	84.4	89.0
ABS Neutrophils	1.80 - 7.50 X10E+09/L	6.80	7.20	**8.4 (H)**
ABS Lymphocytes	1.00 - 5.00 X10E+09/L	1.10	1.20	1.9
ABS Monocytes	0.00 - 0.80 X10E+09/L	0.40	0.40	0.7
Platelets	150 - 450 X10E+09/L	259	272	231
Urea Nitrogen	6 - 24 mg/dL	15	16	15
Creatinine	0.70 - 1.30 mg/dL	1.1	1.1	1.18



1 Proximal Limb of J-Pouch



5 Proximal Limb of J-Pouch



- Infectious etiologies were ruled out with stool tests.
- Obstructive pouch diseases are ruled out with Gastroview enema.
- Pouchoscopy showed ulcers in the pouch body and efferent ileum, suggestive of Crohn's-like disease of the pouch.
- Trial of ciprofloxacin 500 mg twice daily for 3 months was initiated. Symptoms abated, but follow-up endoscopy was unchanged

Questions

- What is your practice in terms of biologic drug holiday with normal pouchoscopy?
- What is the role of Vedolizumab versus other biologics in this case?
- What is your approach in patients with clinical/endoscopic dis-concordance such as in this case?
- Any counsel in regards to anal receptive sexual intercourse in patients with J-pouches?

How Physicians 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

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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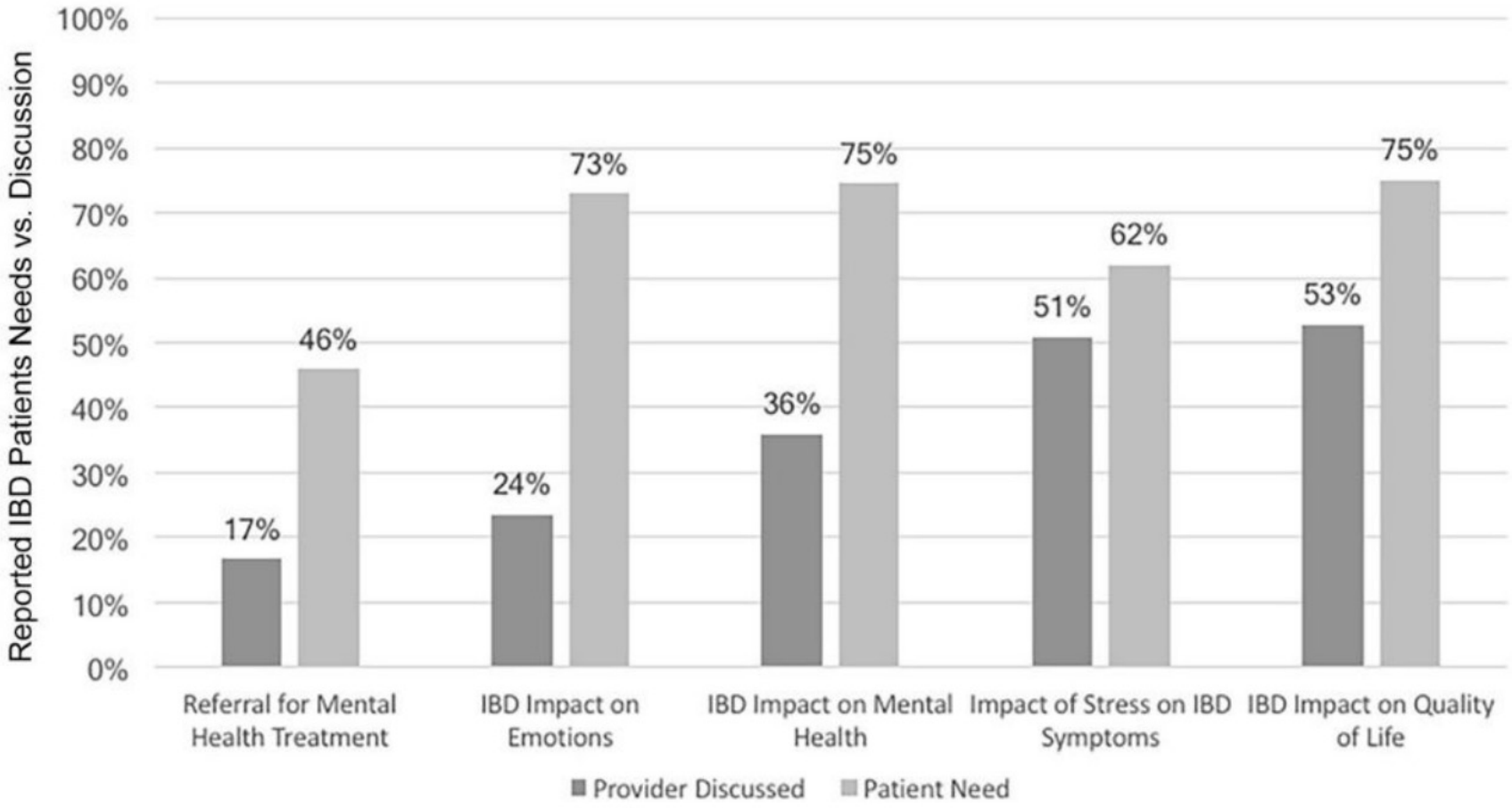
Active Listening

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
- Patients need to feel heard and their concerns and needs 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: Often physicians and patients are not speaking the same language. We are focused on specific treatment goals and objective measures of disease remission: our language might not resonate with patients. How can clinicians and patients work together to 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 and are focused on improving their quality of life 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 quality of life

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

Slide courtesy A Charabaty.

Patient Treatment Goals: Speaking the Same Language

Disease Activity and Severity, Patient's Health Literacy and Activation, 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 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) Physician → patient Medical Minimum legally required	Two way Physician ↔ Patient Medical and personal All relevant for decision-making	One way (largely) Physician → 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)	Physician and patient	Patient

Shared decision making relevant when: More than one reasonable option, 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 physicians get involved in patient advocacy groups (PAGs)?

- Public trust for physicians 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

Earnest MA, et al. *Acad Med.* 2010;85:63-67.

Summary

- Patients and clinicians have a different view of how a 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